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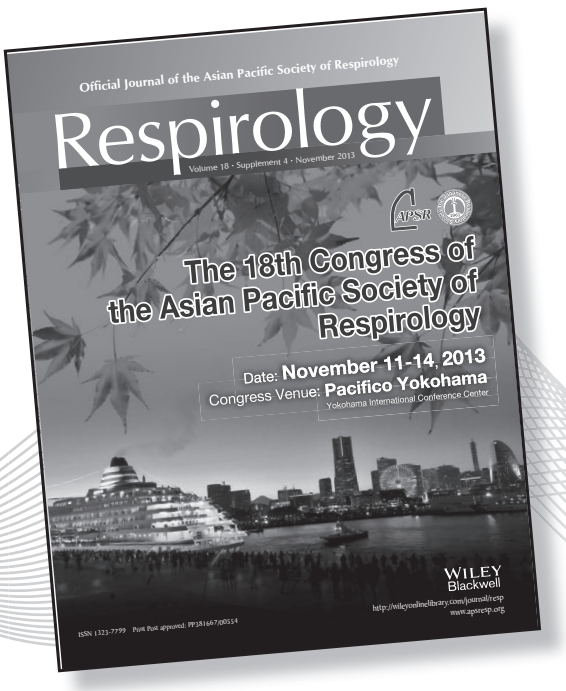

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OS01: LUNG CANCER 1

OS001

EFFICACY AND SAFETY OF PLATINUM-COMBINATION CHEMOTHERAPY RE-CHALLENGE FOR NON-SMALL-CELL LUNG CANCER PATIENTS RELAPSED AFTER ADJUVANT CHEMOTHERAPY OF CISPLATIN PLUS VINORELBINE

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Background There is no standard therapy for relapsed patients who received post-operative platinum based adjuvant chemotherapy for resected non-small-cell lung cancer. We investigated the efficacy and safety of platinum-combination chemotherapy re-challenge for such patients.
Methods Medical records were retrospectively reviewed in three institutions from April 2005 to July 2012. Patients who underwent complete surgical resection were eligible if they once received post-operative adjuvant chemotherapy of cisplatin plus vinorelbine and then re-challenge with platinum-combination chemotherapy.
Results Sixteen patients were enrolled in this study. After re-challenge with platinum-combination chemotherapy, 5 cases showed PR and 8 cases SD. Overall response rate was 31.2% (5/16) and disease control rate was 81.2% (13/16) in the platinum-combination re-challenge patients. Median progression-free survival and overall survival from the start of the re-administration of platinum-combination chemotherapy were 6.5 and 28.0 months, respectively. The main grade 3 or more severe adverse events were neutropenia (31.2%), thrombocytopenia (31.2%), leukopenia (12.5%) and hyponatremia (12.5%). Frequently observed grade 2 or more severe non-hematological toxicities were anorexia (37.5%) and nausea (37.5%). No treatment-related deaths were noted in this study.
Conclusion Re-challenge of platinum-combination chemotherapy was effective and safe, and therefore should be considered as one of treatment option for the NSCLC patients who relapsed after post-operative cisplatinum based adjuvant chemotherapy.

OS002

PHASE I/II STUDY OF AMRUBICIN COMBINED WITH NEDAPLATIN (CDGP) IN UNTREATED NON-SMALL-CELL LUNG CANCER

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We conducted a phase I/II study of combination chemotherapy with nedaplatin and amrubicin for patients with untreated, advanced non-small cell lung cancer (NSCLC). Nedaplatin was given on day 1 and amrubicin on days 1, 2 and 3. The treatment was repeated every 3 weeks. In phase I trial, we fixed the dose of nedaplatin as 100 mg/m^2 and escalated the amrubicin dose from a starting dose of 25 mg/m^2 by 5 mg/m^2 increments until the maximum tolerated dose (MTD). The MTD was defined as the dose level at which at least two of three or two of six patients experienced a dose-limiting toxicity (DLT). In phase II trial, the primary endpoint was overall response rate (ORR). Assuming an ORR of 25% for standard therapy, a target response rate of 50% was established. Alpha = 0.05, beta = 0.10, and the estimated required sample size was 33. Forty-one patients were enrolled in the study. In the phase I study, two DLTs occurred in six patients at level 2, including cerebral infarction and grade 4 thrombocytopenia. Therefore dose level 1 (nedaplatin 100 mg/m^2, amrubicin 25 mg/m^2) was recommended. In the phase II study, a total of 35 patients, including 6 patients from the phase I study, were enrolled and a total of 129 cycles treatment were administered. Grade 3 or 4 neutropenia, grade 3 anemia and grade 3 or 4 thrombocytopenia occurred in 62.9%, 11.4% and 11.4% of cycles, respectively. Febrile neutropenia occurred in 5 cycles (3.9%) but there were no severe infections. Of the 35 patients, 17 achieved a partial response and ORR was 48.6%. The combination of nedaplatin and amrubicin was highly effective and well tolerated in patients with advanced NSCLC.

OS003

PROGNOSTIC FACTORS FOR PATIENTS WITH LUNG CANCER IN THE TERMINAL STAGE

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Background and Aim of Study Lung cancer is the leading cause of cancer-related death. Accurate prediction of survival in the terminal stage is important since it may help patients make a rational decision (quitting chemotherapy or being admitted to a palliative care unit [PCU]). Some prognostic scores have been described as effective indicators of prognoses. However, these scores were intended for patients with other types of cancers. There is no prognostic score for terminal-stage lung cancer patients. The aim of this study was to reveal prognostic factors for patients with terminal-stage lung cancer.
Methods Two independent groups (the training and testing sets) were selected from our PCU patients retrospectively. In the training set, univariate and multivariate analyses were performed to detect independent prognostic factors. The patients in the testing set were then analyzed to validate whether our prognostic factors could predict near-term death, compared with the palliative prognostic score (PaP) and the palliative prognostic index (PPI).
Results Ninety-three patients (69 in the training set and 24 in the testing set) were included. Multivariate analysis showed that fatigue, anorexia, desaturation, hyponatremia, and hypoalbuminemia were independent prognostic factors in the training set. Mean survival time in a group that had more than 3/5 factors was 9.2 ± 2.6 days. In the testing set, the presence of more than 3/5 factors predicted death within 2 weeks with a sensitivity of 100% and specificity of 75%. In comparison, the PaP predicted death with a sensitivity of 21% and specificity of 100% versus the PPI with a sensitivity of 66% and specificity of 100%.
Conclusion This study revealed that fatigue, anorexia, desaturation, hyponatremia, and hypoalbuminemia may be short-term prognostic factors in terminally ill lung cancer patients. In particular, the presence of more than 3 of these factors could suggest death within 2 weeks.

OS004

THE OUTCOME OF PATIENTS WITH RESECTED CLINICAL N3 OR M1 LUNG CANCER

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Introduction As the efficacy of chemotherapy for advanced lung cancer patients has been increased, some patients may benefit from surgery like other kinds of cancers.
Patients and Methods Between 1996 and 2013, 34 lung cancer patients whose clinical stage were N3 positive and/or M1 positive at diagnosis underwent surgery at Juntendo University. We retrospectively reviewed their clinical records and evaluate patients' characteristics, progression free and overall survival.
Results The median age was 59 (range 37–90). 10 patients were female and 24 were male. 13, 17, 3 and 1 patients had performance status of 0, 1, 2 and 3 at diagnosis, respectively. 27, 3 and 4 patients had adenocarcinoma, squamous cell carcinoma and others. 6 patients had sensitive EGFR mutation and 1 patient had EML4/ALK fusion gene. The primary treatment was chemotherapy in 10 patients, local therapy to metastatic lesion in 11 patients and pulmonary surgery in 13 patients which was followed by chemotherapy in 5 patients. Lobectomy, pneumonectomy, sleeve lobectomy, bilobectomy and partial resection were performed in 26, 3, 2, 2 and 1 patient, respectively. Median progression-free survival from operation was 261 days, and 2 year progression-free survival rate was 41.3%. 2 year survival rate from operation was 75.8%. In the multivariate analysis, response to preoperative therapy and solitary brain metastasis at diagnosis were statistically significant good prognostic factors. There was no surgical mortality independence of the mode of surgery.
Conclusion The feasibility of salvage or upfront surgery was acceptable for stage IIIB or IV lung cancer. Oligometastasis and/or response to definitive medical treatment could be predictors for long-term survival which may due to additional local control.

OS005

PROGNOSIS AND PROGNOSTIC FACTORS IN ADVANCED LUNG CANCER PATIENTS DIAGNOSED FOLLOWING EMERGENCY ADMISSION: A SINGLE CRITICAL CARE MEDICAL CENTER STUDY

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Introduction Currently, there is little data on prognosis and prognostic factors in advanced lung cancer patients diagnosed following emergency admission in Japan. Our objective was to review the medical charts of those patients to determine the prognosis, prognostic factors, and main causes of emergency admission.
Methods Between January 2004 and April 2012, we retrospectively analyzed 1244 advanced lung cancer patients (1045 patients with non-small cell lung cancer (NSCLC), 185 with small cell lung cancer (SCLC) and 14 with others).
Results There were 130 patients with advanced lung cancer who were diagnosed following emergency admission. Of them, 103 patients (79%) had non-small cell lung cancer and 27 (21%) had small cell lung cancer. In NSCLC patients, the main reasons for emergency admission were brain metastasis symptoms (23%), pleural effusion (16%), and pneumonia (15%). By multivariate analysis, good performance status (PS) just prior to opting for chemotherapy and emergency admission due to brain metastasis symptoms were good independent predictors of overall survival (OS) (hazard ratio (HR) 0.27 (95% CI, 0.12–0.58), $P < 0.001$; and HR 0.51 (95% CI, 0.28–0.87), $P = 0.016$; respectively). In SCLC patients, the main reasons for emergency admission were brain metastasis symptoms (22%), pneumonia (19%), and pleural effusion (7%). Good PS just prior to opting for chemotherapy and chemotherapy after diagnosis were good independent predictors of OS (HR 0.24 (95% CI, 0.07–0.87), $P = 0.031$; and HR 0.21 (95% CI, 0.06–0.81), $P = 0.024$; respectively).
Conclusions Our study showed that emergency admission due to symptoms of advanced lung cancer before diagnosis is a relatively common event and some simple prognostic factors were also identified.

OS006

A RETROSPECTIVE ANALYSIS OF THE EFFECT OF CONTINUING BEVACIZUMAB BEYOND DISEASE PROGRESSION IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Background and Aim of Study Randomized studies showed that the addition of bevacizumab to standard chemotherapy regimens significantly improved outcome in previously untreated patients with advanced non-squamous non-small cell lung cancer (NSCLC). However, there is no evidence to support the benefit of continued usage of bevacizumab beyond disease progression in patients with non-squamous NSCLC treated with the bevacizumab-based chemotherapy in first-line therapy. We retrospectively analyzed the efficacy and safety of docetaxel plus bevecizumab beyond progression (BBP) patients with non-squamous NSCLC whose disease has progressed after first-line treatment with bevacizumab.
Methods We retrospectively reviewed advanced non-squamous NSCLC patients who were treated with docetaxel plus BBP as second-line after disease progression in first-line treatment with bevacizumab plus a platinum-based doublet between November 2009 and March 2013.
Results Twenty two patients received the combination chemotherapy of docetaxel plus BBP as second-line. Sixteen were male, and median age was 63 (40–75). Twenty one patients received CBDCA plus pemetrexed in the 1st line, and one patient received CDDP plus gemcitabine. Objective responses were observed in 6 (27.3%) patients (6 PR) and stable disease in 12 (54.5%). Total clinical benefit (CR + PR + SD) was observed in 18 (81.8%). The median number of cycle was 5.5, progression free survival (PFS) was 4.2 months and overall survival (OS) was 8.5 months. Severe adverse events were observed in 17 (77.3%) patients. Seventeen patients experienced neutropenia (include one febrile neutropenia) and three had general fatigue.
Conclusion Although retrospective analysis, these results suggest that docetaxel plus BBP in second line setting shows sufficient clinical benefit compared with historical control with favorable toxicity profile.

OS02: TUBERCULOSIS 1

OS007

PROFILE AND TREATMENT OUTCOME OF EXTENSIVE DRUG RESISTANT TUBERCULOSIS (XDR-TB) PATIENTS IN PERSAHABATAN HOSPITAL, JAKARTA INDONESIA

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Background Multi-drugs resistant tuberculosis (MDR) becomes a threatening condition in TB eradication and in adequate treatment will lead to Extensive Drug Resistant (XDR-TB). Studies show poor outcome of XDR-TB treatment. Since Programmatic Management Drugs Resistant TB (PMDT) in 2009 underwent, we have treated 485 patients and 20 confirmed XDR-TB.
Methods These are cases report of all XDR TB patients that have been treated in Persahabatan Hospital since 2009 until 2013. All MDR-XDR TB patients have been asked to consent-for evaluation and research of PMDT before treatment.
Result There are 27 XDR-TB cases that have been treated in all PMDT sites in Indonesia, 20 (74%) cases are in Persahabatan Hospital. The median age is 38 years old (16–76), equal between male and female (11 : 9), 95% are relapse cases that have been treated more than 2 times using first line drugs plus Kanamycin and quinolone, one patient was primary XDR-TB. The DST result confirm XDR-TB with varies lesion but 2 cases with very minimal lesion and 65% have diabetic mellitus. The regimen consists of Capreomycin, high dose Levofloxacin, Cicloserin, Ethionamide, Pirazinamid and PAS, but recently using Moxifloxacin. Outcome shows the median time to treatment is 29 (2–425) days, the conversion time is 79 (30–339) days, duration of intensive phase is 237 (173–561) days, length of treatment 566 (10768) days with the end result are 6 (30%) cured, 2 (10%) failure, 4 (20%) default, 4 (20%) died and 4 (20%) still on continue phase. Among early conversion, mean less than 2 months, we cured and who never or delay conversion cases, means more than 6 months therapy, are that death and default.
Conclusion Inadequate treatment of MDR-TB will develop XDR-TB. The outcome of XDR-TB treatment still poor.

OS008

INTERFERON-GAMMA RESPONSES TO TUBERCULOSIS-SPECIFIC ANTIGENS DURING TREATMENT COURSE AND RECURRENCE OF TUBERCULOSIS

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Background and Aim of Study Recurrence of tuberculosis (TB) is a major obstacle to success in TB control worldwide. Interferon (IFN)-gamma release assay (IGRA) is an immunological test to detect cellular response to TB antigens and many researchers believe that IGRA response would be decreased in parallel with reduced bacterial antigen load as a result of successful anti-TB treatment. We investigated the relationship between longitudinal change of IGRA response during the treatment period and TB recurrence after the end of treatment.
Methods The study was approved by the relevant ethical committees. In total, 506 adult patients with new smear- and culture-positive pulmonary TB were enrolled in Hanoi, Viet Nam. They were tested for IGRA before (month 0) and after two and seven months of treatment (months 2 and 7), and were followed up for 16 months after the end of treatment. In 407 HIV-negative patients without multidrug-resistant TB, risk factors for recurrence were assessed by the log-rank test and analyzed using Cox proportional hazard models. Random coefficient models were also used to compare longitudinal patterns of IFN-gamma responses between recurrent and non-recurrent groups.
Results Of the 381 patients cured (93.6%), 372 entered the post-treatment follow-up period and 27 had recurrence (7.3%). Positive-to-negative change of IGRA results from month 0 to month 2 was significantly associated with earlier recurrence (log rank test, $P = 0.0001$), even after adjustment for body mass index and smear results at month 2 (hazard ratio = 4.87, 95% CI 2.03–11.71). By using a random coefficient model with log-transformed IFN-gamma values as outcome, changes of IFN-gamma values during the course were also significantly different between recurrent and non-recurrent groups ($P < 0.0001$).
Conclusion Difference in longitudinal patterns of cellular immune responses to TB-specific antigens during treatment may provide an insight into the host immune status leading to TB recurrence.

OS009

ANTI-TUBERCULOSIS DRUG RESISTANCE PATTERN AMONG DIFFERENT CATEGORY OF TUBERCULOSIS PATIENTS IN BANGLADESH

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Background Anti-tuberculosis (TB) drug resistance is emerging as a new global health problem. No national data on drug resistance in Bangladesh. The absolute number of multidrug resistant TB (MDR-TB) is expected to be high considering high TB burden. This study was aimed to determine the resistance pattern of mycobacterium tuberculosis (MTB) isolates among different category of patient.
Method A total 1123 randomly selected patients having clinical and or radiological features of tuberculosis attending patients department of NIDCH were enrolled in this study during January to December, 2008. Sputum were collected and processed for culture by digestion, decontamination and concentration following modified Petroff's method and were inoculated on to 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) were performed.
Result Drug susceptibility testing for Isoniazid (INH), Rifampicin (RIF), Ethambutol (EMB) and Streptomycin (SM) was done among 363 cases. Resistance rates for INH, RIFR, EMB and SM were under 73.03%, 71.63%, 27.55% and 55.65% respectively. According to DST report total 221 cases were detected as multi drug resistant TB (MDR-TB). Among them, 87% cases were MDR-TB in category II (CAT-II) failure and 13% were MDR-TB in category I (CAT-1) failure and it was 0% in new cases.
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.

OS010

EFFICACY OF REAL-TIME POLYMERASE CHAIN REACTION FOR RAPID DIAGNOSIS OF ENDOBRONCHIAL TUBERCULOSIS

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Background and Objective The diagnosis of endobronchial tuberculosis (EBTB) is challenging due to its variable and non-distinctive manifestations and the low rate of acid-fast bacilli (AFB) positive sputum smears. To evaluate the efficacy of real-time polymerase chain reaction (PCR) of bronchoscopic biopsy specimens in the diagnosis of EBTB.
Methods Real-time PCR for M tuberculosis DNA in biopsy tissue from EBTB patients was performed prospectively. The yields of real-time PCR, sputum smear and bronchial brush smear (BBS) were compared. The impact of bonchoscopic types of EBTB on diagnostic yields were also evaluated.
Results The yields of sputum smear and BBS by AFB auramine O fluorescent stain, and bronchoscopic biopsy tissue by real-time PCR were 4.1% (3/74), 39.2% (29/74) and 82.4% (61/74), respectively. Real-time PCR (CT35) of bronchial biopsy samples yielded better than AFB stain of BBS, especially in granular and caseating types ($p < 0.01$). A significant difference was found between bronchoscopic types of EBTB in the yields of real-time PCR (CT35) ($\chi^2 = 11.87$, $P = 0.007$).
Conclusions The detection of M. tuberculosis DNA in EBTB biopsy tissue by real-time PCR is more sensitive than sputum smear and BBS. Its yield could be influenced by the bronchoscopic types of EBTB; the early stages appear to yield better.

OS011

LINEZOLID FOR THE TREATMENT OF EXTENSIVELY DRUG RESISTANT TUBERCULOSIS: MULTICENTER, RANDOMIZED CONTROLLED STUDY

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Objective To evaluate the clinical efficacy and safety of Linezolid for the treatment of XDR-TB.
Methods We enrolled 59 patients who had sputum-culture-positive XDR-TB tuberculosis in 5 major tuberculosis specialized hospital in China. Patients were randomly assigned to linezolid therapy group (n = 30) and control group (n = 29). Patients in two groups were adopted two years of individual-based chemotherapy regimens. Meanwhile, linezolid therapy group was added to linezolid that started at a dose of 1200 mg per day for 4 to 6 weeks, followed by 300 to 600 mg per day for at least 6 months.
Results 4 Patients in linezolid therapy group discontinued therapy because of side effects or other reasons, and 3 Patients in control group discontinued therapy because of side effects or other reasons. In linezolid therapy group, the longest period of applying linezolid for treatment was up to 24 months, the minimum was 6 months with the average of about 12 months. The sputum culture conversion rates in the linezolid therapy group were 73.07% in the 12th month after treatment, significantly higher than those of control group (30.76%). The cavity closure or reduced rates in the linezolid therapy group were 57.69% in the 12th month after treatment, significantly higher than those of control group (26.92%). Of 20 patients completed therapy in the linezolid therapy group, 14 (70%) had treatment success (cured and treatment completion). Of 21 patients completed therapy in the control group, only 7 (30%) had treatment success. In the linezolid therapy group, 13 (50%) had adverse events such as peripheral neuropathy, leucopenia and anaemia, gastrointestinal reactions, liver injury etc.
Conclusions Linezolid containing chemotherapy for treatment of XDR-TB may significantly promote cavity closure, accelerate sputum culture conversion and improve treatment success rates. Meanwhile adverse reaction might be tolerated and resolve after suitable intervention.

OS012

CLOFAZIMINE FOR THE TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS: MULTICENTER, RANDOMIZED CONTROLLED STUDY

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Objective Clofazimine has shown activity against Mycobacterium tuberculosis, including MDR-TB strains in vitro and in animal studies. However, clinical experience with clofazimine in MDR-TB is scarce. To evaluate the clinical efficacy and safety of using clofazimine to treat MDR-TB.
Methods We enrolled 92 patients who had sputum-culture-positive MDR-TB in 8 major tuberculosis specialized hospital in China. Patients were randomly assigned to clofazimine therapy group (n = 46) and control group (n = 46). All patients had positive sputum-smear microscopy results at the time of MDR-TB diagnosis. Patients in two groups were adopted individual-based chemotherapy regimens based on the patient medication history and drug susceptibility test results. Meanwhile, clofazimine therapy group was added to 100 mg of clofazimine once daily for 21 months.
Results 3 patients in each group discontinued therapy because of side effects or other reasons. The sputum culture conversion rates of clofazimine therapy group were 74.41% (32/43) in the 21th month after treatment, higher than those of control group (58.13%, 25/43). The lesions absorption rates of clofazimine therapy group were 81.39% (35/43) in the 21th month after treatment, higher than those of control group (60.46%, 26/43). Of clofazimine therapy group, 39 had cavitary changes noted on initial chest CT, and of control group, 38 had cavitary changes. The cavity closure or reduced rates of clofazimine therapy group were 71.79% (28/39) in the 21th month after treatment, higher than those of control group (57.89%, 22/38). Side-effects of skin such as skin discolouration, ichthyosis only occurred in 40 patients of clofazimine therapy group. Other Side-effects are similar in two groups.
Conclusions Using clofazimine to treat MDR-TB can significantly improve clinical symptoms, promote lesion absorption and cavity closure, and accelerate sputum negative conversion. Clofazimine can help MDR-TB patients to improve life quality with mild adverse reaction but good drug tolerance.

OS03: CLINICAL RESPIRATORY MEDICINE 1

OS013

SINOBRONCHIAL SYNDROME(SBS) NOT UPPER AIRWAY COUGH SYNDROME(UACS): CLINICAL EXPERIENCE WITH LOW DOSE ERYTHROMYCIN (LDEM) THERAPY IN THAILAND

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Background Sinobronchial Syndrome (SBS) is not widely recognized as upper airway cough syndrome (UACS). The former is a well known and common in Japan but not in the western countries. The presentations seem clinically indistinguishable from each other, but SBS responds well to low dose erythromycin (LDEM). In this regard SBS could be easily mistaken for UACS. As the diagnosis and treatment is simple and according to the Japanese Respiratory Society guideline, it is reasonable to treat these patients with LDEM when they failed to benefit from current appropriate therapy.
Aim of Study To characterize the clinical presentation of SBS in our experience.
Methods Retrospective study was conducted in Central Chest Institute of Thailand between 2010–2013. Patients were carefully evaluated and diagnosis of SBS was made as following: (1) chronic productive cough but unremitting despite appropriate treatment (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, and (2.4) imaging evidence of sinusitis, and (3) these responded to LDEM, 500 mg/day.
Result SBS was diagnosed in 68 males and 109 females [N = 177], ages 16–94 years [mean 65.1]. Remarkably, they all had symptoms indistinguishable from UACS in addition to their persistent cough of bronchiectasis with or without old pulmonary TB (93), asthma (35), bronchitis (23), COPD (10) and UACS (14). It is worth to note that they all had SBS but not UACS as they responded well and even excellently to LDEM. The longer the LDEM therapy the better the result.
Conclusion From our study, SBS should be carefully considered in patients with (1) productive cough with or without chronic airway disorders and (2) symptoms mimicking UACS, and (3) their cough satisfactorily relieved with LDEM,but not with their usual concurrent therapy. Clarification of long term remission and recurrence is needed.

OS014

THE PREVALENCE AND OUTCOMES OF CO-MORBID ILLNESSES IN ELDERLY PATIENTS WITH RESPIRATORY DISEASES

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Introduction The elderly population is getting increased in worldwide. Lung diseases are major cause of illness, disability and death among elderly patients. This group is also more prone to suffering other nonrespiratory chronic diseases and more than half of elderly people have at least three chronic medical diseases.
Aim We aimed to determine clinical findings, outcomes, patterns of hospitalization, the prevelance and impact of comorbidities in very elderly patients with repiratory diseases.
Methods 243 patients (80 years or older) who had hospitalised in our clinic between 2009–2011 years were included Data were recorded from patients files retrospectively. The Charlson comorbidity index (CCI) was used to quantify co-morbidity.
Results 144 (59.3%) of them were male, 99 (40.7%) were female. The mean age was 82.85 ± 2.64 (80–92). The rates of hospitalization was increased between 2009–2011 years respectively (6.9%, 7.1%, 7.9%) The indications of hospitalization were COPD acute exacerbation (43.2%), pneumonia (32.1%), lung cancer (8.6%), congestive heart failure (CHF) (4.5%), pulmonary embolus (4.1%) tuberculosis (3.7%), hemoptysis and pleural effusion of unknown etiology (3.7%). The prevalance of comorbidite was 75.7%. The most common comorbid diseases were cardiovascular diseases 30.5%, hypertension 20.2%, diabetes mellitus 18.9%, and cerebrovascular diseases 7.4%. 208 (85.5%) patients were discharged, 16 (6.6%) patients were transferred to ICU and 19 (7.8%) patients dead. The most of deaths occured in first 48 hours. CCI and comorbidity number were higher in dead patients than others (1.42 ± 0.7 vs 1.20 ± 0.9 comorbity no: 1.57 ± 0.83 vs 1.08 ± 0.82 respectively).
Conclusion Our results suggested that rates of hospitalization in patients aged 80 or older were increased, 75.7% of them have at least a chronic medical diseases. In clinical practise, chronic diseases and multipl comorbidities are ignored mostly in elderly patients. Awareness of comorbidities in this patients with respiratory diseases who need special care, will result in appropriate medical support and treatment.

OS015

PATIENT SAFETY IN RESPIRATORY AND CRITICAL CARE MEDICINE: FROM ERRORS TO SOLUTIONS

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Background and Aims We describe the impact of an incident reporting, analysis and intervention program implemented by Respiratory and Critical Care Medicine (RCCM) physicians on patient safety.
Methods All clinicians in RCCM voluntarily reported adverse/near miss/error events. The individual narratives and chart reviews were discussed and coded with a classification framework. (Refs 1–2) We grouped recurrent events into distinct clinical problems. We implemented systemic safety and quality improvement solutions. We also integrated patient safety into our teaching curriculum.
Results From 2005 to 2012 we analyzed safety events in 691 patients. This constitutes about 1/4 of all cases reported. The majority were not detected by the formal safety processes of the hospital. There were 450 (65%) diagnostic errors. And 14 distinct clinical problems were identified in 71% of cases. The most common being pleural disease, breathlessness, cancer, tuberculosis and pneumonia. Either deaths or patient harm occurred in 59%. We detected human errors in 88% of cases. They were compounded by systems errors in 56%. We implemented a large number of safety solutions grouped into 8 different categories: feedback, oversight, rule, checklist, red flag, closed loop, handoff and asking the patients. The greatest improvements in patient safety were measured in pleural disease, non-invasive ventilation and severe pneumonia while the quality of care was improved in cancer diagnosis, neuro-muscular weakness and liberation from mechanical ventilation.
Conclusions We believe that, in a deliberate process of creating new solutions from voluntary error reporting by clinicians, we have achieved sustained improvements in patient safety in RCCM.

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OS016

IN VIVO IMAGING OF DIFFUSE PULMONARY OSSIFICATION

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Background and Aim of Study Diffuse pulmonary ossification (DPO) is a rare disease characterized by diffuse small bone fragments in the lung tissue. The majority of cases had been diagnosed on autopsy. Living cases are rarely encountered. To our knowledge, this is the first report of an impressive in vivo imaging by a video-assisted thoracoscopic surgery (VATS).
Methods A 43-year-old healthy woman presented at our hospital in 2008 to undergo detailed investigations as part of a routine health examination. She had no symptoms at the first visit. Chest computed tomography showed small nodular opacities in the lung fields bilaterally. Normal vesicular sounds were heard on auscultation. Transbronchial lung biopsy (TBLB) was not conclusive. After 4 years of follow-up, her dry cough deteriorates with age. In 2012, for the second time the TBLB showed no significant findings. Therefore, we performed the VATS lung biopsy.
Results Gross pathological image gives pulmonate limpet-like appearance. We will present a first case of the VATS image in vivo. The histological findings obtained from the VATS-biopsy showed dendriform mature bone formations with marrow in the aleveolar spaces. Only minimal interstitial fibrosis was observed in the alveolar septum. Consequently, we diagnosed the patient with idiopathic DPO of the dendriform type.
Conclusion DPO is found associated with several conditions, such as chronic pulmonary inflammation, histoplasmosis, chronic therapy with busulfan, pulmonary metastases of osteogenic sarcoma, pulmonary amyloidosis, areas of dystrophic calcifications, and Goodpasture's syndrome. In the present case, the patient has no underlying disease. There is no known treatment for the disease. We will carefully follow up.

OS017

IMPORTANCE OF RECOGNITION OF SINOBRONCHIAL SYNDROME (SBS) BECAUSE OF EXCELLENT EFFECT OF LOW DOSE ERYTHROMYCIN (LDEM) THERAPY IN THAILAND

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Background Sinobronchial syndrome (SBS) is a well characterized chronic neutrophilic inflammation of upper and lower airways in Japan but rare in western countries. According to the Japanese Respiratory Society guidelines the diagnosed of SBS could be simply made when all of 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 and/or mucolytics.
Aim of Study To clarify the existence of SBS and efficacy oflow-dose erythromycin (LDEM) therapy.
Methods Retrospective study was conducted in Central Chest Institute of Thailand between 2010–2013. Patients were carefully evaluated. Those who met the above 2 criteria were included for therapeutic LDEM (500 mg/day). SBS was diagnosed when all the criteria were met. Response was considered (a) good when cough decreased by more than half (b) excellent when cough remained free or almost free.
Results SBS was uncovered in 68 males and 109 females [N = 177], ages 16–94 years [mean = 65.1]. The concurrent diseases were as following: bronchiectasis with or without old pulmonary TB (93), asthma (35), bronchitis (23), COPD (10) and allergic rhinitis (14). Notably, it could be found in association with chronic airway inflammation. Following LDEM therapy, 92 and 85 out of 177 had good 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.

OS018

TREATMENT OF PULMONARY MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA WITH CLARITHROMYCIN: A CASE REPORT

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A 54 year-old male presented cough and expectation for 3 years and computed tomography (CT) showed multiple lesions and bronchiectasis in bilateral lungs. Lung biopsy revealed diffuse hyperplasia of small lymphocytes and histopathologic examination was positive for B-cell marker. There was no metastasis to any lymph nodes and intra-abdominal organ and no Helicobacter pylori (H.P.) infection in the patient. The patient was diagnosed with pulmonary MALT (p-MALT) lymphoma. In this case, chemotherapy or radiotherapy may be a better choice since CT showed large and multiple lesions in bilateral lungs, but the patient refused to these treatments. Considerate the stable physical condition of this patient, we tried to use clarithromycin (CAM) (500 mg/d), and fortunately the lesions reduced significantly after 20 months treatment.
Discussion Mucosa-associated lymphoid tissue (MALT) lymphoma is a low grade B-cell extra-nodal lymphoma from marginal zone and rarely seen in lung. There is non-uniform treatment of p-MALT lymphoma. It's reported that p-MALT lymphomas may be associated with chronic inflammation. Researches found that anti-H.P. infection could reduce the size of the gastrointestinal MALT lymphoma and stimultaneously lessen the size of p-MALT. Our results were similar with previous reports, but there was no gastrointestinal MALT lymphoma in our case. We reported the first report of p-MALT lymphoma without any extra-pulmonary lesions of MALT lymphoma that was regressed with CAM (500 mg/d) treatment. Therefore, CAM may be a promising choice for p-MALT lymphoma treatment without any adverse reactions in chemotherapy or radiotherapy or surgery. Further a trial of massive patients may lead to a better support of CAM treatment of p-MALT.
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OS04: LUNG CANCER 2

OS019

THE RISK FACTORS FOR SEVERE ADVERSE EVENTS OF CHEMOTHERAPY FOR ADVANCED NON-SMALL CELL LUNG CANCER

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Background Chemotherapy is a standard treatment for patients with advanced non-small cell lung, but occasionally causes some adverse events. Serious adverse events, which cause immediate hospitalization, prolonged hospitalization, permanent damage, or death, are clinically defined as severe adverse events (SAE). However, as few studies have reported on the risk factors for SAE, we investigated those in the prediction of SAE in non-small cell lung cancer.
Patients and Method The medical records of the patients who were treated with pemetrexed or docetaxel monotherapy at Juntendo University Hospital between January 2010 and March 2012 were retrospectively reviewed. A multivariate analysis was performed to identify the independent risk factors among the following factors; age (<75 vs. >74), PS (0–1 vs. 2–3), lines of previous chemotherapy (1 line vs. more than 2 lines), coexistence of interstitial pneumonia (IP) before chemotherapy (yes vs. no), and regimen (docetaxel vs. pemetrexed).
Result A total of 151 patients received pemetrexed monotherapy or doetacxel monotherapy (male/female, 99/52; median age (range), 70 (41–92) years; stage III/stage IV/postoperative recurrence, 39/79/33; adenocarcinoma/squamous cell carcinoma/NOS, 117/24/10; pemetrexed monotherapy/docetaxel monotherapy, 67/84). Of these, 16 patients experienced SAE. The causes of SAE were occurrence or exacerbation of IP in 7 patients, febrile neutropenia (FN) in 3 patients, decreased performance status in 2 patients, and anemia, allergic reaction, infection, and appetite loss in one patient, respectively. 2 patients died due to drug-induced IP and 1 patient died due to FN. Multivariate analysis revealed that coexistence of IP before chemotherapy (OR = 3.45; P = 0.0247) and docetaxel monotherapy (OR = 8.14; P = 0.0026) were significantly associated with SAE.
Conclusion IP associated with lung cancer and docetaxel monotherapy are the risk factors in the prediction of SAE in clinical practice.

OS020

DISTINCT CHARACTERISTICS OF BRAIN METASTASES FROM NON-SMALL LUNG CANCER WITH EGFR MUTATION

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Background EGFR-TKIs have been reported effective for brain metastases (BMs) from non-small cell lung cancer (NSCLC) with major EGFR mutation. However, the characteristics of BMs from EGFR-mutant NSCLC have been not adequately understood.
Material and Methods All NSCLC patients with synchronous and metachronous BMs detected with Gd enhanced brain MRI from March 2005 to December 2012, were divided according to the EGFR mutation status. The radiographic characteristics including number of BMs, tumor sizes, and brain edema sizes, and the prognostic factor were analyzed.
Results One hundred and seventy-three patients included were divided into three groups: wild-type EGFR group (90 patients), exon 19 deletion group (47 patients), and exon 21 point mutation group (36 patients). The exon 19 deletion group had more multiple small synchronous BMs with smaller brain edema compared with the wild type EGFR group (P = 0.017, 0.0021, >0.0001). The exon 19 deletion group also had smaller metachrnous BMs with smaller brain edema than the wild-type group (P = 0.03, 0.0016) although the number of BMs was not statistically different (P = 0.54). In the exon 21 point mutation group, the same trends were observed with regard to number, tumor size, and edema size, regardless of the time of BMs diagnosis although the difference was not significant. In the univariate analysis, the number of BMs > 5 was only a prognostic factor (P = 0.00011) in patients with EGFR-mutant NSCLC although the frequency of neurological symptom was not statistically different between the patients with = <5 and those with BMs > 5 (P = 0.58).
Conclusions BMs with major EGFR mutation, especially exon 19 deletion, presented some distinct characteristics compared with those with wild-type EGFR. Because the number of BMs was a prognostic factor, regular evaluation should be performed to detect BMs early, even in asymptomatic NSCLC patients with EGFR mutation.

OS021

THYMIDYLATE SYNTHASE EXPRESSION CAN GUIDE ANTI-CANCER DRUG SELECTION FOR ADVANCED NON-SMALL CELL LUNG CANCER PATIENTS

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Background Combination cisplatin plus pemetrexed (PMT) and carboplatin plus paclitaxel (PAC) with bevacizumab are standard first-line chemotherapies for advanced non-small cell lung cancer (NSCLC). However, it is unclear whether a PMT-based regimen or PAC-based regimen should be selected for patients with advanced NSCLC. Thymidylate synthase (TS) is an important enzyme in DNA synthesis and influences sensitivity to several anti-cancer drugs. The purpose of this study is to determine whether TS expression affects the therapeutic efficacy of PMT or PAC.
Methods Participants were 94 patients with advanced NSCLC treated with PMT or PAC. Samples were obtained by tumor biopsy prior to treatment. Cancer cells were isolated from formalin-fixed paraffin-embedded tissue using laser microdissection, and mRNA levels were analyzed using real-time reverse transcription polymerase chain reaction. Protein expression was evaluated using immunohistochemistry. The association between TS expression and therapeutic efficacy was evaluated.
Results Fifty patients received PMT, 51 patients received PAC, and 7 patients received both regimens. TS expression was significantly lower in PMT responders compared with PMT non-responders (p = 0.0142), but significantly higher in PAC responders compared with PAC non-responders (p = 0.0486). In patients with low expression of TS, progression-free survival (PFS) was prolonged for the PMT-based regimen compared with the PAC-based regimen (21.9 versus 18.7 weeks, p = 0.5661). Conversely, in patients with high expression of TS, PFS for the PAC-based regimen was superior to that for the PMT-based regimen (19.9 versus 13.3 weeks, p = 0.2433).
Conclusion The PMT-based regimen afforded better outcome in patients with low expression of TS, whereas the PAC-based regimen was better in patients with high expression of TS. Thus, TS expression could be a useful biomarker for anti-cancer drug selection in NSCLC patients receiving PMT- or PAC-based chemotherapy.

OS022

LUNG CANCER IN PATIENTS WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Background Combined Pulmonary Fibrosis and Emphysema (CPFE) is a new category of smoking-related diseases named in 2005 by Cottin et al. The syndrome is frequently combined by lung cancer, but the clinical course of those patients have not comprehensively described.
Method A review of patients of lung cancer admitted to our hospital from January 2009 to March 2013 was conducted.
Result CPFE were identified in 59 patients, 19 in adenocarcinoma, 15 in squamous cell carcinoma, 6 in non-small cell carcinoma (NSCLC), and 19 in small cell carcinoma (SCLC). Chemotherapy was given to 39 patients and drug-induced acute lung injury was occurred in 1 patient (G4, 2.5%). Seven patients underwent chemo-radiotherapy, and radiation pneumonitis was observed in 5 patients (G2 = 4; 51%, G3 = 1; 14%). Thirteen patients underwent surgical operation. Pathological findings of resected lung including fibrotic change was as follows; 2 fibrotic-NSIP, 2 UIP, 2 non-specified fibrosis, 1 OP. Two of these patients, one with OP and one with fibrotic-NSIP, had acute exacerbation of interstitial pneumonitis after the operation (15%). Overall survival of patients with NSCLC and SCLC treated by chemotherapy was 7.8 months and 6.5 months, respectively.
Conclusions In this study, the incidence rate of treatment-related lung injury after chemotherapy was not so high as reported in previous study about lung cancer with idiopathic interstitial pneumonitis (IIPs). Since the pathogenesis and the definition of CPFE is still unclear, the differentiation between this syndrome and IIPs can be suggested. More investigation about CPFE is needed and the appropriate treatment to combining lung cancer should be considered.

OS023

A CASE OF SMALL CELL LUNG CANCER WITH CANCER-ASSOCIATED RETINOPATHY (CAR) ACCOMPANIED BY CIRCULATING ANTI-CRMP5/CV2 ANTIBODIES

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Background Cancer-associated retinopathy (CAR) is one of the paraneoplastic syndromes and characterized by retinal degeneration. Anti-recoverin antibodies have been mainly identified in blood sample from CAR patients. Meanwhile, antibodies against collapsing-response mediator protein 5 (CRMP5)/CV2 that bind exclusively to oligodendorcytes often cause optic neuropathy as well as neurological deficit including peripheral neuropathy. Here, we report a rare case of small cell lung cancer with CAR accompanied by circulating anti-CRMP5/CV2 antibodies.
Case A 60-year-old man was aware of visual disturbance and mild sensory abnormality of extremities at first. Though several ophthalmologists pointed out uncertain-caused retinal degeneration, they could not reach definitive diagnosis. Four months later, hoarseness and dysphagia developed. In other hospital, chest CT revealed a tumor in left lower lung and mediastinal lymphadenopathies. He was admitted to our hospital. The imaging studies and histological examinations showed a stage IV small cell lung cancer (SCLC). Serum autoantibodies screening test indicated high titer of anti-CRMP5/CV2 antibodies and low titer of anti-Hu antibodies. Presence of CAR was confirmed by medical history and optical examinations. An anti-CRMP5/CV2 antibodies seemed to be related to retinopathy rather than optical neuropathy. Findings related to paraneoplastic neurological syndrome were uncertain. Treatment of chemotherapy shrank the primary tumor but did not lead to obvious improvement of both sensory disturbance and visual deficit.
Conclusion Anti-CRMP5/CV2 antibodies accompanied by SCLC may be related to the development of CAR. It is important to consider the possibility of malignancy in the case that unexplained visual disturbance develops abruptly.

OS024

PHASE II STUDY OF AMRUBICIN FOR PATIENTS WITH NON-SMALL CELL LUNG CANCER AS THIRD-LINE OR FOURTH-LINE CHEMOTHERAPY: UPDATED RESULTS

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Backgroud Recently, NSCLC patients (pts) receive third-line chemotherapy with the established benefit of second-line chemotherapy. However, the role of cytotoxic agent in this setting has not yet been defined prospectively. Amrubicin (AMR), third-generation synthetic anthracycline agent, has favorable clinical activity and acceptable toxicity for non-small cell lung cancer (NSCLC). This prospective trial was conducted to evaluate the efficacy and safety of AMR for NSCLC pts as third-line or fourth-line chemotherapy (Hokkaido Lung Cancer Clinical Study Group Trial 0901).
Methods Eligible pts had a performance status 0 to 2, after failure of second-line or third-line chemotherapy, and adequate organ function. Pts received AMR 35 mg/m^2 intravenously on days 1–3 every 3 weeks. The primary endpoint was disease control rate (DCR: CR + PR + SD). Secondary endpoints were overall survival (OS), progression-free survival (PFS), response rate (CR + PR), and toxicity profile. The estimated accrual was 37 pts.
Results From August 2009 to May 2011, 41 pts were enrolled from 10 institutions. Patient characteristics were: male/female 29/12; median age 66 (range 43–74); performance status 0/1/2 16/24/1; adenocarcinoma/squamous cell carcinoma/large cell carcinoma/not other specified 30/8/2/1; EGFR mutation positive/negative/unknown 7/26/8; treatment lines 3rd/4th 26/15. The median number of treatment cycles was 2 (range 1–9). The objective responses were CR 0, PR 4, SD 22, PD 14, and NE 1, giving a DCR of 61.0% (95% CI, 46.0–75.9%). Overall response rate was 9.8% (95% CI, 0.6–18.8%). Updated median PFS was 3.0 months, whereas median overall survival time was 12.6 months. Grade 3/4 hematological toxicities were neutropenia (68%), anemia (12%), thrombocytopenia (12%), and febrile neutropenia (17%). Grade 3/4 non-hematological toxicities were anorexia (12%), nausea (10%), and pneumonitis (2%). No treatment-related death was observed.
Conclusions AMR shows significant clinical activity with acceptable toxicities as third-line or fourth-line chemotherapy for advanced NSCLC.

OS05: TUBERCULOSIS 2

OS025

ADENOSINE DEAMINASE LEVELS IN CEREBROSPINAL FLUID FOR DIAGNOSIS OF TUBERCULOUS MENINGITIS (TBM) AND ITS CORRELATION WITH ADVERSE NEUROLOGICAL OUTCOME

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Objectives In spite of the common occurrence of TBM it is often misdiagnosed. The aim of this study was to evaluate the usefulness of CSF ADA for diagnosis of TBM and to correlate the initial levels of CSF ADA with the neurological outcome.
Methods This is a prospective cohort study including 83 patients. Patients with history and clinical features suggestive of TBM were analysed using the Thwaites criteria. CSF ADA levels were estimated in patients fulfilling these criteria. ADA levels higher than 10 IU/L were taken as positive, and these patients were followed up at 30 and 90 days and the neurological outcome was assessed using the modified Rankin scale (MRS).
Results CSF ADA levels in all 83 patients labelled as TBM using the Thwaites criteria was found to be above 10 IU/L (10.64–25). The mean ADA was 30.01 IU/L. A total of 6 patients expired, the mean ADA in this group was 100.4, which was significantly more than the mean ADA levels. 30 patients had residual disability at discharge (MRS greater than 1). The mean ADA levels in this group were 33.12 IU/L.
Conclusions CSF ADA levels were elevated in all 83 patients (100% sensitivity) implying its usefulness as a simple, inexpensive test to aid in the diagnosis of TBM. The initial CSF ADA levels were much higher than the mean in patients who expired, suggesting its role as a marker in predicting mortality in these patients, however there was no significant difference in ADA levels in patients with mild to moderate CNS sequele.

OS026

IMPACT OF SOCIO ECONOMIC STATUS ON NET OUTCOME DOTS CAT I & CAT II CASES

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Background Tuberculosis in developing countries like India has historically been associated with poverty and low socioeconomic status. The purpose of this study was to assess the association of socio economic status (SES) on the outcome of tuberculosis drug therapy in patients of direct observed therapy (DOTS).
Methods Total 300 cases of tuberculosis, diagnosed by sputum microscopy & Chest radiography, were put on DOTS therapy. Cases were divided in two groups. Group A included 213 patients (73 patients of cat I & 140 patients of cat II) who were mostly patient belonging to low SES (below poverty line). Group B included 93 patients (53 cases of CAT I & 30 of CAT II) who could afford satisfactory lifestyle.
Results 11 of 73 cases on CAT 1 in group A resulted in treatment failure & became smear positive after 3rd month of treatment (failure rate 15.06%) & 53 of 73 patients were cured (cure rate 78.08%). 9 patients defaulted during treatment. In group A cat II cases 53 of 140 patients came out MDR (Multi Drug Resistance) cases and were sputum positive after the 5th month of treatment as Gene xpert (MTB RIF) was showing R resistance (failure rate: 37.85%). 63 patients of CAT II completed the treatment of 6 months & were declared cured. 24 patients defaulted during treatment. In group B 41 of 53 cat I patients were cured (cure rate 77.35%). 5 cases failed treatment (9.4%). 7 cases defaulted. In group B cat II cases 22 of 30 cases were cured (cure rate 73.33%). 4 were MDR. 4 defaulted during treatment.
Conclusion Failure rates & MDR were alarmingly high in group A (low SES) & most of them were smokers or drug addicts with poor adherence to treatment.

OS027

DOUBLE BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL IN TUBERCULOSIS PATIENTS WITH TUBERCULOSIS TREATMENT SUPPLEMENTED WITH MORRINDA-ZINGER EXTRACT: THE SPEED OF SPUTUM CONVERSION

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Background and Aim of Study We studied treatment outcome of TB Patient who are managed with DOTS strategy in Persahabatan hospital. The objective of the study is to compare the treatment outcome of TB patient treated with Anti TB drugs using Fixed Dose Combination (FCD) plus placebo versus those who treated with FDC plus Morrinda citrifolia 125 mg and Zinger officinale 125 mg extract. Fortibi is a supplement contained Morrinda citrifolia 125 mg and Zinger officinale 125 mg extract mix in one capsule. Previous study revealed that there is synergy effect of Morrinda citrifolia and Zinger officinale of antimicrobial.
Method This was a clinical trial with Double blind approach with 100 TB patients, new cases diagnosed from November 2010 until October 2011. Each patient underwent sputum smear evaluation at week 2, week 4, week 6 and week 8. Sputum conversion was evaluated in each group for 6 months.
Result In total 100 positive AFB TB patients with standard TB treatment, there are 51 patient Morrinda citrifolia 125 mg and Zinger officinale 125 mg extract arm and 49 patients at placebo arm with 27 males and 24 females and 18 males and 31 females respectively. Age, sex, body mass index, extend of disease and cavities do not give significant differences in treatment outcome. However, at week 6 observations, conversion of exposure group showed rapid respond than placebo group ($p < 0.05$). Others factor identified influencing the rapid of sputum conversion are positive of AFB.
Conclusion Morrinda citrifolia 125 mg and Zinger officinale 125 mg extract additional to FDC in the study give more rapid respond based on sputum at week 6 observations.

OS028

LONGER DELAYS IN DIAGNOSIS OF TUBERCULOSIS IN A TOKYO METROPOLITAN AREA

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Background and Aim of Study Delays in the diagnosis of tuberculosis (TB) results in excess morbidity and mortality. Early diagnosis and immediate initiation of treatment are essential for an effective TB control program. Despite of appropriate diagnostic methods to identify people suspected of having TB, some patients had longer delays until diagnosis. The aim of this study was to assess longer delay in the diagnosis of TB and risk factors for this delay and consequences.
Methods We retrospectively reviewed 133 cases of tuberculosis (PTB alone 109 cases/EPTB 24 cases) from 1998–2012 at a single university hospital. Medical records were reviewed to patient demographic and clinical characteristics.
Results Long total delay (over 12 weeks) as the time from first consultation was observed for 12/133 (9%) of patients (PTB alone 10 cases/EPTB 2 cases). The median providers delay was 13 weeks in patients with PTB alone and 19 weeks in patients with EPTB, respectively. Seven (58%) of patients needed repeat examination due to initial diagnostic failure. Asymptomatic, under age 59, never smoking patients were associated with longer delays in diagnosis.
Conclusions Repeat testing is recommended for patients who were strongly suspected to have active TB. Interventions to expedite TB diagnosis in primary care and non-infectious disease specialist need to be developed and evaluated in this setting.

OS029

THE INCIDENCE OF MULTI DRUG RESISTANT TUBERCULOSIS AMONG PATIENTS RECEIVING STANDARDIZED TREATMENT REGIMEN FOR SUSPECTED MDR-TB

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Introduction The LCP-PMDT through the WHO started the use of Standardized treatment regimen for all smear positive drug resistant tuberculosis suspects. Two regimens were used namely STR A, used for cases of category 1 and 2 Relapse, RAD and those with single non-DOTS treatment. The 2nd regimen is STR B, which included category 1 and 2 failure and those with multiple non-DOTS treatment.
General Objective To determine the Incidence of Multi-drug resistant tuberculosis among patients receiving Standardized Treatment regimen for suspected Multi-Drug Resistant Tuberculosis.
Study Design Descriptive Study.
Results Of the 179 patients, 101 belonged to STR B and 78 to STR A. The incidence of MDR-TB was 81.2% (82 out of 101) for STR B and 39.7% (31 out of 78) for STR A. MDR-TB occurred most frequently among Category 1 failure 94% (17 of 18 patients), followed by Category 2 failure 90.1% (10 of 11 patients) and 76.3% (55 of 72 patients) for patients with Multiple non-DOTS treatment. Incidence of MDR-TB was 55% and 30.4% for Category 2 relapse and single non-DOTS treatment, and respectively 45.5% and 33.3% for Category 1 RAD and Category 1 relapse.
Conclusion Base on the available data, we conclude that MDR-TB occurs more frequently among the STR B group (category I failure, category II failure, and other Non-DOTS with multiple treatment). Our study recommends initiation of standardized regimen for MDR-TB for patients with Category I failure, Category II failure, category II relapse and those with Non-DOTS with multiple treatment should be considered while awaiting the results of the DST this is due to the high frequency of MDR-TB cases among the following group of patients. As for the use of category II treatment regimen, this should be used in category I RAD and category I relapse pending the results of the DST.

OS030

DELAY IN DIAGNOSIS OF PULMONARY TUBERCULOSIS AND RISK OF NOSOCOMIAL TRANSMISSION AMONG INTENSIVE CARE UNITS: A NATIONAL SURVEILLANCE IN TAIWAN

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Background Tuberculosis, a global public health threat, is still a leading cause of death worldwide. Although its incidence and mortality rates have steadily declined since 1950, TB remains a leading infectious disease in Taiwan. The presentation of tuberculosis is versatile and diagnosis of tuberculosis is frequently delayed for months. Failure to recognize active tuberculosis in the patients admitted to intensive care unit (ICU) can potentially cause nosocomial transmission.
Methods The whole National Health Insurance Research Database were surveyed. Among all ICU admissions, prevalence of pulmonary tuberculosis and delay in diagnosis were studied to evaluate the risk of nosocomial transmission.
Results During 2004–2010, a total of 1,354,244 ICU admissions were identified. The mean age was 66.6 ± 17.0 years with a male-female ratio of 1.6. The mean duration of ICU stay was 7.1 ± 8.9 days. Pulmonary tuberculosis was associated with 23,724 (1.8%) of these ICU admissions. Among these, diagnosis was delayed until after admission in 8,389 (35.4%) or even within 3 months after discharge in 5,767 (24.3%). For patients with delayed diagnosis, 74.2% required mechanical ventilatory support while nebulizer therapy and non-invasive positive pressure ventilation were applied in 48.2% and 11.3%, respectively. Only 13.8% of patients with delayed diagnosis of tuberculosis have received negative pressure isolation.
Conclusions Delay in diagnosis of tuberculosis is common among patients admitted to ICU. In area with TB endemics, nosocomial transmission poses a serious risk to not only patients but also health care workers in ICU. Intensive care practitioners should be aware of such risk and receive routine screening for tuberculosis infection.

OS06: CLINICAL RESPIRATORY MEDICINE 2

OS031

POINT-OF-CARE DISCRIMINATION OF EXUDATIVE AND TRANSUDATIVE PLEURAL EFFUSIONS IN THE EMERGENCY DEPARTMENT

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Background and Objective The ability of reagent strips to distinguish exudative or transudative pleural effusions in primary care of the emergency department has not yet to be evaluated. The purpose of the study was to investigate the value of the strips in distinguishing transudative or exudative, pleural effusion, and also in discrimination of infectious or noninfectious in the exudative pleural effusion.
Methods A chest radiograph will obtained to make sure the diagnosis. Each of the sample was collected and the strip was inserted into the reader machine (Clinitek Status, Bayer Diagnostics); after 2 minutes, this reader will shown the possible results.
Results Totally, 200 patients were enrolled into this study. The cost of a strip was USD0.67 per test compared to USD15.8 per test for a conventional test. Reagent strip with protein greater than 3 was significantly differentiated exudates and transudates with the Sn, 94%; Sp, 65%; PPV, 83%; NPV, 72%; OR, 4.67; and 95% CI, 1.45–19, p = 0.01). A leukocyte esterase greter than 2 with the Sn, 81%; Sp, 69%; PPV, 72%; NPV, 89%; OR, 3.47; and 95% CI, 1.23–15, p = 0.02) was significantly predictive in the pleural infection.
Conclusion The results suggest that the reagent strips not only speed up to distinguish exudative or transudative pleural effusions in the emergency department, but also a rapid tool in the discrimination of infectious exudative effusions. A good discriminatory properties were found in this simple and cheaper test.

OS032

PULMONARY COMPLICATIONS AS AN INDEPENDENT PROGNOSTIC FACTOR IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES

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Background and Aim of Study Patients with hematologic malignancies may complicate with various pulmonary diseases, such as infections, lung involvement of hematologic malignancies, alveolar hemorrhage, pulmonary edema, drug-induced pneumonitis, and so on. To identify the incidence, risk factors of pulmonary complications, and the influence of pulmonary complications on in-hospital mortality of hematologic malignancies.
Methods Medical records and chest computed tomography of patients, who were admitted to our university hospital since Jan 2010 to Dec 2011 for the treatment of hematologic malignancies, were reviewed and analyzed retrospectively.
Results Two hundred seventy six patients were admitted mainly for chemotherapy of malignant lymphoma (58.3%), leukemia (22.1%), or multiple myeloma (19.6%). Fifty eight patients (21.0%) had underlying pulmonary comorbidities, mostly COPD (n = 25). Eighty five patients (30.8%) suffered from pulmonary complications. Pulmonary complications developed higher in current or ex-smokers than non-smokers. Nineteen patients (6.9%) died from pulmonary complications (pneumonia 9 cases, acute respiratory distress syndrome 6 cases, alveolar hemorrhage 3 cases, acute exacerbation of interstitial pneumonia 1 case). Underlying pulmonary comorbidities was not associated with survival, however, the development of pulmonary complications was associated with higher in-hospital mortality (31.8% vs 9.9%). Multivariate analysis revealed old age and the development of pulmonary complications as independent poor prognostic factors during the treatment of hematologic malignancies.
Conclusion Smoking history was related to the development of pulmonary complications. Pulmonary complication is an independent prognostic factor during the treatment of hematologic malignancies.

OS033

COMPARISON OF CORB-65 AND CURB-65 AS A PROGNOSTIC SCORING SYSTEM FOR ADULT PATIENTS WITH PNEUMONIA

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Background and Aim of Study CURB-65 is a well known prognostic score for patients with community acquired pneumonia (CAP). Measurement of urea takes longer time and needs more laboratory resource than measurement of peripheral oxygen saturation (SpO2) with fingertip pulse oxymeter. We compared the performance of CURB-65 and CORB-65 (with SpO2 as an exchange for urea) in predicting the mortality of adult patients with CAP in Cipto Mangunkusumo Hospital (CMH), a tertiary referral center in Indonesia.
Methods A prospective cohort study was performed on adult patients with CAP in Emergency Department (ED) of CMH between October and December 2012. Age, blood pressure, respiratory rate, level of conciousness, peripheral oxygen saturation, and blood sample for urea were obtained at admission. Confusion, urea blood level above 7 mmol/L, respiratory rate above 30 per minute, diastolic blood pressure below 60 mmHg or systolic blood pressure below 90 mmHg, age above 65 year-old were given 1 point in CURB-65 (SpO2 below 92% was given 1 point in CORB-65). The outcome was 30-day mortality. Calibration was evaluated with Hosmer-Lemeshow test. Discrimination was evaluated with area under the receiver operating characteristic curve (AUC).
Results 30-day mortality was observed in 73 (32.0%) from 228 patients. Hosmer-Lemeshow test showed a good calibration of CORB-65 ($P = 0.159$) and CURB-65 ($P = 0.041$). The AUC of CORB-65 and CURB-65 were 0.76 (95% CI 0.685 to 0.825) and 0.77 (95% CI 0.706 to 0.832), respectively.
Conclusions CORB-65 showed a better calibration than CURB-65 and both score demonstrated similar discrimination capability. Given the rapid and ease of SpO2 measurement, CORB-65 can be considered as a prognostic scoring system for adult patients with CAP. Nevertheless, further validation of this new score is still needed with larger sample size.
Key Words Comunity acquired pneumonia, prognostic scoring system.

OS034

HUGOS SCORE: A NEW PROPOSED PROGNOSTIC SCORE FOR ADULT PATIENTS WITH PNEUMONIA

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Background and Aim of Study Cipto Mangunkusumo Hospital (CMH) is a tertiary referral hospital in Indonesia where most of the patients come with multiple and complicated diagnosis. For this reason, many of our patients with community acquired pneumonia (CAP) cannot be predicted with CURB-65 prognostic score. The original study of CURB-65 excluded patients with malignancies, immunocompromised, tuberculosis, and terminal events. Our previous study showed that Heart rate above 110 beat per minute, Urea blood level above 60 mg/dL, Glasgow coma scale below 12, peripheral Oxygen saturation below 92% and the presence of Sepsis were the independent predictors for mortality in our setting. We compared this new prognostic score (HUGOS) and CURB-65 in predicting the mortality of adult patients with pneumonia in our setting.
Methods We performed a prospective cohort study on all adult patients with CAP in Emergency Departmentt of CMH between October and December 2012. Variables in HUGOS and CURB-65 were obtained at admission. We assigned 1 point for each variable found in HUGOS score that we mentioned above. The outcome was 30-day mortality. Calibration was evaluated with Hosmer-Lemeshow test. Discrimination was evaluated with area under the receiver operating characteristic curve (AUC).
Results Mortality in 30 days was observed in 73 (32.0%) from 228 patients. HUGOS score showed a better calibration than CURB-65 (Hosmer-Lemeshow test $p = 0.975$ and $p = 0.041$, respectively). The AUC of HUGOS and CURB-65 were 0.79 (95% CI 0.726 to 0.845) and 0.77 (95% CI 0.706 to 0.832), respectively.
Conclusions HUGOS score showed a better calibration than CURB-65 in our setting. Both scores demonstrated equal discrimination in predicting the mortality of adult patient with CAP who also has multiple and complicated diagnosis. Nevertheless, further validation of HUGOS score with larger sample size is still needed.
Key Words Pneumonia, prognostic score.

OS035

CLINICAL FEATURES AND GREMLIN FLCN MUTATIONS IN THE 152 UNRELATED FAMILIES WITH BIRT-HOGG-DUBÉ SYNDROME

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Background and Aim of Study Birt-Hogg-Dubé syndrome (BHDS), a rare inherited autosomal genodermatosis first recognized in 1977, is characterized by fibrofolliculomas of the skin, an increased risk of renal tumors and multiple lung cysts with spontaneous pneumothorax. The objectives of our study were to investigate clinical features of BHDS whose pulmonary manifestations prompted *FLCN* genetic testing for the diagnosis of BHDS and their germline *FLCN* mutations.
Methods and Results We reviewed clinical pictures and the results of *FLCN* genetic testing of the probands of 152 unrelated families with BHDS. Pneumothorax episode led to FLCN genetic testing under the suspicion of BHDS in 144 probands while multiple lung cysts on chest CT prompted in 8 probands. Germline *FLCN* mutations identified were distributed throughout the entire exons, but frequently demonstrated in the exons 11, 12, and 13 (58.6%). Skin manifestation was identified in 27% of probands while renal tumors only in 3.9% of probands. Family history of pneumothorax was revealed in 64.5%, that of skin manifestation in 15.1% and that of renal tumor in 5.3%. The first episode of pneumothorax occurred at the age of 33.8 ± 13.2 years. A total of 530 episodes of pneumothorax was noted in the entire study population. Pneumothorax occurred most frequently between the late 20s and early 30s. A bilateral and simultaneous pneumothorax episode was demonstrated in 12.5% of the probands.
Results In the cohort of BHDS whose pulmonary manifestation prompted the diagnosis, the frequencies of skin and renal manifestation were low. In this clinical setting, family history of pneumothorax is common and a bilateral and simultaneous episode of pneumothorax may develop frequently.

OS036

CORRELATION OF EXHALED NITRIC OXIDE, NASAL NITRIC OXIDE AND ATOPIC STATUS IN BRONCHIAL ASTHMA AND ALLERGIC RHINITIS: AN INDIAN EXPERIENCE

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Background and Objective Exhaled nitric oxide (FE_{NO}) and nasal nitric oxide (n NO) measurement is an area of ongoing research in the study of airway inflammation. The atopic status is known to influence the levels of FE_{NO} and n NO. This study was undertaken to study the relationship between the noninvasive methods of nitric oxide measurements in bronchial asthma and allergic rhinitis and their correlation with atopic profile of Indian population.
Methods Ninety subjects were recruited for the study comprising 25 each of bronchial asthma (BA), allergic rhinitis (AR), bronchial asthma with allergic rhinitis (BA-AR) and 15 healthy controls. These were assessed for atopy and exhaled breath analysis of nitric oxide. The measurements of FE_{NO} and n NO levels was done using NIOX chemiluminescence analyzer. Atopy was assessed by skin prick testing (SPT) against 58 common aero-allergens and subjects with atleast 1 positive SPT were labeled as atopic.
Results The FE_{NO} levels in BA-AR (41.44 ± 29.9 ppb) and BA (34.96 ± 17.2 ppb) groups were higher in comparison to control (12.73 ± 7.8 ppb) ($p < 0.05$) and AR group (16.40 ± 10.3 ppb) ($p < 0.05$). The AR (271.44 ± 120.3 ppb) and BA-AR (336.42 ± 124.6 ppb) groups had higher n NO levels compared to control group (114.50 ± 76.0 ppb) ($p < 0.05$) and BA group (100.58 ± 111.2 ppb) ($p < 0.05$). The increasing FE_{NO} levels significantly correlated with the increase in number of allergen sensitization in patients suffering from BA-AR ($r = 6.856$; $p < 0.05$). However, the BA group showed a weaker positive correlation ($p = 0.07$).
Conclusion FE_{NO} is a non-invasive marker of airway inflammation. Also, FE_{NO} levels correlate with presence and degree of atopy in BA and AR. Simultaneously, n NO could be a surrogate marker of rhinitis.

OS07: ASTHMA 1

OS037

THE EFFECTS OF AN ARG16GLY ADRB2 POLYMORPHISM ON RESPONSES TO SALMETEROL OR MONTELUKAST IN JAPANESE PATIENTS WITH MILD PERSISTENT ASTHMA

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Long-acting β2-agonists (LABAs) and leukotriene receptor antagonists (LTRAs) are two principle agents that can be added to inhaled corticosteroids (ICS) for patients with asthma that is not adequately controlled by ICS alone. Several studies have shown that the Arg16Gly genotype of the β2-adrenergic receptor (ADRB2) gene may influence the bronchodilator effects of β2-agonists and that subjects with Arg/Arg show deterioration in peak flow with LABA treatment. We hypothesized that differential responses to LABA or LTRA might be partly determined by the Arg16Gly polymorphism in Japanese subjects with asthma. This randomized, genotype-stratified, two-period crossover study included 80 subjects with mild to moderate asthma; 35 subjects were Arg/Arg, and 45 were Gly/Gly. Morning peak expiratory flow (PEF) was measured daily during each 16-week treatment course, and the primary study endpoint was the difference between salmeterol treatment and montelukast treatment in deltaPEF (change in PEF, L/min); this difference, calculated as deltaPEFsal-deltaPEFmon, was then assessed according to the ADRB2 genotype. Additionally, multivariate analyses were used to identify independent factors that were predictive of responses to each treatment. The mean deltaPEFsal-deltaPEFmon was 19.3 ± 46.6 (SD) among Arg/Arg asthmatics, and 16.8 ± 51.5 (SD) among Gly/Gly asthmatics, indicating that the Arg/Arg genotype did not influence the bronchodilator effect of the two agents. Multivariate analysis revealed that higher peripheral eosinophil counts were associated with better response to salmeterol ($P < 0.05$). In Japanese patients with mild to moderate asthma, the Arg16Gly genotype on the ADRB2 gene did not influence the differential bronchodilator effect of salmeterol or montelukast as an add-on therapy to ICS within 16 weeks of follow-up. Higher peripheral eosinophil counts may be associated with better responses to salmeterol in combination with ICS.

OS038

EFFICACY OF TIOTROPIUM AS ADD-ON THERAPY FOR ADULTS WITH UNCONTROLLED ASTHMA: A META-ANALYSIS

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Tiotropium, a long-acting anticholinergic used in COPD, has been shown to be potentially efficacious in patients with uncontrolled asthma.
Trials evaluating tiotropium as add-on therapy for uncontrolled asthma among patients > 18 years old, of any ethnicity or gender and without other respiratory illnesses, versus placebo or alternative controller, measuring the following outcomes – FEV1, morning and evening PEF, number of exacerbations, use of rescue medications, and quality of life – were included. After a thorough search across databases, three authors independently assessed trial eligibility and validity using predefined criteria, with disagreements resolved by consensus, after which data extraction of selected studies was performed using a customized data extraction form. Analysis was done using RevMan 5.1 software. Results were presented as mean differences, standard errors, and 95% confidence intervals, and shown as forest plots. Estimates were calculated using the inverse variance method for continuous variables and pooled using the random effects model. I-square and Chi-square tests were used to assess heterogeneity. Adverse events were reported as dichotomous variables.
Of the 19 studies retrieved, four were included, totalling 1617 participants. The tiotropium group had a significant improvement in FEV1 (95% CI, 0.14 [0.09, 0.19], $p < 0.00001$), morning PEF (95% CI, 20.03 [11.71, 28.35], $p < 0.00001$), and evening PEF (95% CI, 23.13 [15.18, 31.09], $p < 0.00001$). Moreover, there was trend towards benefit in reduction of rescue medication use and improvement in quality of life, but were not statistically significant, (95% CI, 0.12 [–0.17, 0.4], $p = 0.42$) and (95% CI, 0.1 [–0.05, 0.25], $P = 0.20$) respectively. Significant reduction ($p < 0.0001$) of exacerbations was also found in the tiotropium group. Homogeneity ($I^2 = 0\%$, $Chi^2 = 0.47–3.22$) was found across studies in all outcomes.
Tiotropium is associated with a significant improvement in pulmonary function among patients with uncontrolled asthma, with possible reduction in rescue medication use and improvement of quality of life.

OS039

HIGH ASTHMA PREVALENCE IN SCHOOLCHILDREN FROM METRO ANTANANARIVO (MADAGASCAR): THE INFLUENCE OF THE GENETIC LINK TO POLYNESIA?

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Asthma seems to be an underestimated disease for many African countries. We performed a cross-sectional study in Antananarivo, Madagascar's capital, investigating the prevalence of asthma in schoolchildren. They belong to the population of the Merina people which live in the highlands of Madagascar, are of Polynesian descent and speak an Austronesian language.
As part of the VAVANY-study, which included a questionnaire and lung function for 1236 schoolchildren, we consecutively collected data from 111 children aged 7–15 years from two private schools in Metro Antananarivo using spirometry with Bronchodilator Responsiveness (BDR) and a survey based on the International Study of Asthma and Allergies in Childhood (ISAAC) – study questionnaire.
Median age of children under study, 57% of which were male, was 10.4 years (SD 1.6). As expected in light of growing poverty, we found BMIs to be generally low with a mean BMI being 15.6 (SD 3.4).
Asthma point prevalence, defined on clinical base as a change in FEV1 in the BDR > 12%, was found to be 9% for the two schools. We established a negative correlation between wheezing and the number of older siblings (odds ratio 0.76) through an ISAAC questionnaire for all children (n = 1236). This trend could be demonstrated in the subgroup as well but didn't reach significance due to the small group size. All other factors were without any influence on schoolchildren with or without asthma: gender, BMI, lung volumes, smoking at home, means of cooking.
Asthma is a substantial chronic health problem in schoolchildren living in Antananarivo. The clinical data in this subgroup confirmed the trend already demonstrated in the VAVANY-study through questionnaire that the number of older siblings has an influence on the prevalence of asthma. Whether this high rate is partly due to the Southeast Asian Island genetic background still has to be proven.

OS040

FACTORS ASSOCIATED WITH UNCONTROLLED SEVERE ASTHMA IN PATIENTS WITH ASPIRIN-EXACERBATED RESPIRATORY DISEASE

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Background Aspirin intolerance is an important factor for severe asthma, but some of the patients with aspirin-exacerbated respiratory disease (AERD) have mild asthma. There have been no studies that clarified the factors for asthma severity and heterogeneities of asthma phenotypes according to the clinical characteristics of AERD patients.
Objective We attempted to identify the factors for severe asthma in AERD patients and novel AERD phenotypes.
Methods This study included 102 AERD patients, who were classified into "controlled mild-to-severe" AERD and "uncontrolled severe" AERD. We explored the risk factors for asthma severity in AERD patients by multivariate logistic regression analysis. Cluster analysis was also performed on 75 AERD patients.
Results By multiple regression analysis, age (at 10-year interval) (OR, 1.5; 95% CI, 1.0–2.2), nonatopy (OR, 3.7; 95% CI, 1.2–11.5), peripheral eosinophil count (OR, 8.0; 95% CI, 1.7–36.8), and U-LTE4 concentration (OR, 13.3; 95% CI, 3.7–48.5) were found to be strong independent predictors of uncontrolled severe asthma in AERD patients. Three independent clusters were identified in cluster analysis. The patients in cluster 2 suffered from most severe asthma. Most of the patients in cluster 2 were female and showed middle age at onset of asthma and a lowest frequency of allergic rhinitis and/or urticaria.
Conclusion Cysteinyl-leukotriene (cysLT) overproduction, eosinophilic inflammation, non-atopy and old age were found to be risk factors for asthma severity in AERD patients. Furthermore, patients could be classified into three unique clusters, which supported the clinical heterogeneity in AERD patients.

OS041

COMPARISON OF DISTAL AIRWAY NITRIC OXIDE DERIVED BY 2 CM AND TMAD AS AN INDEX OF INOS MRNA EXPRESSION

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Backgrounds and Aim of Study It is already reported that fraction of exhaled nitric oxide (FeNO) is an indicator of asthmatic airway inflammation. Tsoukias et al. established that the measuring of distal airway NO (Calv) based on two compartments model (2 CM) is useful for evaluation of distal airway inflammation. On the other hands, Condorelli et al. established Trumpet model with axial diffusion (TMAD) that considered both the trumpet geometry and gas-phase axial diffusion of NO. TMAD is recognized to provide a more accurate estimation of NO concentration from 17th generation of bronchus to alveoli (CANO). Between 2 CM and TMAD, we examined which is a good marker of distal airway inflammation using iNOS mRNA expression in distal bronchial epithelial cells (dBECs). To compare 2 CM and TMAD as an index of distal airway inflammation by means of iNOS mRNA expression of distal BECs in asthmatic subjects.
Methods Distal BECs were isolated from generation of 10th to 15th bronchi with bronchial brushings from 13 of mild-moderate steroid naive bronchial asthma (snBA), 9 of steroid treated BA (stBA), and 23 of disease control subjects. Total RNA was extracted from dBECs and iNOS mRNA was measured by qRT-PCR. We also measured Calv and CANO at multi flow rates and derived by 2 CM and TMAD. We studied correlation between Calv or CANO and iNOS mRNA expression in dBECs. HE stain and immunohistochemistry (IHC) for TBLB specimens were performed.
Results Calv, CANO and iNOS mRNA expression were significantly higher in snBA. Calv was significantly correlated with iNOS mRNA expression, but CANO was not. TBLB revealed abundant inflammation in bronchi but not in alveoli. Furthermore IHC revealed iNOS protein expression in dBECs, but not in alveolar epithelial cells.
Conclusion These findings suggest that 2 CM is more useful for distal airway inflammation in asthma.

OS042

ASSOCIATION STUDIES OF SNPS IN ASTHMA CANDIDATE GENES IN PAKISTANI ASTHMATIC CASES AND CONTROLS

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Asthma is a chronic disease of the airways. Its symptoms are caused by inflammation and constriction of the bronchial muscles. The prevalence of asthma in Pakistani adults is approximately 10%, but higher (16.3%) in children. The present study was conducted to determine association of 33 SNPs in 21 candidate genes with asthma in Pakistani population. Genes and SNPs in these genes that were previously associated with asthma in different populations were selected for the present study to assess their role in asthma in the Pakistani population. We conducted this study in 333 asthmatic cases and 220 healthy controls, recruited from outpatient clinics in Islamabad, Rawalpindi and Lahore Pakistan. Genomic DNA was extracted from blood lymphocytes using a phenol chloroform extraction protocol. Genotyping was performed using the Sequenom Mass ARRAY iPLEX platform (26 SNPs) and TaqMan assay (7 SNPs). The minor allele at two of the SNPs showed modest evidence of association with protection from asthma, rs1131882 in the *TBXA2R* gene (OR 0.73, 95% CI 0.52–1.01, P = 0.05) and rs2280091 in the ADAM33 gene (OR 0.69, 95% CI 0.50–0.97, P = 0.03). The minor allele at two additional SNPs showed modest evidence of association with risk for asthma, rs1800896 in the *IL10* gene (OR 1.38, 95% CI 1.01–1.88, P = 0.04) and rs1800925 in the *IL13* gene (OR 1.45, 95% CI 1.04–2.02, P = 0.03). In conclusion, the A allele in rs1131882 (*TBXA2R*) and G allele in rs2280091 (ADAM33) may be protective for asthma, whereas the G allele in rs1800896 (*IL10*) and the T allele in rs1800925 (*IL-13*) may be important in susceptibility to asthma in the Pakistani population. Further studies will be needed to replicate these associations in the Pakistani population and then to elucidate the mechanism for these observations.

OS08: CRITICAL CARE MEDICINE 1

OS043

ACUTE PRESENTING SYMPTOMS, CLINICAL PROFILES AND OUTCOME OF ADULT MEDICAL PATIENTS IN EMERGENCY ROOM OF CIPTO MANGUNKUSUMO HOSPITAL

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Background and Aim of the Study Cipto Mangunkusumo Hospital (CMH) is a national referral center in Indonesia. Most of the patients come with multiple and complicated diagnosis. The aim of the study was to describe clinical profiles and in-hospital prognosis in adult medical patients who admitted to Emergency Room of CMH.
Methods We performed a prospective cohort study on adult medical patients in Emergency Department (ED) of CMH between October and December 2012. Acute presenting symptoms and diagnosis were made by resident of Internal Medicine incharge. Outcome was assessed when the patients were discharge from the hospital (alive or dead).
Results A total of 815 nonsurgical patients attended during the study (51.7% was male). Mean age was 47.3 (SD 15.2) year old, mean arterial pressure was 91.7 (22.0) mmHg, mean heart rate was 101.3 (SD 23.4) bpm, mean respiratory rate was 25.0 (SD 6.8) bpm, mean body temperature was 36.9 (SD 1.1) oC, mean peripheral O2 saturation 96.2 (SD 4.2) %, median Glasgow coma scale was 15 (3 to 15). The frequent chief complaints found were shortness of breath (25.1%), general weakness (16.2%), and loss of conciousness (12.7%). The frequent diagnosis found were pneumonia (35.6%), dyspepsia (33.2%), hypertension (28.5%), renal failure (27.7%), malignancy (24.7%), sepsis (23.1%), anemia (22.0%), and diabetes mellitus (17.3%). Median length of stay was 5 (0 to 63) days. Mortality was observed in 145 patients (17.8%). The causes of death were irreversible septic shock (53.8%), respiratory failure (24.8%), cardiac arrest (11.0%), cardiogenic shock (6.9%), and pulmonary embolism (3.4%).
Conclusions Clinical profile and outcome of adult medical emergency patients in Cipto Mangunkusumo Hospital differs from other hospital in Indonesia. As a national referral center, a long length of stay and high mortality was observed.

OS044

[redacted]

OS045

EFFICACY AND SAFETY OF DEXMEDETOMIDINE FOR SEDATING PATIENTS WITH ACUTE EXACERBATION OF CHRONIC RESPIRATORY FAILURE DURING NON-INVASIVE VENTILATION

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Background and Aim of Study Patients developing acute exacerbation of chronic respiratory failure (AE-CRF) such as chronic obstructive pulmonary disease (COPD) or tuberculosis sequelae may need non-invasive positive pressure ventilation (NPPV). However, they often denied NPPV for its discomfort and/or due to delirium. Dexmedetomidine (DEX), commonly used to sedate patients with endotracheal intubation, is an $\alpha 2$ adrenoreceptor agonist featuring mild sedation without respiratory depression. Since there are few studies examining safety and efficacy of DEX for NPPV, we investigated whether DEX was also useful to sedate patients with AE-CRF in need of NPPV.
Methods DEX was administered to ten patients under the NPPV in their clinical course of AE-CRF. We retrospectively assessed Richmond agitation sedation scale (RASS), adverse effects, blood gas analysis, before and 24-hour after initiation of DEX.
Results The eight male and two female patients with average age of 76.6 (62–92) years were examined. Their underlying diseases are tuberculosis sequelae (n = 3), interstitial pneumonia (n = 2), pulmonary aspergillosis (n = 2), COPD (n = 1), etc. The RASS score was decreased after initiation of DEX. As for adverse effects, mild hypotension occurred in four patients, and controllable oversedation in one patient. DEX didn't deteriorate respiratory conditions in the others. Case 1. 70 year-old man; He had chronic respiratory failure due to tuberculosis sequelae. He was admitted due to AE-CRF. His arterial blood gas revealed pH 7.079, partial pressure of carbon dioxide and oxygen 167.8 mmHg and 91.0 mmHg on 15 L/min oxygen inhalation. Although NPPV was immediately initiated, he couldn't tolerate NPPV due to delirium. DEX was, therefore, initiated on 0.2 μg/kg/hour, to decrease RASS score from +1 to –2. His blood pressure and heart rate slightly decreased. His respiratory conditions were improved.
Conclusion This study indicated that dexmedetomidine was effective and safe for patients with AE-CRF in need of NPPV and may be a unique option for sedating such patients.

OS046

PREOPERATIVE RISK SCORING SYSTEM FOR INFANTS AND YOUNG CHILDREN UNDERGOING CARDIOTHORACIC SURGERY (PREDICT)

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Background Predicting the risks of developing postoperative pulmonary complications in infants and young children undergoing cardiothoracic surgery has always been a challenge. This study proposed a risk stratification method for postoperative pulmonary complications among children 6 years old and below who will undergo cardiothoracic surgery.
Methodology We prospectively followed 286 children, aged 6 years old and below, who underwent cardiothoracic surgery from September-March 2013. Preoperative risk factors included age, gender, weight, cardiac diagnosis, type of surgery, history of respiratory tract infection and reactive airways disease and the need for preoperative mechanical ventilation. Laboratory data included complete blood count, blood gas, serum albumin, bleeding parameters,2D echocardiogram and tidal breathing analysis. ASA and RACHS-1 scoring were also included. Primary outcome measure is postoperative pulmonary complication and secondary outcome measures included duration of postop mechanical ventilation, recovery room and PICU stay, overall length of post-operative hospital stay and death.
Results Two hundred eighteen (76%) out of the 286 children developed postoperative pulmonary complications, with atelectasis, pneumonia and air leaks as the most frequent complication noted. Among the clinical variables analyzed, 14 variables were independent predictors of postoperative pulmonary complications: age <28 days old, weight of <8.85 kg, history of RTI and reactive airways disease, use of mechanical ventilation preop, pulmonary hypertension, pH < 7.35 and >7.45, pO2 <80, wbc < 5 and >10, neutrophils >39.5, lymphocytes <47.5, serum albumin <32 g/L, high ASA and RACHS-1 score. ROC analysis derived the best minimum cut off score of 7 points, with a lowest and highest achievable score of 1 and 20 respectively and with a sensitivity of 86.7% and specificity 55.9%.
Conclusion The use of this scoring system will help us screen, categorize, and risk stratify children 6 year old and below before subjecting them to surgery.

OS047

NON-INVASIVE VENTILATION FOR ACUTE RESPIRATORY FAILURE: ONE YEAR OBSERVATIONAL STUDY

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Introduction Noninvasive mechanical ventilation (NIV) is a front-line therapy for the management of acute respiratory failure (ARF) due to various origins. However there is less data to compare about each disease directly in a single center. Now, we tried to evaluate the effect of NIV in patients with ARF and difference about each basic disease.
Methods This study is observational study during one year in a single center. We identified patients with ARF who were treated with NIV in the Department of Respiratory Medicine and Allergy, Tosei General Hospital between January and December 2011. Clinical characteristics were collected from patient's record. We evaluated success rate of NIV and 28th day mortality. Furthermore, we compared about each basic disease. NIV success was defined as a leave from NIV on survival without tracheal intubation or barotrauma.
Results 135 patients were included in this study (Age: 74.2 ± 9.5 y.o.). 72 patients had ARF without hypercapnea (ARDS: 28 (Berlin stage: severe 1, moderate 18, mild 9), Interstitial lung disease (ILD): 37, other 7) and 63 Patients had ARF with hypercapnea (acute exacerbation of COPD: 26, Late sequelae of pulmonary tuberculosis: 13, bronchial asthma 7, other 17). Overall success rate of NIV was 82.2%. 28th day mortality and hospital mortality was 18.5% and 27.4% respectively. There was no difference in the success rate of NIV between respective basic diseases (ARDS 82.1%, ILD 78.4%, COPD 96.2%). However, hospital mortality in patients with ILD was higher than other disease. (ARDS 14.3%, ILD 40.5%, COPD 26.9%).
Conclusion This single center observational study showed that the success rate of NIV for ARF was no difference between each disease. However, it was suggested that long term mortality was contributed by the each basic diseases.

OS048

OS09: CELL AND MOLECULAR BIOLOGY

OS049

CAVEOLIN-1 CONTRIBUTES TO CIGARETTE SMOKE EXTRACT (CSE)-INDUCED MUC5AC HYPER-SECRETION IN HUMAN BRONCHIAL EPITHELIAL HBE16 CELLS

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Background and Aim of Study Airway mucus hyper-secretion is a major regulator for the pathological progress in chronic obstructive pulmonary disease (COPD) and MUC5AC is the chief secretory mucin in the airway. Caveolin-1 is a membrane marker protein of caveolae, which involved as the hub of several cell signaling pathways. Caveolin-1 was recently considered to be a significant modulator of the development of airway inflammation. In this study we aim to investigate the role of caveolin-1 in cigarette smoke extract (CSE)-induced MUC5AC hyper-secretion, and explore the underlying mechanism.
Methods The human bronchial epithelial HBE16 cells were exposed to CSE to establish mucus hyper-secretion model in vitro. HBE16 cells were transfected with caveolin-1 cDNA over-expressed plasmid or pretreated by Methyl-β-cyclodextrin (MβCD) 10 μM for 30 mins before exposure to CSE. The level of MUC5AC mRNA and protein in each were detected by RT-PCR and ELISA respectively, and the expression caveolin-1 protein was measured by Western Blotting.
Results Mucus hyper-secretion model was successfully established by CSE. 10% CSE treatment for 24 h significantly increased MUC5AC mRNA and protein in dose- and time-dependent ways ($p < 0.05$). There was no effect of CSE on the expression of caveolin-1 protein ($p > 0.05$). The caveolin-1 cDNA plasmid transfection increased the expression of caveolin-1 and CSE-induced MUC5AC secretion; Moreover, MβCD down-regulated the expression of caveolin-1 and MUC5AC secretion induced by CSE ($p < 0.05$).
Conclusion Based on our research, we can confirm that caveolin-1 can promote the MUC5AC secretion induced by CSE.

OS050

A CRITICAL ROLE OF PHOSPHORYLATION OF THE PTEN C-TERMINUS IN TGFB-INDUCED B-CATENIN TRANSLOCATION INTO CYTOPLASM DURING EMT IN EPITHELIAL CELLS

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Current evidence suggests that the pathogenesis of pulmonary fibrosis might involve the recruitment of endothelial and alveolar/epithelial cell (AEC)-derived fibroblasts through Epithelial/Endothelial-Mesenchymal Transition (EMT), as well as bone marrow (BM)-derived fibroblasts. Fibrotic lesions contribute the development of new fibrosis lesion as tissue microenvironment through the supply of TGFβ stimulation. TGFβ-induced translocation of β-catenin from E-cadherin complexes into cytoplasm is involved in the transcription of EMT target genes. Although PTEN (phosphatase and tensin homologue deleted from chromosome 10) exerts phosphatase activity by binding to E-cadherin complexes via β-catenin, recent studies suggested that phosphorylation of the PTEN C-terminus tail might cause loss of the PTEN phosphatase activity. Nevertheless, whether TGFβ can modulate the β-catenin translocation and PTEN phosphatase activity via phosphorylation of the PTEN C-terminus remains elusive. Furthermore, the role of phosphorylation of the PTEN C-terminus in TGFβ-induced malignant phenotypes has not been evaluated. To investigate whether modulation of phosphorylation of the PTEN C-terminus could regulate the malignant phenotypes, we established epithelial cells with mutation of phosphorylation sites in the PTEN C-terminus. TGFβ yielded a 60% increase in the p-PTEN/PTEN ratio. Expression of a PTEN protein with mutation of phosphorylation sites in its C-terminus (PTEN4A) repressed TGFβ-induced EMT and cell motility through complete blockade of β-catenin translocation into cytoplasm, besides the inhibitory effect of PTEN4A on TGFβ-induced activation of smad-independent signaling pathways. Thus, this exploration leads to illuminate the mechanisms, by which lung fibrosis develops.

OS051

OS052

THE INVOLVEMENT OF IL-8 AND LEPTIN IN REGULATION OF RSV INFECTED BRONCHIAL EPITHELIAL CELLS ON TH SUBSETS DRIFT

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Objectives The mechanisms of Respiratory syncytial virus (RSV)-induced asthma are incompletely understood. Asthma is characterized by help T (Th) subsets drift. More, respiratory epithelium is the main and first target of RSV. In our previous study, RSV-infected human bronchial epithelial cells (HBECs) can induce Th subsets drift. So, in this study, we intend to explore why Th subsets drift can be caused by RSV-infected HBECs.
Methods First, analyze the differences of mRNA expression between normal and RSV-infected HBECs by micro-array and pick out the obviously up-regulated genes 1 and 2. Then identify the expression of genes 1 and 2 by real-time PCR and ELISA. Second, lymphocytes isolated from peripheral blood were treated by human recombinant products encoded by gene 1 and 2, the distribution of Th subsets and protein level of extra-cellular signal-regulated kinase1/2 (ERK1/2) and phosphorylated ERK1/2 in lymphocytes were detected individually by flow cytometry and western blotting, immuno-fluorescence.
Results Micro-array results showed that, compared with normal HBECs, there were 349 up-regulated and 154 down-regulated genes in RSV-infected cells. Among them, the expression of LEP and IL8 were obviously increased. And the expression of IL8 and LEP in HBECs was significantly up-regulated after RSV infection also tested by real-time PCR. The levels of their encoded proteins interleukin (IL-8) and leptin in supernatant from RSV-infected group were higher than control. After lymphocytes were treated by IL-8 and leptin, we found both IL-8 and leptin contributed to differentiation of Th2 and Th17 subsets and ERK1/2 phosphorylation. But they had no effect on Treg differentiation.
Conclusion There were significant changes of mRNA expression in RSV-infected HBECs. IL-8 and leptin over-secreted by RSV infected HBECs may promote differentiation of Th2 and Th17 subsets by activating the signal molecule ERK1/2.

OS053

ABSTRACT WITHDRAWN

OS054

IDENTIFICATION OF A FACTOR RESPONSIBLE FOR BRONCHIOLAR PROGENITOR CELL KINETICS

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Background and Aim of Study Bronchiolar progenitor (BP) cells are attracting research attention as a potential therapeutic tool in regenerative medicine, but the cellular biology remains elusive.
Method To gain the insight, we performed microarray analysis by using Agilent microarray system to analyze the gene expression pattern of BP cells that were sorted as the surface phenotype of $CD45^{neg}CD31^{neg}CD34^{neg}Sca1^{low}$auto-$fluorescence^{low}$ from the mouse lung.
Result Among 36391 genes evaluated, we found 16918 genes representing significant differences between BP cells and Clara cells; the expression of 6172 genes and 3587 genes were upregulated and downregulated, respectively, by more than 2-fold in BP cells as compared with Clara cells. We identified the "*Bronchiolar progenitor factor 1(Bpf1)*" gene whose expression was significantly upregulated in BP cells as compared with Clara cells (gScale: 21364 versus 11841, $p < 0.05$). In BPF1-deficient mice, the number of BP cells significantly increased as compared with wild-type mice (43834 versus 23485 cells/mouse, $p < 0.05$). When exposed intraperitoneally to 200 mg/kg naphthalene as a lung inflammatory model, BPF1-deficient mice revealed reduced inflammation as compared with wild-type mice (total BAL cell number: 1.9×10^5 versus 6.8×10^5 cells/mouse, $p < 0.005$).
Conclusion BPF1 has a pivotal role for the cellular kinetics of BP cells, which may be useful to ameliorate lung inflammation.

OS10: ASTHMA 2

OS055

OBSERVATION OF AUTOPHAGY IN ALLERGIC ASTHMA MICE MODELS AND THE EFFECTS OF NERVE GROWTH FACTOR ANTIBODY INTERVENTION

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Background and Aim of Study Nerve growth factor can promote dendritic cell maturation and function. Autophagy-mediated DC activation is essential for innate cytokine production and Antigen presenting cells (APC) function. This study was aimed at determining the effect of nerve growth factor antibody on autophagy of dendritic cells in mice.
Methods BALBc mice were sensitized with ovalbumin and treated with anti-NGF. the control group treated with saline accordingly. At 1 day after the last challenge, their airway responsiveness and inflammation were examined and the levels of autophagy of dendritic cells in the lungs were determined, The expression of MHC-II molecule and co-stimulus molecule CD80, CD86 and CD40L were mesured, and the levels of Th1 and Th2 cells were determined.
Results OVA challenge induced severe inflammation and airway resistance, higher levels of autophagy, significantly high expression of CD80, CD86, CD40L and MHC II, and decreased Th1 and increase Th2 cells responses. Treatment with anti-NGF antibody significantly reduced inflammation and allergic airway resistance, inhibited autophagy, down-regulated CD80, CD86, CD40L and MHC II expression, and increased Th1 and decreased Th2 cells responses.
Conclusion anti-NGF antibody can degrade the antigen presenting function of dendritic cells by affecting autophagy of dendritic cells in the lungs of mice, resulting Th1 promoting and Th2 inhibiting response.
Key Words asthma mice; Autophagy; Nerve growth factor; Dendritic cells; Antigen presenting function; anti-NGF antibody.

OS056

PLUME CHARACTERISTICS OF FLUTICASONE PROPIONATE/FORMOTEROL PMDI COMPARED WITH FLUTICASONE PROPIONATE/SALMETEROL PMDI

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Background It has been suggested that aerosol inhaler characteristics such as fine particle size distribution, low plume velocity, and long duration of the aerosol cloud may assist coordination of inhalation with actuation, improve lung deposition, and reduce oropharyngeal deposition. This study compared 2 ICS/LABA combination HFA pMDI inhalers: fluticasone propionate/formoterol 125/5 μg (FP/FORM; *flutiform*(R)) and fluticasone propionate/salmeterol 125/50 μg (FP/SAL; *Seretide*(R) *Evohaler*(R)).
Methods Inhalers were operated according to their respective patient information leaflets, and were fired into still air. Plume data were recorded using an Oxford Lasers EnVision Pharma system with high speed CMOS camera and short-pulse laser light source. VidPIV 4.6 & EnVision 1.1.5 software was used to analyse the data and assess velocity and other characteristics of the plume at set intervals from the actuator (up to 9.5 cm which is representative of the distance from mouth to throat).
Results FP/FORM pMDI had slower maximum velocity of plume than did FP/SAL at the distances measured (table). Furthermore, the duration of plume lasted approximately 50% longer over the distance measured with FP/FORM than with FP/SAL.

FR/FORM	
Plume Duration over 95 mm (ms)	168.3
Max velocity @ 30 mm (m/s)	20.3
Max velocity @ 60 mm (m/s)	15.2
Max velocity @ 95 mm (m/s)	10.1
Plume Duration over 95 mm (ms)	114.0
FR/SAL	
Max velocity @ 30 mm (m/s)	26.5
Max velocity @ 60 mm (m/s)	21.8
Max velocity @ 95 mm (m/s)	15.6

Conclusion FP/FORM has a slower and more prolonged plume compared with FP/SAL. This may help synchronise aerosol availability and inhalation and may lead to less oropharyngeal deposition and better lung deposition.

OS057

COMPARISON OF THE FINE PARTICLE FRACTION OF FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE COMBINATION WITH OTHER COMBINATION PRODUCTS

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Background and Aim of Study A combination of the inhaled corticosteroid, fluticasone propionate, and the long-acting β_2-agonist, formoterol fumarate has been developed in an aerosol inhaler (FP/FORM). As changes in flow rate have been shown to affect the *in vitro* performance of inhalers, which could compromise *in vivo* performance, this study evaluated the effect of flow rate on fine particle fraction (FPF) and dose (FPD) of FP/FORM and three available combination products.
Methods Dose strengths used to deliver comparable treatment doses (FP/FORM, 250/10 μg; beclomethasone/formoterol (BDP/FORM) pMDI, 200/12 μg; fluticasone/salmeterol (FP/SAL) DPI, 250/50 μg; budesonide/formoterol (BUD/FORM) DPI, 400/12 μg) were compared. Aerodynamic particle size distribution was determined by Andersen Cascade Impaction at 28.3 L/min and 60 L/min flow rates with a cut-off diameter of 5.0 μM and was calculated as % of label claim.
Results FP/FORM provided a consistent and high FPF of approximately 40% for each component, with less than a 10% relative difference in the FPD emitted between flow rates. FP/FORM provided the highest FPF at both flow rates with BUD/FORM and FP/SAL delivering a FPF of less than 20% at 28.3 L/min. The FPD of all three comparator products evaluated were affected by increases in flow rate from 28.3 L/min to 60 L/min, with BUD/FORM having a ~5 fold increase in FPD between flow rates and BDP/FORM showing a 50% difference.
Conclusion The data confirm that FP/FORM emits a high FPF of approximately 40%. These data also demonstrate that FP/FORM has a higher FPF, that is less affected by changes in flow rate, than other combination products assessed.

OS058

IL-17A AND TNF-α SYNERGISTICALLY STIMULATE IL-8 PRODUCTION IN HUMAN AIRWAY EPITHELIAL CELLS

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Background Asthma is characterized by airway hyper-responsiveness and reversible airflow limitation. Airway inflammation is considered as an important underlying condition, which is usually characterized by Th2 cells and eosinophils. Recent reports, however, have suggested an involvement of neutrophilic inflammation by Th17 cells, especially in severe, refractory asthma.
Purpose We examined the ability of IL-17 to promote airway epithelial cells to IL-8 expression alone or in combination with TNF-α.
Materials and Methods We evaluated the expression of IL-8 by ELISA and real-time PCR, and investigated whether MAPK and NF-κB signaling pathway contributed to their expressions by using thier inhibitors, and measuring protein phosphorylation. Additionally, we examined the effect of anti-asthma drugs on the release of proinflammatory cytoines from the cultured cells.
Results IL-17A alone induced only a minimal effect on IL-8 expression. TNF-α showed a concentration-dependent stimulatory effect on IL-8 expression. Interestingly, IL-17A in combination with TNF-α showed a synergistic effect on IL-8, but such effect was not observed with LPS or IL-1β. This effect by TNF-α and IL-17A was significantly inhibited by MAPKs inhibitors.
Conclusions We found that IL-17A alone had a minimal enhancing effect on airway epithelial cells, whereas the combination of TNF-α and IL-17A induced a synergistic increase in the expression of IL-8. Both cytokines of IL-17A and TNF-α have shown to be expressed within the lungs of asthmatic individuals. Therefore, our findings suggest that IL-17A is thought to contribute to the pathogenesis of neutrophilic inflammation in severe persistent asthma.

OS059

OVER-EXPRESSION OF THE LTC4 SYNTHASE GENE IN MICE REPRODUCES HUMAN ASPIRIN-INDUCED ASTHMA

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Background The pathogenesis of aspirin-induced asthma (AIA) is presumed to involve the NSAID-induced abnormal metabolism of arachidonic acid, resulting in an increase in 5-LO metabolites, particularly leukotriene C(4) (LTC(4)). However, the role of LTC4 in the development of AIA has yet to be conclusively demonstrated.
Objective The aim of this study was to evaluate the contribution of the lipid product LTC4 secreted by the 5-LO pathway to the pathogenesis of AIA.
Methods To evaluate antigen-induced airway inflammation, the concentrations of T-helper type 2 cytokine in bronchoalveolar lavage fluid (BALF) obtained from LTC4 synthase-transgenic (Tg) and wild-type (WT) mice after challenge with ovalbumin were measured. Subsequently, the ex vivo and in vivo effects of the NSAID sulpyrine were investigated in these Tg and WT mice by measuring the secretion of LTC4 from sulpyrine-treated BAL cells and the levels of LTC4 in BALF following challenge with sulpyrine. Finally, the sulpyrine-induced airway response by the administration of pranlukast, an antagonist of the cysteinyl (cys)-LT1 receptor, was analysed.
Results The concentrations of IL-4, -5, and -13 in BALF from Tg mice were significantly higher than those in WT mice. In addition, sulpyrine augmented the secretion of LTC4 in BALF and by BAL cells in Tg mice, but not in WT mice. Additionally, the increased airway resistance induced by sulpyrine could be reduced by treatment with pranlukast. Furthermore, the secretion of LTC4 from mast cells, eosinophils, and macrophages was increased in the allergen-stimulated LTC4 synthase gene Tg mice, even in the absence of sulpyrine, as well as in BAL cells after sulpyrine.
Conclusion The over-expression of the LTC4 synthase in a mouse asthma model also replicates the key features of AIA. And our study supports that cys-LTs play a major role in the pathogenesis of AIA in patients with chronic asthma.

OS11: CRITICAL CARE MEDICINE 2

OS060

THROMBOCYTOPENIA AS AN INDEPENDENT PREDICTIVE FACTOR OF MORTALITY IN ICU-ADMITTED PATIENTS WITH HIGH-RISK COMMUNITY ACQUIRED PNEUMONIA

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Objective It is the primary objective of this study to determine the prevalence of thrombocytopenia in ICU-admitted patients with high-risk Community Acquired Pneumonia (CAP). Furthermore, the study aimed to evaluate the prognostic value of thrombocytopenia in these patients.
Methods This is a cross-sectional study of ICU-admitted patients in Chinese General Hospital and Medical Center for a period of 14 months (February 2012 to March 2013). The primary outcome measure was ICU mortality.
Results One hundred twenty patients were included in the study. Thrombocytopenia with platelet count below 150×10^9/L was seen in 37 (31%) patients. Platelet count was noted to be $101–149 \times 10^9$/L in 15 (12.5%) patients, $51–100 \times 10^9$/L in 10 (8.33%), $21–50 \times 10^9$/L in 7 (5.83%) patients and less than or equal 20×10^9/L in 5 (4.17%) of patients. ICU mortality rate was 44.17%. There is an apparent trend showing that the lower platelet count, the greater the mortality. In a logistic regression analysis, thrombocytopenia (less than 150×10^9/L) appeared to be an independent predictor of mortality wherein the risk is twice than that of those with normal values.
Conclusions Thrombocytopenia is only prevalent in one-third of ICU-admitted patients with high-risk CAP. The increased severity of thrombocytopenia is directly proportional to mortality. Thrombocytopenia increases the risk of dying and could be considered as an independent predictor of mortality.

OS061

INCIDENCE, ANTIBIOGRAM OF PATHOGENS ISOLATED AND CLINICAL OUTCOME OF VENTILATOR ASSOCIATED PNEUMONIA, A PROSPECTIVE COHORT STUDY

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Background Ventilator associated pneumonia (VAP) is an important cause of poor outcome in mechanically ventilated patients. The aim of this study was to find out the incidence of VAP at our institution, to evaluate the antibiotic sensitivity pattern of microorganisms isolated and to assess clinical outcome in VAP.
Methods A total of 107 patients who were not having pneumonia at presentation and who were mechanically ventilated for more than 48 hours for various indications were included in the study. APACHE II score of first day was recorded. The diagnosis of VAP was established using clinical pulmonary infection score of more than 6. Gram staining and culture sensitivity was performed on all endotracheal aspirates and antibiotics modified accordingly.
Results 30 out of 107 patients (28.03%) developed VAP. 25 patients developed late onset VAP while 5 developed early onset VAP. Most common isolates were Pseudomonas aeruginosa (9 isolates) followed by MRSA (8 isolates), Klebsiella pnueumoniae (7 isolates) and Acinetobacter baumanii (6 isolates). Klebsiella pnueumoniae and Acinetobacter baumanii were found to be most lethal. Most isolates of Klebsiella were extended spectrum Beta Lactamase producing and all Acinetobacter were carbapenem resistant. Mortality in VAP was 46.67% and correlated well with a higher mean APACHE II score of 18.3 as compared to a mortality of 28.57 in non VAP group with a low mean APACHE II score of 13.1.
Conclusion The development of VAP was associated with increased morbidity and mortality and a higher mean APACHE II score at admission. The incidence of multidrug resistant pathogens is rising and therefore it is important to identify them as this information will help in the selection of an appropriate antibiotic regimen and decrease the treatment costs and improve outcome.

OS062

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 the 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 the 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 or 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 decremental PEEP titration method. The 'only RM' group patient was put on baseline ventilator settings after manoeuvre.
Results Out of the total 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.

OS063

COMPARISON OF SERIAL RAPID SHALLOW BREATHING INDEX TO SERIAL CROP INDEX IN PREDICTION OF WEANING OUTCOME IN CRITICAL CARE PATIENTS

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Purpose To compare serial CROP and serial RSBI in predicting weaning success.
Methods This is a prospective cohort study of the Philippine Heart Center done from December 2011-November 2012. All patients > 18 yo on mechanical ventilator for >48 hours capable of being weaned. Serial RSBI and CROP was taken 30 minutes, 60 minutes and 120 minutes prior to extubation. ABG was taken at the end of each cycle. Extubation was a success if patient could sustain spontaneous breathing >48 hours.
Results Total of 61 patients 33 (54.1%) males and 28 (45.9%) females. Most common indication for intubation was ARF typeI (26%) and ARF TypeII secondary to AECOPD 16 (26%). Longest duration on ventilator was 14 days mean 6 ± 2.78. It was observed that an increasing trend of CROP predicted weaning success. Increasing values of RSBI was related to weaning failure. There were 6 patients who underwent facilitated extubation with NIV, their CROP score were noted to be low. A cut off value of both parameters noted a sensitivity of 78.6% and 72.3% for CROP < 16. RSBI value > 52 had a 71.4% sensitivity and 70.2% specificity. Areas under the curve generated by ROC yielded 0.679 ± 0.075 for RSBI and 0.735 ± 0.087 for CROP. CROP having a greater value is more predictive, thus a better parameter.
Conclusions Trends of weaning can detect deteriorating pulmonary mechanics. An increasing RSBI was noted in weaning failures. Conversely, an increasing CROP can predict weaning success. In this study a CROP value > 0.16 had a sensitivity of 78.6 and specificity of 72.3. RSBI > 52 had a 71.4 sensitivity and 70.2 specificity. CROP index having a higher sensitivity and specificity makes it a better predictor for weaning success.

OS064

EARLY PREDICTORS OF MORTALITY IN PATIENTS WITH MECHANICAL VENTILATION

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Background and Aim of Study Mechanical ventilation (MV) is one of the most essential modality that supports many critically ill patients in the intensive care unit (ICU). A high mortality rate was observed in mechanically ventilated patients. The prediction of patients outcome at initiation of MV is important in decision-making process. This study was designed to determine early predictors of mortality in patients with MV.
Methods We performed a retrospective cohort study on 242 ICU patients who used MV for more than 24 hours between January 2009 to December 2012. Data were collected at initiation of mechanical ventilation and the main outcome was all-cause mortality during ICU. We analyzed age, sepsis, hypoalbuminemia, shock, post surgical, acute kidney injury, hyperglicemia, cerebrovascular disease, malignancy, cardiac arrest, respiratory failure and APACHE II score at initiation of MV. Multivariate logistic regression analysis was performed to identify independent predictors of mortality.
Results Of the 242 patients admitted, overall mortality rate in the ICU was 45.5%. Multivariate analysis showed that APACHE II score >= 16 [OR 10.2 (95% CI 4.50–23.18), p < 0.001] was the only independent factor.
Conclusion The APACHE II score measured at initiation of MV is an early predictors of mortality in patients with MV.
Key Words Mechanical ventilator, predictors of mortality.

OS065

SERUM ALBUMIN LEVEL AS A PREDICTOR OF MORTALITY IN PATIENT WITHVENTILATOR-ASSOCIATED PNEUMONIA

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Background and Aim of the Study Ventilator-associated pneumonia (VAP) is considered as the most common nosocomial infection in the intensive care unit (ICU) with high mortality rates. Hypoalbuminemia has been recognized as poor prognostic indicator in critically ill patient but its role in patient with VAP is not fully known. The aim of this study is to evaluate the role of initial serum albumin in predicting the mortality of patient with VAP.
Methods We designed a retrospective study to analyze data from patients with VAP between 2003 ± 8211; 2012 in Cipto Mangunkusumo Hospital, a tertiary hospital in Indonesia. Patient was devided based on initial serum albumin level into: Group-1 (less than 2.7 mg/dL), Group-2 (2.7 to 3.5 mg/dL), and Group-3 (above 3.5 mg/dL). We analyzed the hazard of inhospital mortality with cox proportional hazard model.
Results Out of 196 patients evaluated in this study, 95 patients (49%) were included in Group-1, 83 patients (42.8%) in Group-2, and 16 patients (8.2%) in Group-3. Overall mortality rate was 58.2%. The hazard of in hospital mortality in Group-1 and Group-2 were 2.48 (95% CI 1.07 ± 8211; 5.74; p = 0.033) and 1.42 (95% CI 0.60 ± 8211; 3.34; p = 0.43), respectively, compared to Group-3.
Conclusion Initial serum albumin level was a good prognostic indicator of mortality in patients with VAP.

OS067

ABSTRACT WITHDRAWN

OS12: PULMONARY CIRCULATION

OS066

THREE DIMENSIONAL ECHOCARDIOGRAPHY IS USEFUL FOR ASSESSING RIGHT VENTRICULAR FUNCTION IN PATIENTS WITH PULMONARY HYPERTENSION ASSOCIATED WITH LUNG DISEASES

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Right heart catheterization is a standard procedure to evaluate pulmonary hypertension (PH). Thus, mean pulmonary artery pressure (mPAP) has been widely accepted as a physiologic maker for the diagnosis, not only in the case of idiopathic pulmonary artery hypertension (IPAH), but also in the PH associated with lung diseases (PHALD). However, mPAP often conflicts with their symptoms and cardiac function, especially in the advanced cases. The right ventricular (RV) end diastolic volume has been proposed as an alternative marker of IPAH, which predict the prognosis. However, since right ventricle is not grove shape like left ventricle, but awkward shape, it is difficult to determine the RV volume using M-mode echocardiogram. To date, cardiac MRI is an only technique to determine RV volume and function, but consumes time and cost. We tried to determine RV volume in patients with PHALD, using 3-dimensional echocardiography (3DEC), which enable non-invasive non-consuming determination of RV volume. 3DEC was carried out in 23 patients with PHALD including 13 COPD, 7 IPF, and other lung diseases. We were afraid that anatomical deformation of the lung interfered displaying the echogram. However, RV diastolic and systolic volumes determined by 3D-UCG were correlated with references determined by MRI (r = 0.877 and 0.870, respectively). Our data suggests that 3D-UCG could be a convenient technique to determine RV volume. Our next goal is to investigate whether RV function determined 3DEC in patients with PHALD could be a surrogate marker, which is associated with disease severity.

OS068

SIMPLE PREDICTION OF RIGHT VENTRICULAR EJECTION FRACTION USING TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION IN PULMONARY HYPERTENSION

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Aims The present study examined whether tricuspid annular plane systolic excursion (TAPSE) can simply predict right ventricular ejection fraction (RVEF) in patients with pulmonary hypertension (PH). The TAPSE cut-off value to predict reduced RV EF was also evaluated.
Methods and Results The association between TAPSE and cardiac magnetic resonance imaging (CMRI)-derived RVEF was examined in 53 PH patients (mean pulmonary artery pressure 39 ± 11). The accuracy of the prediction equation to calculate RVEF using TAPSE was also evaluated. In PH patients, TAPSE was strongly correlated with CMRI-derived RVEF in PH patients (r = 0.86, p ± 0.0001). We then examined the accuracy of the two equations: the original regression equation (RVEF = 2.01 × TAPSE + 0.6) and the simplified prediction equation (RV EF = 2 × TAPSE). Bland-Altman plot showed that the mean difference ± limits of agreement was 0.0 ± 10.6 for the original equation and −0.6 ± 10.6 for the simplified equation. Intraclass correlation coefficient was 0.84 for the original and 0.82 for the simplified equation. Normal RV EF was considered to be > or = 40% based on the data from 53 matched controls, and the best TAPSE cut-off value to determine reduced RV EF (± 40%) was calculated to be 19.7 mm (sensitivity 88.9%, specificity 84.6%).
Conclusion A simple equation of RV EF = 2 × TAPSE enables easy prediction of RV EF using TAPSE, an easily measurable M-mode index of echocardiography. TAPSE of 19.7 mm predicts reduced RV EF in PH patients with clinically acceptable sensitivity and specificity.

OS069

FAVORABLE EFFECT OF ORAL COMBINATION VASODILATOR THERAPY FOR TWO CASES WITH SEVERE PORTOPULMONARY HYPERTENSION

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Portopulmonary hypertension (PoPH) is defined as pulmonary arterial hypertension associated with portal hypertension, with or without advanced hepatic disease. The prognosis of PoPH is reportedly poor and medical therapeutic strategy for PoPH has not been established. We here report two cases of severe PoPH who were treated with oral combination vasodilator therapy. Case 1: A 55-year-old man was referred to our hospital in 2010 due to suspected pulmonary hypertension by echocardiography. Right heart catheterization (RHC) exhibited elevated mean pulmonary artery pressure (MPAP) of 40 mmHg, and pulmonary vascular resistance (PVR) was 510 dyn*s*cm^{-5}. He had a past history of liver cirrhosis with portal hypertension and was diagnosed with PoPH. After this, he noted a worsening of dyspnea and syncope (WHO-functional class (FC) IV), and was treated with an oral combination therapy of ambrisentan 10 mg qd and tadarafil 40 mg qd. At 6-month follow-up, WHO-FC improved to class III, MPAP improved from 55 mmHg to 33 mmHg, and PVR also decreased from 871 dyn*s*cm^{-5} to 263 dyn*s*cm^{-5}. Case 2: A 70-year-old man with cirrhosis (Child-Pugh B) was referred to our hospital due to progressive dyspnea and palpitation in Apr 2013. RHC indicated pulmonary hypertension (MPAP: 62 mmHg, PVR: 1478 dyn*s*cm^{-5}), and we diagnosed him with PoPH. Oral combination vasodilator therapy (ambrisentan 10 mg qd and tadarafil 40 mg qd) was started. In four weeks, WHO-FC improved from IV to III, BNP level decreased from 1896.7 pg/ml to 139.1 pg/ml, and tricuspid regurgitant pressure gradient also decreased from 117 mmHg to 63.6 mmHg in echocardiography. 3-month follow-up is scheduled in Oct 2013. In the presented two cases with WHO-FC IV PoPH, oral combination therapy of ambrisentan and tadarafil improved functional capacity and pulmonary hemodynamics without remarkable adverse events.

OS070

WAVE INTENSITY ANALYSIS OF THE PULMONARY CIRCULATION IN HEALTH AND DISEASE

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Background The assessment of right ventricular (RV) afterload is of fundamental importance in pulmonary arterial hypertension (PAH). Conventional haemodynamic assessment fails to account for the pulsatile component of RV afterload and wave reflections that occur in PAH. Wave Intensity Analysis (WIA) is a recently developed time-domain model that allow insights into forward and backward-travelling waves, and ventriculo-vascular interactions.
Methods Simultaneous invasive pressure and Doppler flow-velocity measurements were undertaken in Controls (n = 7) and PAH subjects (n = 6) in the lower lobe pulmonary artery. Pulmonary angiograms were performed to define vascular anatomy. WIA modelling was performed offline using custom MatLab software.
Results Controls (age 69 ± 9 yrs, 3 females) had normal pulmonary haemodynamics (mPAP = 16 ± 5 mmHg; PVR = 1.5 ± 0.7 WU) vs. PAH subjects (age 56 ± 13 yrs, 4 females) with moderate-severe disease (mPAP = 41 ± 5 mmHg; PVR = 6.4 ± 4.4 WU). Total forward compression wave intensity was higher in PAH subjects compared to controls (164.5 ± 39.7 vs. 88.3 ± 20.7 × 102 W.m^{-2}.s^{-1}, $p < 0.001$), consistent with increased RV ejection workload. Importantly, PAH subjects displayed a markedly enhanced systolic backward-travelling (reflected) compression wave (56.9 ± 14.6 vs. 10.7 ± 5.6 × 102 W.m^{-2}.s^{-1}, $p < 0.001$ vs. controls) representing 35 ± 5% of the total forward compression wave intensity. Furthermore, the backward-travelling wave arrived earlier in PAH during ventricular systole (45 ± 20 vs. 89 ± 30 ms, $p < 0.001$) due to higher wave speed from arterial stiffening (6.9 ± 1.3 vs. 2.7 ± 0.8 m.s^{-1}, $p < 0.001$). The estimated reflection site in PAH patients was 15 ± 5 cm from the measurement point.
Conclusions WIA in the pulmonary circulation is feasible and reveals important changes in PAH. In particular, markedly enhanced backward compression waves together with faster wave speeds considerably raise RV afterload, with significant implications for understanding right sided ventriculo-vascular coupling.

OS071

THE PULMONARY HYPERTENSION REGISTRY IN THE PHILIPPINES: RESULTS FROM THE PHILIPPINE HEART CENTER – CENTER FOR PULMONARY VASCULAR DISORDERS

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The Pulmonary Hypertension Registry in the Philippines was formed to determine the number of Filipino patients with pulmonary hypertension; to classify all patients based on the 2008 Dana Point Classification of Pulmonary Hypertension; to collate all diagnostic examinations and results; and, to know the management initiated among these patients. Cases with pulmonary hypertension were prospectively collected at the Center for Pulmonary Vascular Disorders, Philippine Heart Center since 2009. Data gathered were analyzed using Chi square and T-test. There were 104 patients included. 82 (78.8%) (31 ± 12) on classification 1, majority were congenital heart diseases; 6 (5.8%) (44 ± 12) on classification 2; 8 (7.7%) (49 ± 24) on classification 3; 3 (2.9%) (33 ± 9) on classification 4; and, 5 (4.8%) (45 ± 24) on classification 5. Female (76%) prevail on all groups. 100% have dyspnea and easy fatigability. 78 (73.1%) were in New York Heart Association functional class III. 57 (54.8%) have RV heave and 92 (88.5%) have accentuated pulmonic heart sound. 58 (55.8%) have right ventricular hypertrophy and 102 (98.1%) have dilated pulmonary artery segment on chest x-ray. 98 (92.3%) have sinus rhythm on electrocardiograph. Hypoxemia (70.22 ± 21.75) was present on 83 patients. PFT showed chest restriction (FVC 63 ± 17). On echocardiogram, pulmonary artery pressure using tricuspid regurgitant jet (TRJ) was 86.3 + 26.4 mmHg and 14 (13.5%) has pericardial effusion. Six minute walk test was 253 ± 55 meters. Mean pulmonary artery pressure, cardiac output, cardiac index and pulmonary vascular resistance were 67.7 ± 26.3 mmHg, 3.8 ± 1.5 L/min, 2.7 ± 1.04 L/min/m^2 and 1383 ± 915.05 dynes/cm^2, respectively, implying severe hemodynamic status. Except for classification 4, management was medical using a phosphodiesterase^{-5} inhibitor (80.8%), furosemide (97.1%), spironolactone (95.2%), digoxin (98.1%) and oxygen (84.6%). 18 patients died (17.3%). In conclusion, pulmonary hypertension exists among Filipinos. Predominant cases are pulmonary hypertension associated with congenital heart diseases. Majority of all patients seen are on New York Heart Association functional class III and with severe hemodynamic status. All cases were managed medically except for classification 4. 17.3% have already died.

OS13: LUNG CANCER 3

OS072

QUANTITATIVE EVALUATION FOR THE COMPLEXITY OF THE OUTLINES OF PULMONARY NODULES

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Backgrounds The outlines of primary lung cancers are more complicated than those of metastatic lung tumors on computed tomography (CT) images of the chest. This feature is useful for clarifying the diagnosis of pulmonary nodules. Up to now there have been no established methods for evaluating complexity of tumor outline numerically. We applied fast Fourier transform (FFT) analysis for quantification of complexity of tumor outline.
Methods Sequential cases of 72 histologically proven primary lung cancers (Group PL), 54 metastatic lung tumors (Group MT), and 24 benign lesions (Group BN) were included. The diameters of tumors in groups PL and MT were 18.9 ± 7.4 mm, 12.2 ± 6.1 mm, and 18.0 ± 5.3 mm respectively. The outline of each tumor on chest CT images was described using polar coordinates, and converted to rectangular coordinates, yielding wave data of the tumor outline. The FFT was then used to analyze the wave data. The complexity index (Cxi) was defined as the sum of the amplitude of all harmonics over a fundamental frequency.
Results The Cxi was higher for group PL (10.3 ± 6.7 mm, $p < 0.0001$) and group BN (7.9 ± 3.9 mm, $p < 0.0001$) than for group MT (3.2 ± 2.4 mm), and it was correlated with tumor diameter in each group: PL ($r = 0.667$, $P < 0.0001$), MT ($r = 0.809$, $P < 0.0001$), and BN ($r = 0.826$, $P < 0.0001$). The cut-off equation $Cxi = 0.127\ DT + 2.23$ provided the highest diagnostic accuracy for distinguishing Group PL from Group MT such as a sensitivity of 95.8%, a specificity of 81.5%, and an accuracy of 89.7%.
Conclusion FFT analysis appears useful for quantification of complexity of the tumor outline.

OS073

PULMONARY THROMBOEMBOLISM IN LUNG CANCER PATIENTS AND EGFR MUTATIONS

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Background Venous thromboembolism (VTE) occurs more frequent in patients with malignant diseases including lung cancer. Pulmonary thromboembolism (PTE) is a part of VTE and symptomatic PTE is sometime a fatal disease. Recently, it is found that there are subgroups with driver mutations in non small cell lung cancer (NSCLC), and epidermal growth factor receptor (EGFR) mutation is most frequent. At present, there is little information of the relationship between PTE and EGFR mutations.
Methods We retrospectively investigated lung cancer patients diagnosed PTE in a single institution, Saitama Medical University International Medical Center, from April, 2007 to March, 2012. Screening of EGFR mutations, which are tested by the PNA LNA PCR-Clamp, has started since 2007, and PTE was diagnosed by contrast enhanced CT or autopsy. Relationship between PTE and EGFR-mutation status were analyzed by Fisher's exact test.
Results A total of consecutive 1953 lung cancer patients were treated in this period. A total of 18 patients (0.92%) were diagnosed PTE. PTE occurred more frequently in progressive disease (14 patients), adenocarcinoma histology (15 patients), distant disease (11 patients), and periods under chemotherapy including EGFR-TKI or radiation therapy (13 patients). While, 1643 tests for EGFR mutations were done, and there were 391 patients harboring EGFR mutations and 1252 patients without EGFR mutations. Incidence of PTE in patients with EGFR mutations (9 patients, 2.3%) was significantly higher than that in patients without EGFR mutations (6 patients, 0.48%) (Fisher's exact test: $p < 0.01$).
Conclusion EGFR-mutated patients are more often experienced PTE than patients without EGFR mutations. It is considered, when EGFR-mutated NSCLC with advanced stages is progressing, coagulation testing including D-dimer or FDP should be done.

OS074

THE ROLE OF CYTOKINE-INDUCED KILLER (CIK) CELLS THERAPY IN MODULATING TREGS IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC)

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Objective Recent studies have revealed that Foxp3(+)CD25(+)CD4(+) regulatory T cells (Tregs), which are physiologically engaged in the maintenance of immunological self-tolerance, play critical roles for the control of antitumor immune responses. Targeting Tregs has the capability to augment cancer vaccine approaches. The current study was therefore designed to evaluate the role of cytokine-induced killer (CIK) cells infusion in regulating Tregs in patients with non-small cell lung cancer (NSCLC).
Methods Fifteen patients with advanced NSCLC were treated by infusion of CIK cells derived from autologous PBMC. By FACS and Liquid Chip, T, NK, DC cell subsets in peripheral blood (Pb) and plasma cytokine profiles in the treated patients were tested at two and four week intervals post infusion of CIK cells.
Results Analysis of the immune cell populations before and after the administration showed an increase in NK cells concomitant with a decrease in Tregs at two week after infusion of CIK cells. We found increased NKG2D expression on NK cells along with a rising percentage of NK cells. There was a positive correlation between NKG2D expression and the number of CIK cells infused. Correspondingly, plasma cytokine profiles demonstrated elevated levels of anti-tumor cytokines including IFN-gamma, IP-10, TNF-alpha, GM-CSF, MCP-3, IL-21 and reduced TGF-beta1 level that is mainly produced by Tregs over the same time frame. We found that Tregs in the treated patients' Pb still maintained a lower level at four week post CIK infusion.
Conclusion CIK cells therapy can suppress Tregs and enhance anti-tumor immunity in the patients with advanced NSCLC. This therefore may represent a more promising therapeutic setting against advanced NSCLC combined with chemotherapy, radiotherapy and cancer vaccines targeting tumor-associated self-antigens in the future.

OS075

BONE METASTASES ARE MORE FREQUENT AND MULTIPLE IN EGFR MUTATION POSITIVE NSCLC PATIENTS

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Background Non-small cell lung cancer (NSCLC) patients with EGFR mutation are different from other NSCLC patients in their smoking status and prognosis. Aim of this study was to clarify the difference in metastatic pattern between EGFR mutation positive and negative NSCLC patients.
Methods We checked the EGFR mutation status, Clinical staging and metastatic pattern in 409 NSCLC patients who visited Kyushu University Hospital or Fukuoka Higashi Medical Center and who were examined about their EGFR mutation status between Jan 2007 to Dec 2011. In addition, we checked bone metastatic pattern of 73 patients whose imaging data, FDG-PET or bone scintigraphy, could be referred. We used OSS point for quantification of bone metastasis, which was given respectively if there were bone metastasis in 17 osteal regions (MAX 17 points).
Results EGFR mutation positive patients were 153 (37.4%) and negative were 256 (62.6%). Clinical Staging and metastatic pattern other than bone metastasis were not significant between EGFR positive and negative patients. Bone metastases were statistically more frequent in mutation positive than negative patients (35.9%, 23.8%, $p < 0.05$). Average OSS point was also higher in mutation positive than in negative patients (4.62, 3.25, $p < 0.05$).
Conclusions EGFR mutation positive NSCLC patients may be suffered from multiple bone metastases more frequently than negative patients.

OS076

DIAGNOSTIC VALUE OF TUMOR M2 PYRUVATE KINASE IN PATIENTS WITH LUNG CANCER

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Introduction Tumour M2-pyruvate kinase (Tu-M2-PK), the inactive dimeric form of the M2 isoenzyme of PK was described as a tumour characteristic metabolic marker. The aim of this study was to investigate the diagnostic value of (Tu-M2-PK) as a tumor marker in patient marker in patients with lung cancer.
Methods In this prospective study we included 98 patients who were newly diagnosed lung carcinoma of different histological cell types (study group) and 90 cases who have no malignancy as control group. Control cases were divided into two groups; 45 of them had lung disease (group 1) the rest 45 were healthy people (group 2). The levels of Tu-M2-PK in plasma were measured by a commercially available sandwich enzyme-linked immunosorbent assay (Schebo, Biotech AG Giessen, Germany). Analysis of the receiver operator characteristics (ROC) curve used with the MEDCalc program.
Results The mean plasma Tu-M2-PK levels for study group was 16.73 ± 7.24 IU/ml, and for group1 4.53 ± 2.15 and for group2 4.08 ± 2.87 IU/ml. At a diagnostic cut-off value of 8.9 IU/ml for Tu- M2-PK in EDTA plasma was calculated using the ROC curve (AUC 0.991% confidence interval: 0.965–0.999; significance level P (Area = 0.5) $p < 0.0001$). In our patient population, Tu-M2-PK showed a diagnostic sensitivity of 100% and a specificity of 97.8%, according to cut-off of 8.9 IU/ml for lung carcinoma.
Conclusion We think that plasma Tu-M2-PK levels can be utilized for the differential diagnosis of and in screening for lung cancer.

OS077

EFFECT OF CEFEPIME (CFPM) OR MEROPENEM (MEPM) FOR FEBRILE NEUTROPENIA PATIENTS WITH LUNG CANCER. RANDOMIZED PHASE II STUDY (LOGIK1003)

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Objective The objective of this study is to determine the efficacy and safety of cefepime or meropenem for febrile neutropenia in lung cancer patients by prospective randomized study.
Endpoint Primary endpoint: Response rate (response was defined as fever resolution for 5 consecutive days without switching the drug, and without sever medical complication). Secondary endpoint: Defervescence at 72 hours, 7 days, 14 days.
Safety Results 21 patients and 24 patients were enrolled into cefepime (CEPM) arm and meropenem (MEPM) arm, respectively. Response rate was 17.65% (95% CI: 0.00–35.77) in CEPM arm, and was 38.10% (95% CI: 17.35–58.87%). Response rates of both groups were relatively low. it may be because the definition of response rate in the present study may not reflect true clinical efficacy. Defervescence at 72 hours, 7 days, 14 days were 70.59%, 86.67%, 100% in CFPM arm, and 65.00%, 84.21%, 92.31% in MEPM arm. There were no significant difference between the two group. We observed adverse event with 33.33% in CFPM arm and with 45.83% in MEPM arm. No severe adverse event was observed in the both arms.
Conclusion In the presents study, there were no significant difference between CFPM and MEPM in the efficacy and the safety for febrile neutropenia in lung cancer patients.

OS14: COPD 1

OS078

FACTORS ASSOCIATED WITH OUTCOME AMONG COPD PATIENTS UNDERGOING PULMONARY REHABILITATION

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Introduction Pulmonary Rehabilitation provides a comprehensive intervention for patients with chronic respiratory diseases. Outcome assessments are used to quantify the improvement in various areas of therapy like optimizing functional status. Since identification of additional benefits cannot be detected by usual measures, determination of other factors are considered to ensure success.
Methods Patients with COPD were enrolled in an 8 week out-patient program. They underwent pre and post-rehab evaluation that included Spirometry, Six-Minute Walk Test (6 MWT) and cardiopulmonary exercise testing. Subjects completed a self administered respiratory questionnaire using St. George Questionaire (SGRQ) and Medical Research Council Dyspnea Scale (MMRC). Successful primary outcome was defined as greater than the minimum clinically important difference in one or more areas of attendance, MMRC, SGRQ and 6MWT.
Results In total, 320 patients completed the study. At baseline, data showed educational attainment and distance between the facility and patients' residence were signficant factors that determine success in the program at p-value 0.009 and 0.013 respectively. Age, gender, civil status, weight, height and Body Mass Index (BMI) showed no significant correlation. Impact of single or aggregated co-morbidities on the effect of the program was also significant at p-value 0.004. Advanced stage of COPD is associated with poor outcome. Significant correlations were found with outcome, presence of hypoxemia and episodes of exacerbations. Patients with partial pressure of oxygen at >80 mm Hg (72.8%) and experiencing less than twice a year exacerbations (97.8%) were noted to have more successful outcome.
Conclusion Educational attainment, distance between the facility and patient's residence, number of co-morbidities, severity of COPD, degree of hypoxemia and episodes of exacerbations determined the outcome of pulmonary rehabilitation program. These were statistically significant and clinically important in the improvement of the quality of life of COPD patients.

OS079

CONCURRENT USE OF TIOTROPIUM AND SALMETEROL/FLUTICASONE PROPIONATE COMBINATION IN COPD: EFFECTS ON AIRWAY DIMENSIONS AND AIRFLOW LIMITATION

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Background and Aim of Study Concurrent administration of tiotropium (Tio) and salmeterol/fluticasone propionate combination (SFC) are commonly used treatments in chronic obstructive pulmonary disease (COPD). However, there are few data on their effects of airway structural changes. The aim of the study is to assess the effects of Tio plus SFC on airway dimensions in COPD compared with Tio or salmeterol (SM) alone, or SFC.
Methods Patients with COPD were randomized to receive 16-week treatment periods in one of four-way study: (1) Tio (18 μg once daily; n = 15), (2) SM (50 μg twice daily; n = 14), (3) SFC (50/250 μg twice daily; n = 16), (4) Tio plus SFC (n = 15). Airway dimensions were assessed by a validated CT technique, and airway wall area corrected for body surface area (WA/BSA), percentage wall area (WA%), airway wall thickness (T), and luminal area (Ai)/BSA at the right apical segmental bronchus were measured. Pulmonary function and the St. George's Respiratory Questionnaire (SGRQ) were evaluated.
Results Concurrent therapy of Tio plus SFC resulted in a significant decrease in WA/BSA, WA%, and T compared with Tio, SM and SFC ($p < 0.05$, respectively), and showed a significant increase in Ai/BSA compared with Tio ($p < 0.05$). Tio plus SFC provided greater improvements in FVC, FEV_1 and RV/TLC than monotherapy ($p < 0.05$, respectively). In the Tio plus SFC group, the changes in WA% and Ai/BSA were significantly correlated with changes in FEV_1 ($r = -0.86$, $p < 0.001$ and $r = 048$, $p < 0.05$). There were more significant improvements in SGRQ scores after treatment with Tio plus SFC than the three other treatments.
Conclusion The superiority of triple inhalation therapy may reflect improvements of the range of airway dimensions and pulmonary function measurements in COPD.

OS080

SUBGROUPS OF COPD PATIENTS WITH DISTINCT PHENOTYPES IN FOUR REGIONS OF TEN ASIAN CITIES

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Background Various phenotypes were observed in COPD patients. We evaluated whether there are subgroups of COPD patients with distinct phenotypes in four regions of ten Asian cities.
Methods We evaluated a total of 1022 COPD patients recruited from ten Asian cities which were classified into four regions of China/Taiwan, India/Sri Lanka, Philippines/Thailand/Malaysia/Vietnam, and Korea/Japan. To find principle variables for the phenotype of COPD patients, we performed factor analysis using the variables of age, body mass index, modified Medical Research Council dyspnea scale, Charlson comorbidity index, cigarette smoking amount, the St. George Respiratory Questionnaire (SGRQ) score, FEV1, FVC, and the ratio of FEV1/FVC. To find subgroups of COPD with distinct phenotypes, we performed hierarchical cluster analysis of Wald's method with the principle variables found by factor analysis.
Results We found age, Charlson index, SGRQ score, and FEV1 as principle variables for phenotyping the COPD patients. The cluster analysis for the total 1022 patients revealed three subgroups of COPD patients with distinct phenotypes, 'milder severity' (59%), 'milder severity but more comorbidity' (14%), and 'severe severity' (27%). The fractions of the three subgroups were different among the four Asian regions ($p < 0.001$). The fractions of the COPD phenotype with 'milder severity but more comorbidity' were 30%, 5%, 13%, and 11% in the regions of China/Taiwan, India/Sri Lanka, Philippines/Thailand/Malaysia/Vietnam, and Korea/Japan, respectively. The fractions of 'severe severity' were 20%, 42%, 33%, and 22% in the same order of the four regions.
Conclusion We found subgroups of COPD patients with distinct phenotypes. The difference in the fractions of the COPD subgroups might suggest that there are substantial differences in the severity and a potential subtype in the four Asian regions.

OS081

THE 0.70 FIXED RATIO AND LOWER LIMIT OF NORMAL OF FEV1/FVC IDENTIFY AN POSTOPERATIVE RISK IN PATIENTS UNDERGOING THORACIC SURGERY

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Objective Although there is an ongoing debate about the validity of the 0.70 fixed ratio and lower limit of normal (LLN) of FEV1/FVC to diagnose chronic obstructive pulmonary disease (COPD), whether or not the FEV1/FVC ratio below 0.70 but above the LLN (the in-between) could identify patients at risk in COPD-related clinical outcomes remains elusive. Because the incidences of prolonged postoperative stay (PPS) increase in the patients with COPD undergoing thoracic surgery, appropriate preoperative pulmonary assessment is warranted. Nevertheless, whether or not the combined assessment could be applied to identify patients at risk has not fully been evaluated.
Methods Postoperative risks were evaluated in patients undergoing thoracic surgery by the 0.70 fixed ratio and LLN of FEV1/FVC.
Results The COPD group had a three fold increase in prolonged oxygen therapy (POT) and 50% increase in PPS, as compared with the in-between group. When the minimal clinically important difference (MCID) in FEV1 is assumed to be 100 ml after intervention, the patients in the in-between and COPD groups could be categorized into the non-COPD and in-between groups, respectively. Nevertheless, the patients in the COPD group did not appear to be categorized into the non-COPD group.
Conclusions Our data suggest that the in-between group can identify patients at risk and improve the precision of risk stratification. This classification of three groups by the 0.70 fixed ratio and LLN of FEV1/FVC might provide a new useful strategy to improve postoperative outcomes by drug interventions in the patients undergoing thoracic surgery.

OS082

EFFECTS OF INDACATEROL IN ADDITION TO TIOTROPIUM IN PATIENTS WITH COPD

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Background and Aim of Study Current guidelines (GOLD2010) recommend treatment with single or combined long-acting bronchodilators for patients with moderate or more severe chronic obstructive pulmonary disease (COPD). Indacaterol, an inhaled long-acting beta-agonist, can produce 24 hours of bronchodilation and reduce symptoms with only once-daily use. In this study, we compared combined use of indacaterol and tiotropium with tiotropium alone to evaluate the combined effect.
Methods In 18 patients with persisted COPD symptoms who received tiotropium treatment and needed additional treatment, we measured each lung volume using spirogram, gas dilution, and body plethysmography at baseline and after 4, 8, and 24 weeks as well as MostGraph, 6MD, and CAT score.
Results Improved FEV1 in each stage and remarkably improved breathing resistance and reactance in stageIV were found. In stageIIItoIV, FVC and IC were also improved. High scores were achieved in CAT score in stageIV.
Conclusion Indacaterol may be effective in improving obstructed airway, air trapping, and ventilation-perfusion mismatch.

OS083

HIGHER PREVALENCE OF AORTIC ANEURYSM IS ASSOCIATED WITH THE SEVERE LUNG DESTRUCTION AND AORTIC WALL CALCIFICATION IN PATIENTS WITH COPD

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Background and Aim of Study Chronic obstructive pulmonary disease (COPD) and aortic aneurysm (AA) shared the risk factor of smoking, and COPD has been reported to be associated with the development of AA. However, it remains unclear what kind of patients would have a higher risk of AA.
Methods A total of 238 eligible patients with COPD participated. To evaluate the existence of AA, participants underwent CT scanning of chest, abdomen and pelvis, in addition to the regular COPD workup. Emphysema severity was analyzed by Goddard classification. We also evaluated the aortic wall calcification by selecting a slice with the most severe calcification in thoracic artery and calculating the percentage of calcification area (aortic wall calcification score) as follows; score 0, no calcification; score 1, calcification area was <25%; score 2, 25%> and <50%; score 3, 50%> and <75%; and score 4, >75%.
Results AA was detected in twenty-six patients (10.9%) by CT screening, while six patients (2.5%) had already diagnosed with a history of repair operation. We designated them "AA group (n = 32)" and classified enrolled 238 patients into two groups; AA group and non-AA group (n = 206). AA group had a higher age, smoking status, Goddard and aortic wall calcification scores, while a lower value of FEV1 and FEV1/FVC than non-AA group. Gender, body mass index, and FEV1 % predicted were not different between two groups. Meanwhile, multivariate analysis showed that aortic wall calcification score (HR, 17.63; 95% CI, 1.62–3.79, $p < 0.001$) and Goddard score (HR, 3.96; 95% CI, 1.01–1.20, $p = 0.047$) were independently associated with existence of AA in COPD patients, but other factors did not prove to be statistically significant.
Conclusion Patients with severe lung destruction and aortic wall calcification in thoracic artery had a higher risk of AA in COPD.

OS085

INHALED CORTICOSTEROIDS AND RISK OF ADMISSION FOR EMERGENCY DEPARTMENT CHILDREN WITH ACUTE ASTHMA: A META-ANALYSIS

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Background Inhaled corticosteroids (ICS) are widely used for chronic management of asthma and also have been reported its efficacy in emergent treating adults with acute asthma.
Object This meta-analysis aimed to investigate if ICS are related to a reduced risk of admission for emergency department children with acute asthma as comparing with either placebo or systemic corticosteroids (SC).
Materials and Methods Randomized controlled trials were indentified from PubMed, EMBASE, Google Scholar, and the Cochrane Library using the following search terms: asthma, acute asthma, inhaled corticosteroids, nebulized corticosteroid, systemic, oral, intramuscular, intravenous, emergency department, and child. Outcome was admission rate of emergency department.
Results Ten randomized controlled trials were included. The overall combined odds ratio (OR) revealed that there was no significant reduction in hospital admissions for children treated with ICS (OR = 0.74, 95% CI = 0.13 to 1.27, P = 0.277). Closer inspection of analysis for ICS versus placebo subgroup, ICS treatment significantly reduced hospital admission rate (OR = 0.15, 95% CI = 0.03 to 0.93, P = 0.042). For ICS versus SC subgroup, it revealed no significant different in hospital admissions for children treated with ICS versus SC (OR = 1.54, 95% CI = 0.30 to 7.83, P = 0.604). For ICS plus SC versus SC only subgroup, there was no significant difference in hospital admissions between patients treated with ICS plus SC and SC only (OR = 0.87, 95% CI = 0.49 to 1.53, P = 0.618).
Conclusion Among emergency department children with acute asthma, those on ICS had a similar risk of admission to those treated with SC, but a lower risk of admission than those with placebo.

OS15: CLINICAL RESPIRATORY MEDICINE 3

OS084

PROSTACYCLIN AND COUGH IN PATIENTS WITH BRONCHIAL ASTHMA

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Inflammatory mediators are involved in the pathogenesis of airway inflammation, but the role of prostacyclin remains obscure. This study was designed to investigate the role of prostacyclin in cough reflex sensitivity of the asthmatic airway, which is characterized by chronic eosinophilic airway inflammation. The effect of beraprost, a chemically and biologically stable analogue of prostacyclin, on cough response to inhaled capsaicin was examined in 21 patients with stable asthma in a randomized, placebo-controlled cross over study. Capsaicin cough threshold, defined as the lowest concentration of capsaicin eliciting five or more coughs, was measured as an index of airway cough reflex sensitivity. The cough threshold was significantly ($p < 0.05$) decreased after two weeks of treatment with beraprost [17.8 (GSEM 1.20) μM] compared with placebo [30.3 (GSEM 1.21) μM]. Prostacyclin increases cough reflex sensitivity of the asthmatic airway, suggesting that inhibition of prostacyclin may be a novel therapeutic option for patients with asthma, especially cough predominant asthma.

OS086

EFFECT OF NAIL POLISH AND ARTIFICIAL ACRYLIC NAILS ON OXYGEN SATURATION DETERMINED BY PULSE OXIMETRY IN NORMOXIC ADULTS

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Background Varieties of nail polish colors had been reported to affect the accuracy of pulse oximeter from less than 2 to 10%. Newer styles of nail polishing including acrylic nail become popular in recent years. Their effects on oxygen saturation (SpO2) had not been studied. Moreover, different types of pulse oximeter especially finger pulse oximeter may be affected by these newer styles of nail polish.
Objective To determine if fingernail polish and acrylic nails affect SpO2 measured by 3 different models of pulse oximeter.
Methods Prospective research. Eleven colors of nail polish (white, yellow, orange, black, brown, green, blue, purple, pink, metallic silver, and red) and 1 painted acrylic nail were used. Sixty volunteers had these nail polish applied on their fingers. Three models of pulse oximeter (Oxiwatch, Mini-Torr Plus, and Mindray PM-7000/Masimo) were used to measure SpO2 prior to and after nail polish application.
Results Baseline SpO2 were not different among 3 models of pulse oximeter. Red, orange, pink nail polish and acrylic nail did not show statistically significant decrease in SpO2. The others showed statistically significant decrease in SpO2 measured by Oxywatch and Mini-Torr Plus ($p < 0.05$). These 2 models of pulse oximeter were not able to measure SpO2 in some subjects using green, black, blue, metallic, purple and brown nail polish while Mindray PM-7000/Masimo was able to measure all subjects and all nail polish colors.
Results Commonly used nail polish colors (pink, orange and red) and acrylic nails did not affect SpO2. Some models of pulse oximeter may be affected by nail polish.

OS087

IT'S TIME TO CALL ATTENTION TO CLINICAL SIGNIFICANCE OF BASIDIOMYCETOUS FUNGI IN CHRONIC COUGH

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Background and Aim of Study To clarify the clinical significance of basidiomycetous (BM) colonization in chronic cough patients, we report the results of a preliminary study regarding the recent prevalence of chronic cough in our hospital, and the positive rates of both BM colonization and a peculiar laryngeal sensation presenting as a sensation of mucus in the throat (SMIT).
Methods The medical records of 106 patients complaining of cough lasting 8 weeks or more, who visited our clinics from 1 April to 31 December 2012, were collected and reviewed retrospectively.
Results Among the 106 patients who were adequately assessed, a diagnosis was made in 93 patients (87.7%): atopic cough (AC) in 29 (27.4%); cough variant asthma (CVA) in 22 (20.8%); sinobronchial syndrome (SBS) in 21 (19.8%); fungus-associated chronic cough (FACC) in 13 (12.3%); gastroesophageal reflux-associated cough (GER) in 4 (3.8%); psychogenic cough in 4 (3.8%), and unexplained cough (UCC) in 13 (12.3%). BM fungi were detected in 1 AC patient, 3 CVA patients, 3 SBS patients. SMIT was observed in 8 (27.6%) AC patients, 6 (27.3%) CVA patients, 10 (47.6%) SBS patients, 10 (76.9%) FACC patients, 1 (25%) GERD patients, and 0 (0%) psychogenic cough patients. Regardless of diagnosis, the existence of SMIT was significantly correlated with positive results of BM colonization in the sputum of chronic cough patients ($P < 0.05$).
Conclusion Our data showed that SMIT is an important clinical manifestation in FACC patients and may predict the presence of BM colonization in chronic cough patients. It is surprising that the positive ratio of BM colonization in chronic cough patients was shown to be relatively high, and that FACC was demonstrated to be the fourth major cause of chronic cough in this study.

OS088

TO STUDY THE PRESCRIPTION PATTERN OF INHALERS AND MEDICATION IN MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PRIMARY CARE PRACTICE

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Introduction Primary care physicians provide care to the majority of patients of COPD. Although clinical practice guidelines have been developed for COPD, their influence on primary care practice is unclear.
Aims and Objectives The study sought to examine the prescription pattern regarding inhaler devices and medication in management of COPD in primary care practice in relation to guideline-based recommendations.
Materials and Methods We studied the prescriptions details of already diagnosed and on treatment COPD patients and inhaler devices, inhaled medications, oral medications were physically verified.
Results 4287 COPD patients completed the study. Results show that 29.5% patients were on inhalers and 70.5% on oral medications. 57.1% used Dry Powder Inhalers, 28.3% Meter Dose Inhalers, 11.5% Meter Dose Inhalers with spacer devices and 3.1% nebulizers. 35.8% patients were prescribed SABA/ICS, 25.9% LABA/ICS, 13.5% SABA, 11.3% ICS, 7.8% SABA/SAAC and 1.6% of COPD were prescribed LAAC/ICS. A triple drug inhaler with ciclesonide/tiotropium/formoterol was used only by 4.1% patients. Among oral medications methylxanthines were prescribed to 30.5% patients, oral salbutamol and methylxanthines to 19.8%, oral salbutamol to 15.2%, multiple drugs to 24.1% patients and 3.6% patients were prescribed leukotriene modifiers where as 6.9% patients of COPD were given steroids.
Conclusions This study presents a snapshot of primary care physician's prescription patterns in COPD management which is extremely sub optimal. We suggest that extensive surveys should be carried out to audit the prescription in primary care practice to explore the COPD management patterns in an effort to improve COPD care in primary care.

OS089

TO STUDY THE TYPE OF INHALERS USED AND ERRORS IN INHALER TECHNIQUES COMMITTED BY CHRONIC PULMONARY DISEASE PATIENTS IN PUNJAB

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Introduction Effectiveness of inhaled drugs depends on patient's ability to use inhaler device correctly. A less-than-optimal technique results in decreased drug delivery and reduced efficacy.
Aims and Objectives In India, there is paucity of data on error rate in inhaler techniques adopted, so we studied the types of inhalers used and errors in inhaler techniques committed by the patients.
Material and Methods Chronic pulmonary diseases patients already using inhalers were questioned about type of inhaler device, as to who imparted education about inhaler technique and observed their actual inhaler technique. Errors in inhaler techniques were categorized into mild, moderate and sever on basis of subjective assessment by the physician using a 10-item checklist.
Results Data revile that 56.3% patients used DPI 25.7% MDI, 12.8% MDI with spacer and 5.2% used nebulizer. 71.5% patients were self educated to learn inhaler technique, 11.6% by shop keeper chemist, 10.7% by hospital staff and only 6.2% were actually educated by the consultant. Errors in inhaler techniques was observed in 79.8% patients which included 45.5% mild, 21.3% moderate and 33.2% gross errors. Errors were committed by 82.5% patients using DPIs, 93.1% using MDIs, 65.1% using MDIs with spacers and 21.5% using nebulizers. Error rate was 86.3% in self educated patents, 73.9% in shopkeeper chemists educated, 65.2% in health staff educated and was 40.8% in patients educated by the doctor.
Conclusion We conclude that majority of patients' committee errors in taking inhalers, which may result in inadequate drug delivery. We observe that written instructions are not sufficient and that verbal instructions, demonstrations and practice sessions need to be included in education programme for inhaler techniques and simple teaching devices should be built to develop coordination skills needed for inhaler use.

OS090

THE EFFECT OF TAI CHI ON LUNG FUNCTION, EXERCISE CAPACITY AND DIAPHRAGM STRENGTH IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background Although the benefits of exercise on the health of patients with COPD have been widely reported, the effect of Tai Chi as an alternative exercise has not been well evaluated in patients with COPD. This study reported a randomized controlled trial, which investigated the effect of Tai Chi on lung function, exercise capacity, and diaphragm strength in patients with COPD.
Methods 40 patients with COPD were randomized into the control group and Tai Chi group. Patients in the control group received only routine care, while patients in the Tai Chi group received routine care and completed a 6-month Tai Chi exercise program. Lung function parameters, blood gas parameters, 6-min walking distance (6MWD), and diaphragm strength parameters were measured before and after the trial.
Results Lung function parameters (FEV1 and FEV1 predicted), 6MWD, diaphragm strength parameters (TwPes, TwPga, and TwPdi) were found to be significantly increased in COPD patients after completion of the 6-month Tai Chi program ($p < 0.05$). These parameters were also found to be significantly higher in COPD patients who completed the Tai Chi excercise program than in COPD patients who received only routine care ($p < 0.05$). In contrast, no significant differences in PaO_2 and $PaCO_2$ were observed in COPD patients before and after completing a Tai Chi program and between Tai Chi group and control group ($p > 0.05$).
Conclusions Tai Chi exercise enhances lung function, exercise capacity, and diaphragm strength. Our study suggests that Tai Chi may be an effective non-pharmacotherapy for COPD patients.

OS16: LUNG CANCER 4

OS091

CARCINOMATOUS MENINGITIS AND EGFR MUTATION

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Background Carcinomatous meningitis (CM) in non-small cell lung cancer (NSCLC) has no standard treatment, and is treated by almost always palliative care. The prognosis for patients with carcinomatous meningitis is poor, with a median survival up to 2 months. Recently, it is found that there are subgroups with driver mutations in NSCLC, and epidermal growth factor receptor (EGFR) mutation is most frequent, and tyrosine kinase inhibitors (TKIs) are very active for EGFR-mutated tumors.
Methods Screening of EGFR mutations, which are tested by the PNA-LNA PCR Clamp, has started from 2007 in our institution. We performed a retrospective study investigating incidence, clinical course and survival of consecutive patients with CM in a single institution from April. 2007 to June. 2013.
Results During this period, 1677 NSCLC patients were tested by the PNA-LNA PCR Clamp, and there were 397 patients harboring EGFR mutations and 1280 patients without them. A total of 28 patients experienced CM (18 patients with EGFR mutations, 8 patients without them, and 2 patients without information of pathology and mutation status because of poor PS). Incidence of CM in patients with EGFR-mutations was significantly higher than that in patients without EGFR mutations (4.5% vs. 0.6%, respectively, Fisher's exact test: $p < 0.05$). Among the 18 CM patients with EGFR mutations, treatment by whole brain irradiation and TKIs might contribute on long survival after occurring CM. (median survival: 3.3 months).
Conclusions EGFR-mutated patients more often experience CM than patients without it. Treatment by whole brain irradiation and TKIs might be a key treatment for EGFR-mutated patients with CM.

OS092

RANDOMIZED STUDY OF PEMETREXED PLUS CARBOPLATIN FOLLOWED BY PEMETREXED VERSUS PACLITAXEL PLUS CARBOPLATIN FOLLOWED BY PEMETREXED IN NON-SQUAMOUS NSCLC (LOGIK0904)

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Background PARAMOUNT study confirmed the improvement of overall survival with continuation maintenance chemotherapy with pemetrexed (PEM) compared with placebo after 4 cycles of cisplatin plus PEM induction chemotherapy recently. JMEN study also showed the usefulness of switch maintenance with PEM after 4 cycles of platinum doublet without PEM. In this study, we conducted the randomized phase II study comparing switch or continuation maintenance chemotherapy with PEM after standard doublet regimen.
Methods Histologically/cytologically confirmed stage IIIb or IV non-squamous NSCLC patients with mesurable disease, ECOG PS 0–1, age over 20 years and adequate organ function were eligible for the study. Randomization was stratified by gender and stage of disease. Patients received 3 cycles of PEM 500 mg/m^2 plus CB AUC6 (Arm 1) or PAC 200 mg/m^2 plus CB AUC6 (Arm 2). All patients with non-PD after induction chemotherapy continued PEM 500 mg/m^2 until PD. Primary endopoint is progression free survival (PFS).
Results 140 pts were enrolled and assigned to Arm1 or Arm2 randomly. The clinical data of 132 pts were used as full analysis set (median age 64.5 yrs (42–83), 85 male, 120 stage IV, 58 PS0, 127 adenocarcinoma, 46 never smoker). 42 pts had prior treatment including 9 sugery, 1 adjuvant chemotherapy, 24 radiotherapy and 8 others. In both arms, 50% of pts entered into the maintenance treatment with PEM after completion of 3 cycles induction chemotherapy. The median PFS was 113 days in Arm 1 and 143 days in Arm 2, respectively. Cox-proportinal Hazard ratio was 1.047, and 95% HR confidential interval was 0.707–1.549. Stratified Log-Rank test showed no significant difference in both arms.
Conclusion There was no significant difference for PFS in Arm 1 (PEM plus CB follwed by PEM) and Arm 2 (PAC plus CB followed by PEM).

OS093

TREATMENT WITH EGCG IN NSCLC LEADS TO DECREASING IFP AND HYPOXIA TO IMPROVE CHEMOTHERAPY EFFICACY THROUGH REBALANCE OF ANGS

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Background and Aim of Study Microvasculature and microenvironment play important roles in proliferation, invasion, metastasis and prognosis in non-small cell lung cancer (NSCLC), which might be altered by many anti-angiogenic drugs. Epigallocatechin-3-gallate (EGCG), a natural anti-angiogenesis agent refined from green tea, was defined to have multiple effects on angiogenesis factors, such as endothelial growth factor (VEGF) and angiopoietins (ANGs). Hypothesizing that EGCG might regulate microvasculature and microenvironment in NSCLC, the effects of EGCG on microvessel density (MVD), expression of Ang-1 and Ang-2, interstitial fluid pressure (IFP), tumor hypoxia, and chemotherapy sensitivity were examined.
Methods and Results EGCG treatment of A549 cells in mice bearing xenografts in vivo led to a significant decrease of MVD detected by CD31, and of Ang-2 expression detected by quantum dots double-label immunofluorescence assessment, while Ang-1 decreased with no significance. Decreased IFP was measured by the Wink-in-needle method, while hypoxia was assessed by polarographic electrode and pimonidazole (PIMO) immunohistochemistry. Assuming that these changes would increase response to chemotherapy, tumor growth studies were performed in nude mice with xenografts, which were then treated with EGCG and the chemotherapeutic agent cisplatin. EGCG therapy combined with cisplatin led to synergistic inhibition of tumor growth, compared with administration of each treatment separately ($P < 0.001$). According to linear regression analysis, IFP was positively correlated with PIMO staining ($R2 = 0.618$, $P = 0.002$), Ang-2 was correlated with MVD ($R2 = 0.423$, $P = 0.022$), IFP ($R2 = 0.663$, $P = 0.01$) and PIMO staining ($R2 = 0.694$, $P = 0.01$).
Conclusion IFP and delivery of oxygen might be improved by rebalance of Ang-1/Ang-2 under the treatment of EGCG in NSCLC, which also acts as a sensitizer of chemotherapy. These studies established a new mechanism for using EGCG as an adjuvant chemotherapy agent through modifying microvasculature and microenvironment.

OS094

PROGNOSIS OF CANCER PATIENTS IN THE HOSPITAL DAMAGED BY THE JAPAN EARTHQUAKE AND TSUNAMI

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Background Our hospital (previously named Tohoku Kousei Nenkin Hospital) is a community cancer center situated in the coastal place of Sendai City. The giant earthquake and tsunami hit Japan's northeast on March 11, 2011. Our hospital suffered serious damage to buildings, water supply and energy supply. Many patients (pts) in our hospital had been living in the affected areas. Medium-and long-term effect of the earthquake on prognosis of cancer pts is still unclear.
Patients and Methods We investigated the contents of medical records about trends and prognosis of cancer pts. Including pts who were changing hospital, we tracked the prognosis as possible.
Results The number of pts who had been hospitalized on the time of the earthquake was 400 and pts hospitalized with cancer was 101. Median age was 69 years (range, 37 to 88 years), and 59.4% was male. The percentages of pts with gastro-intestinal cancer, thoracic cancer, and other cancers were 52.5%, 36.6%, 10.9%, respectively. Median follow up time was 9.9 months. There was no significant difference in Overall Survival [OS] between pts living in disaster areas and in other area (14.7 v 16.1 months, Hazard Ratio [HR], 2.08, 95% CI 0.73 to 5.92; $P = 0.17$). There was a tendency to be better OS in pts qualified as disaster victim certificate than in other pts (18.3 v 12.6 months, HR, 0.47; 95% CI 0.21 to 1.05; $P = 0.07$).
Conclusion Including the type of cancer and treatment, factors affecting the OS should be further investigated. In particular, meaning that there is a tendency to extend OS in pts with disaster victim certificate is worth considering.

OS095

PHASE II STUDY OF S-1 WITH PATIENT-REPORTED OUTCOME EVALUATION IN ELDERLY PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER

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Background and Aim of Study As the aging of lung cancer patient is in progress, the assessment of the treatment including the evaluation of quality of life is important in the elderly patients. We performed the phase II study to evaluate the efficacy and safety of S-1 and the quality of life in elderly (over 75 years old of age) patients with advanced non-small cell lung cancer.
Methods Patients received S-1 (approximately equivalent to 80 mg/m^2/day) as a first-line treatment for 2 weeks followed by a 1-week rest period every 3 weeks. This treatment course was repeated until disease progression or the emergence of intolerable toxicities. The primary end point was the disease control rate. Secondary end points were progression-free survival, overall survival, toxicity and quality of life.
Results Forty patients were enrolled (male/female; 25/15). The median age was 78 years (75–85). The tumor histology was as follows: adeno/squamous/large/others; 24/10/2/4. The disease control rate was 90.0% (CR/PR/SD/PD; 0/4/32/4). The progression-free survival and overall survival was 4.2 months and 16.6 months, respectively. The grade 4 toxicity (hypokalemia) was observed in one patient (2.5%). The grade 3 toxicities included neutropenia (2.5%), anorexia (7.5%), and hyponatremia (5.0%).
Conclusion S-1 monotherapy was effective and well tolerated as a first-line chemotherapy for elderly patients with advanced non-small cell lung cancer. The evaluation of quality of life using patient-reported outcome will be also presented and discussed in the session.

OS096

WHICH DO NSCLC PATIENTS WITH EGFR MUTATION PREFER AS A FIRST-LINE THERAPY, EGFR-TKI OR CHEMOTHERAPY? A VIGNETTES STUDY (LOGIK0903)

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Background Treatment decision-making is associated with potential decisional conflict of patients. Aim of this study was to determine the preferences of advanced NSCLC patients for EGFR-TKI or chemotherapy as first-line therapy if they were in the situation of having a lung cancer harboring EGFR mutation, and to investigate the variables considered important to that preference.
Methods Three vignettes were designed to assess the patients', the physicians' or medical staff members' preferences for treatment decision-making and the reasons classified into five category such as "evidence level", "type of drug administration", "therapeutic efficacy", "adverse events", and "influence to ordinary life" behind the decision.
Results Total 377 individuals containing 100 patients, 100 physicians, and 177 medical staff members were analyzed in this study, and 322 participants (85.4%) preferred to EGFR-TKI than chemotherapy as a first-line therapy. Preference rate of EGFR-TKI in patients was statistically significantly lower than those in physicians and medical staffs, 73%, 88% and 91%, respectively. Among the reasons we investigated, "therapeutic efficacy" was the only marginal significant reason for preference in patients (odds ratio: 3.88, $P = 0.06$). In addition to "therapeutic efficacy", "type of drug administration" and "influence to ordinary life" was the significant reasons for their preference in physicians (odds ratio: 11.57, 22.57 and 20.5, respectively). In pre-planned analysis, we found the difference of value between the patients and the physicians in "influence to ordinary life".
Conclusions If the patients have an advanced lung cancer with EGFR mutation, they may prefer EGFR-TKI as a first-line therapy to chemotherapy as well as physicians and medical staff members. However the reasons of those preferences among them may be different. We should consider continuation of patients' ordinary life when we discuss about treatment decision-making with patients.

OS17: COPD 2

OS097

THE PREVALENCE RATE OF COPD AS A COMORBIDITY IN JAPANESE PATIENTS WITH LUNG CANCERS UNDERGOING BRONCOSCOPY

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Objective In comparing patients undergoing thoracic surgery, we found that COPD patients with an FEV1/FVC below 0.70 had an average postoperative stay that was 61% higher, and a 100% greater need of prolonged oxygen therapy (POT), than patients without COPD (Matsuo and Hashimoto, et al. 2012 Interact Cardiovasc Thorac Surg 14 (5); p560–564). Although 43.2% of the patients undergoing major lung resection carried COPD, the exact prevalence rate of COPD as a comorbidity and the severity in Japanese patients with lung cancers remain elusive. Because only 10% of the patients with COPD were managed as the patients with COPD, we have been encouraging to perform spirometry as screening for patients undergoing bronchoscopy since our study.
Methods We evaluated the prevalence rate of COPD and the severity in Japanese patients with lung cancers who underwent spirometry.
Results We analyzed 270 cases with lung cancers for which spirometry were performed. Reversibility testing was performed in 168 cases among 270 cases. Only two cases showed the significant reversibility after bronchodilator treatment. Although a new JRS COPD guideline estimates the incidence rate of COPD in the patients over 65 years old with lung cancers to be about 30%, 54.4% of the patients with lung cancers carried COPD (147/270 cases). The incidence rate of ischemic cardiac diseases in the patients with COPD was significantly higher than that in the patients without COPD (11.6% vs 2.4%). The population of GOLD grade I and II were higher than that of Gold grade III in the patients with lung cancers (GOLD grade I/II/III/IV; 95/41/11/0, respectively), compatible with the population of the patients with lung cancers undergoing thoracic surgery.
Conclusions Because most patients with lung cancers may undergo bronchoscopy to diagnose lung cancers, combined assessment of spirometry and bronchoscopy for the patients with lung cancers is desirable for comprehensive assessment.

OS098

CO-ADMINISTRATION OF GLYCOPYRRONIUM AND INDACATEROL IMPROVES LUNG FUNCTION AND SYMPTOMS IN PATIENTS WITH COPD VERSUS INDACATEROL ALONE: THE GLOW6 STUDY

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Background and Aim of Study Current COPD management strategy recommends combining bronchodilators with different mechanisms for treating symptomatic patients with moderate-to-severe COPD. We compared once-daily dual bronchodilation by co-administration of the long-acting muscarinic antagonist (LAMA) glycopyrronium 50 μg (GLY) and long-acting β_2-agonist (LABA) indacaterol 150 μg (IND), to monotherapy with IND 150 μg alone.
Methods In this multicenter, double-blind, parallel group study, patients with moderate-to-severe COPD were randomized (1 : 1) to GLY + IND or IND + Placebo (all delivered via Breezhaler® device) for 12 weeks. We assessed lung function, dyspnea (via the transition dyspnea index [TDI]), patient-reported symptoms, and safety and tolerability over 12 weeks.
Results Of the 449 patients randomized (GLY + IND [n = 226]; IND [n = 223]; male 81.8%; mean age: 63.8 years, mean post-bronchodilator forced expiratory volume in 1 second (FEV_1): 54.8% predicted), 94.0% completed the study. At Week 12, GLY + IND treatment demonstrated a statistically significant greater improvement in mean trough FEV_1 over IND (least squares mean treatment difference [Tx]: 64 mL; $p < 0.001$). Significantly greater improvements in FEV_1 area under curve from 30 min to 4 hours ($AUC_{30min–4h}$) and Forced Vital Capacity (FVC) were observed with GLY + IND vs IND at Day 1 (Tx: 105 mL, 112 mL, respectively) and Week 12 (Tx: 111 mL, 93 mL, respectively], all $p < 0.01$. GLY + IND significantly improved TDI score, mean daytime respiratory symptom score and % days able to perform usual daily activities vs IND at Week 12 (Tx: 0.49, –0.1, 6.2 respectively, all $p < 0.05$). The overall incidence of adverse events (AEs) and serious AEs (SAEs) was comparable for the GLY + IND and IND groups (AEs: 37.6% vs 34.1%; SAEs: 2.2% vs 2.3%).
Conclusion Compared to indacaterol monotherapy, once-daily co-administration of glycopyrronium and indacaterol provided, from the Day 1 of treatment, superior improvements in lung function and dyspnea, without adversely affecting safety and tolerability.

OS099

COMPARISON OF THE EFFICACY AND SAFETY OF ONCE-DAILY GLYCOPYRRONIUM WITH BLINDED TIOTROPIUM IN PATIENTS WITH COPD: THE GLOW5 STUDY

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Background Glycopyrronium (NVA237) is a once-daily LAMA that has demonstrated efficacy similar to open-label tiotropium.[1] The GLOW5 study was designed to compare the efficacy and safety of glycopyrronium with blinded tiotropium.
Methods This multicenter, 12-week, blinded study randomized (1 : 1) patients with moderate-to-severe COPD to once-daily glycopyrronium 50 μg or tiotropium 18 μg. The primary objective was to demonstrate non-inferiority of glycopyrronium versus tiotropium for trough FEV_1 at Week 12 (non-inferiority margin: –50 mL). Other endpoints included FEV_1 area under the curve ($AUC_{0–4hr}$) on Day 1, transition dyspnea index (TDI), St George's Respiratory Questionnaire (SGRQ), rescue medication use, exacerbation rate, safety and tolerability.
Results Of the 657 patients randomized, (glycopyrronium [n = 327]; tiotropium [n = 330]; mean age: 63.5 years, mean post-bronchodilator FEV_1: 53.5% predicted), 95.9% completed. Glycopyrronium demonstrated non-inferiority to tiotropium for trough FEV_1 at Week 12 (Least Squares Mean (LSM) = 1.41 L for both groups, [95% confidence interval (CI): –0.032–0.031 L]). Glycopyrronium had rapid onset of bronchodilation in the morning as demonstrated by a higher FEV_1 $AUC_{0–4hr}$ on Day 1 compared to tiotropium (treatment difference = 58 mL; $p < 0.001$). At Week 12, TDI total score (–0.188; P = 0.385), SGRQ total score (0.65; P = 0.488) and percentage of days with no rescue medication use (–1.5; P = 0.528) were comparable between the two groups. No significant treatment difference was observed with respect to number of moderate/severe COPD exacerbations per year (Glycopyrronium = 0.38 versus tiotropium = 0.35 [95% CI: 0.62 – 1.93]; P = 0.754). Overall, incidence of adverse events was similar in the glycopyrronium (40.4%) and tiotropium (40.6%) groups.
Conclusion Glycopyrronium and tiotropium showed similar effective and sustained bronchodilation with similar impact on dyspnea, health status, exacerbations rate, rescue medication use, safety and tolerability. Glycopyrronium's onset of bronchodilation was significantly more rapid following the first dose.
Reference
1. Kerwin, E, et al. Eur Resp J 2012;40:1106–1114.

OS100

ONCE-DAILY QVA149 IMPROVES LUNG FUNCTION, DYSPNEA AND HEALTH STATUS REGARDLESS OF DISEASE SEVERITY AND PRIOR MEDICATIONS: THE SHINE STUDY

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Introduction The current GOLD strategy recommends combining two long-acting bronchodilators for the maintenance treatment of patients with moderate-to-severe COPD. The SHINE study evaluated the effect of QVA149, a dual bronchodilator combining the LABA indacaterol and the LAMA glycopyrronium (NVA237), compared with glycopyrronium, indacaterol, tiotropium monotherapies and placebo.
Methods In this 26-week, multicenter, double-blind, parallel-group, placebo and active controlled (open-label tiotropium) study, patients ≥40 years with moderate-to-severe COPD (post-bronchodilator $FEV_1/FVC < 0.7$ and $FEV_1 \geq 30\%$ to <80% predicted) and smoking history ≥10 pack-years were randomized to receive once-daily QVA149 (110/50 μg), indacaterol (150 μg), glycopyrronium (50 μg), tiotropium (18 μg) or placebo (2 : 2 : 2 : 2 : 1). Here, we present the improvements in lung function, Transition Dyspnea Index (TDI) and St. George's Respiratory Questionnaire (SGRQ) total score by COPD disease severity and prior medication use.
Results In total, 2144 patients (mean age 63.9 years; mean FEV_1 post-bronchodilator 55.2% predicted) were randomized (QVA149 [n = 475]; indacaterol [n = 477]; glycopyrronium [n = 475]; tiotropium [n = 483]; placebo [n = 234]); 89.1% completed the study. Significant improvements in lung function, dyspnea and health status were observed with QVA149 compared to placebo with a treatment difference of 370 mL and 260 mL in FEV_1 $AUC_{5min–4h}$, 240 and 120 mL in trough FEV_1, 1.17 and 1.00 in TDI and −2.74 and −3.77 in SGRQ score, in patients with moderate and severe COPD, respectively. Compared with placebo, QVA149 demonstrated a significant improvement in lung function, dyspnea and health status with a treatment difference ranging from 300 to 370 mL for FEV_1 $AUC_{5min–4h}$ and 170 to 250 mL for trough FEV_1, 0.71 to 2.27 in TDI and −0.34 to −5.94 in SRGQ total score, respectively in all the subgroups of patients with different prior medications.
Results With once-daily QVA149, similar improvements were seen in both moderate and severe COPD patients independent of medications used prior to recruitment and randomization into the SHINE study.

OS101

THE EFFICACY AND SAFETY OF INHALED FLUTICASONE FUROATE (FF)/VILANTEROL (VI) IN ASIAN PATIENTS WITH COPD

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Background and Aim of Study A once-daily (OD) inhaled corticosteroid (ICS)/long acting $beta_2$ agonist (LABA) is under development for the treatment of COPD. This study evaluated the effect on lung function and safety of three strengths of FF/VI (50/25, 100/25, 200/25 mcg) investigated in a global program, compared with placebo, in an Asian population of symptomatic COPD patients with moderate-to-severe airflow limitation.
Methods This was a randomised, double-blind, placebo-controlled, parallel-group, multi-centre study. Patients were stratified by smoking status (former/current). Study treatment was administered OD via a dry powder inhaler for 24 weeks. Primary endpoint: trough FEV_1 at the end of treatment. Secondary: CRQ-SAS dyspnoea domain. Other endpoints included diary-recorded rescue albuterol use and night-time awakenings requiring albuterol. Safety measures: adverse events (AEs), 24 h urinary cortisol, vital signs, ECG, laboratory evaluation and incidence of pneumonia.
Results The ITT population comprised 643 patients. Statistically and clinically significant increases in trough FEV_1 (L) were observed relative to placebo across all strengths of FF/VI (mean [95% CI] FF/VI 50/25: 0.140 [0.09, 0.19]; 100/25: 0.179 [0.13, 0.23]; 200/25: 0.194 [0.14, 0.25]; all $p < 0.001$, ITT). FF/VI 100/25 and 200/25 showed statistically significant improvement in CRQ-SAS dyspnoea domain despite mean difference from placebo not reaching 0.5 (change of clinical importance). FF/VI 100/25 and 200/25 significantly reduced 24 h rescue medication use and night-time awakenings requiring rescue use compared with placebo. On-treatment serious AEs were similar across all groups, although the frequency of on-treatment AEs was higher in the FF/VI 200/25 group compared with other treatments. Compared with placebo, no effect of FF/VI on urinary cortisol excretion, vital signs, ECG parameters including QTc (F), incidence of pneumonia, or laboratory evaluation including liver chemistry was observed.
Conclusion All strengths of FF/VI improved lung function with an acceptable safety profile consistent with results from the global program.
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OS102

COPD PREVALENCE AND PATIENT BURDEN IN KOREA AND JAPAN: CONTINUING TO CONFRONT (C2C) COPD INTERNATIONAL PATIENT SURVEY 2012–13

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Background and Aim of Study COPD is associated with high disease and societal burden. The C2C Patient Survey aimed to estimate the COPD prevalence and disease burden across 12 countries, including Japan and Korea, among respondents self-reporting COPD.
Methods Using probability sampling of households from the general population aged 40 yrs or older, we identified patients who self-reported either (a) physician diagnosis of COPD/emphysema/chronic obstructive airway disease, (b) physician diagnosis of chronic bronchitis, or (c) chronic bronchitis symptomatology, AND who used medication on most days or reported chronic cough with phlegm/sputum most days. A total of 300 interviews were conducted in each country using face-to-face interviews (Korea) or online survey (Japan). Standardized, translated data collection instruments included: Patient Activation Measure (PAM-13) to assess patient engagement with healthcare and COPD self-management, mMRC, COPD Assessment Test (CAT), and Work Productivity & Activity Impairment Scale (WPAI).
Results Mean age (years) was 62 in Korea and 60 in Japan. The self-reported COPD prevalence was 8% in Korea and 7% in Japan. The proportion of patients with prior diagnosis of COPD/emphysema/chronic obstructive airway disease was lower in Korea (22%) than in Japan (36%). Korean respondents reported higher levels of moderate-to severe dyspnea (46% vs. 25%) and higher mean CAT scores (24 vs. 16) than those from Japan. Korean respondents were also twice as likely to report having >= 50% impairment in daily activities (61% vs. 30%). About one-half of respondents in both countries reported very low levels of engagement with their disease management, not believing in or lacking confidence in an active patient role.
Conclusion The self-reported prevalence of COPD was similar in Korea and Japan, while the perceived burden of illness appeared to be greater in Korean respondents. Sponsored by GSK.

OS18: INTERSTITIAL LUNG DISEASE 1

OS103

HEALTH-RELATED QUALITY OF LIFE IMPACTS ON SURVIVAL IN IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study Recent studies have clarified predictors of survival in idiopathic pulmonary fibrosis (IPF), however, the impact of health-related quality of life (HRQL) on survival has not fully been studied until now. The aim of the study was to investigate relationships between HRQL and survival in IPF.
Methods We retrospectively analyzed the initial evaluation data of consecutive IPF patients who underwent multidimensional evaluation including the HRQL scoring of the St. George's Respiratory Questionnaire (SGRQ) from June 1, 2004 to June 1, 2012. Cox proportional hazard analyses were performed to examine the relationship between HRQL scores and survival.
Results 118 patients (102 men, 63 with surgical lung biopsy, mean age 65.7 ± 7.7 years) were studied. The median survival time was 47.4 (95% CI 37.3–57.4) months. The mean PaO_2, FVC % predicted, DLco % predicted, and mean pulmonary artery pressure (MPAP) were 82.6 ± 11.4 mmHg, 78.3 ± 20.1%, 56.4 ± 19.6%, and 17.1 ± 5.5 mmHg, respectively. The 6-min walk distance (6MWD) and the lowest SpO2 of the 6-min walk test (6MWT) were 570 ± 126 m, 82.4 ± 9.6%, respectively. The symptoms, the activity, the impacts, and the total score in the SGRQ (SGRQ total) were 45.9 ± 22.5, 42.6 ± 24.4, 28.5 ± 19.8, and 36.0 ± 20.0, respectively.
By univariate Cox proportional hazards analysis, the symptoms, the activity, the impacts, and the total score in the SGRQ were significant prognostic factors. BMI, PaO_2, FVC % predicted, FEV1/FVC, DLco % predicted, Baseline Dyspnea Index, 6MWD, lowest SpO_2 during the 6MWT, MPAP, and CT pattern with definite UIP were significantly associated with survival. Multivariate Cox analysis showed FVC % predicted (HR: 0.972, 95% CI: 0.958–0.986, $p < 0.001$) and SGRQtotal (HR: 1.027, 95% CI: 1.012–1.043, $p < 0.001$) were significant predictors of survival.
Conclusion SGRQtotal and FVC % predicted were independent prognostic factors in patients with IPF.

OS104

ANALYSIS OF CLINICAL PROGNOSTIC FACTORS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS LESS THAN 60 YEARS OF AGE

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Background International guidelines for idiopathic pulmonary fibrosis (IPF) recommend lung transplantation for appropriate patients with IPF, and criteria for lung transplantation have been proposed based on prognostic factors. In Japan, indications of lung transplantation are limited to patients less than 60 years old, and little is known about prognostic factors of IPF in this population.
Purpose We aimed to evaluate prognostic factors of IPF patients less than 60 years.
Methods The twenty-eight IPF patients less than 60 years were recruited among the forty-nine patients with IPF who underwent initial evaluation at Tosei General Hospital from May 2007 to December 2010. Several known prognostic factors for IPF such as level of dyspnea (Baseline Dyspnea Index; BDI), % FVC, % DLco, extent of honeycombing on HRCT, and mean pulmonary artery pressure (mPAP) were studied. Fibrosis score (Am J Roentgenol 1997; 169:977–983) was used for the evaluation of extent of honeycombing: e.g., score 2, honeycombing involving <25% of the lobe.
Result Twenty-three male and five female patients with a mean age of 53.7 years. The 2-year survival rate was 74.1%. A univariate Cox proportional-hazard model showed that % DLco (HR, 0.953;95% CI, 0.912–0.997), % FVC (HR, 0.959;95% CI, 0.927–0.993), mPAP (HR, 1.223;95% CI, 1.059–1.412) and Fibrosis score (HR, 0.117;95% CI, 0.015–0.918) at the first visit were significantly predictive of the 2-year survival. Stepwised multivariate Cox proportional analysis showed that mPAP was only a significant predictor (HR, 1.223;95% CI, 1.059–1.412). The optimal points on the receiver operating characteristic (ROC) curves for discriminating between 2-year survivors and nonsurvivors corresponded to mPAP of 18.5 mmHg (AUC 0.861, sensitivity 0.714, specificity 0.778). The 2-year survival rates of mPAP > 18.5 mmHg was 50.0%.
Conclusion The mPAP might be prognostic factors in patients with IPF less than 60 years.

OS105

RESPIRATORY HOSPITALIZATION AS A PROGNOSTIC FACTOR IN IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study The purpose of this study was to evaluate the importance of history of respiratory hospitalization as a prognostic factor in idiopathic pulmonary fibrosis (IPF).
Methods Consecutive patients with IPF who underwent evaluation including pulmonary function test from July 2008 through August 2012 and whose pulmonary function test approximately 6 months before had been available were included in the study. Prognostic significance of age, % predicted FVC, 6-month change in % predicted FVC, and history of respiratory hospitalization in preceding 6 months were analyzed.
Results Fifty-three patients (43 males and 10 females) were included. Baseline characteristics at the registration were as follows: age 72.4 ± 46.9 yrs, FVC 2.4 ± 0.9 L, % predicted FVC 79.8 ± 27.4%, 6-month change in % predicted FVC –1.7 ± 9.3% (range –42.3–25.8%), and history of respiratory hospitalization in preceding 6 months 0.2 ± 0.4 times (range 0–2 times). An observational period was 616 ± 371 days and 13 patients were dead in this period. In univariate Cox proportional analysis, % predicted FVC, 6-month change in % predicted FVC, and history of respiratory hospitalization in preceding 6 months significantly correlated with survival although age did not. In multivariate analysis, only history of respiratory hospitalization significantly correlated with survival.
Conclusion History of respiratory hospitalization in preceding 6 months is important as a prognostic factor.

OS106

CONTINUOUS SUBCUTANEOUS INJECTION OF MORPHINE FOR DYSPNEA IN PATIENTS WITH TERMINAL STAGE INTERSTITIAL PNEUMONIAS

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Background and Aim of Study Dyspnea represents a very frequent and distressing symptom in patients with terminal stage interstitial pneumonias. The purpose of this study was to assess the efficacy of morphine on the intensity of dyspnea and its effect on respiratory rate in patients with interstitial pneumonia.
Methods We retrospectively assessed data of patients with terminal stage interstitial pneumonias who were referred to palliative care team and received continuous subcutaneous injection of morphine for dyspnea between September 2010 and March 2013. We assessed dyspnea measured on Numerical rating scale (NRS) and respiratory rate before treatment (T0), 2 hours (T2) and 4 hours later (T4).
Results Twenty three patients were assessed. Median dose of morphine was 0.25 mg/h (range 0.125–0.25 mg/h), 0.25 mg/h (range 0.25–0.5 mg/h) and 0.25 mg/h (range 0.25–6.25 mg/h), median NRS was 8 (IQR 5–10), 6 (IQR 3–8) and 4 (IQR 3–7) and median respiratory rate was 36 (IQR 29–40), 34.5 (IQR 27–40.5) and 33 (IQR 28–38) at T0, T2 and T4, respectively. A significant improvement was observed in NRS (T0 versus T2; $P = 0.002$, T0 versus T4; $P < 0.001$) but not in respiratory rate. In subgroup analysis, dyspnea significantly decreased in patients using non-invasive positive pressure ventilation (NPPV), but did not significantly decreased in patients without NPPV. Respiratory rate was not significantly decreased in both subgroups.
Conclusion Continuous subcutaneous injection of morphine could be effective for relieving dyspnea of patients with terminal stage interstitial pneumonias and did not decrease respiratory rate at the dose level used. This study was supported by the grant from National Hospital Ornagization.

OS107

USUAL INTERSTITIAL PNEUMONIA IN PRIMARY SJÖGREN'S SYNDROME IN COMPARISON WITH IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study Interstitial lung disease associated with primary Sjögren's syndrome sometimes shows usual interstitial pneumonia pattern (UIP/PSS). There are few reports concerning this disease entity, and the differences from idiopathic pulmonary fibrosis (UIP/IPF) are not fully understood. Although immunosuppressive therapy including corticosteroids is not recommended in the recent guideline for UIP/IPF, whether this is also the case in UIP/PSS is unclear. The aims of this study are to compare UIP/PSS with UIP/IPF from various perspectives, and to evaluate the validity of immunosuppressive therapy on UIP/PSS.
Methods We retrospectively reviewed the medical records of consecutive UIP/PSS and UIP/IPF patients diagnosed by surgical lung biopsy and multidisciplinary discussion in Kanagawa Cardiovascular and Respiratory Center between December 1998 and May 2002. We compared clinical, radiological, and pathological characteristics between the two groups. The treatment responsiveness, if the patients were treated, was also analyzed by comparing the pulmonary function before and 1-year after immunosuppressive therapy initiation.
Results Ten (UIP/PSS) and 22 (UIP/IPF) patients were included in this study. In the UIP/PSS group, females and never smokers were predominant. Radiological honeycombing was more common, and pathological honeycombing and fibroblastic foci were more severe in the UIP/IPF group. Plasmacytes infiltration, lymphoid follicles with germinal center, and pathological changes of bronchioles and pleura were more prominent in the UIP/PSS group. The responsiveness to immunosuppressive therapy in the UIP/PSS group was significantly better than that in the UIP/IPF group.
Conclusion UIP/PSS was greatly distinct from UIP/IPF in clinical, radiological, and pathological features. In contrast to UIP/IPF patients, most UIP/PSS patients on immunosuppressive therapy experienced favorable clinical course. The application of immunosuppressive therapy to UIP/PSS may be recommended.

OS19: ASTHMA 3

OS108

WHAT ARE REASONS FOR NON-ADHERENCE IN PATIENTS WITH ASTHMA? A 24 WEEKS PROSPECTIVE TELEPHONE FOLLOW-UP RESEARCH

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Introduction The low treatment adherence of patients with Asthma is one of the biggest challenge in Asthma management. Although there are lot of research performed, most of them were designed to assessment the adherence and corresponding to influence factors in current. This is a research designed for assessing the reasons for non-adherence patients who had received treatment based on guideline, in current and next 24 weeks, by telephone follow-up.
Methods This is a 24 weeks, prospective, multicenter, telephone follow-up study performed in 12 hospitals from February to October in 2012. The interviewing and administering questionnaires have been performed by the telephone follow-up. (Registration No: ChiCTR-OCH-12002744)
Results A total of 1278 adults and 310 adolescents with asthma were enrolled in this study. The majority of patients were female (56.3%) with a mean age of 46.9 ± 12.5 years in adults. There were 53.9% female and the mean age of 6.8 ± 2.8 years in adolescents. After 24 weeks follow-up, 37.6% adults with asthma complied with treatment and 54.8% adolescents complied. The major reasons for non-adherence were "My symptoms has get control, I am no need to adherence treatment."(50.5%), "I feels the treatment is useless." (16.8%) and "Too expensive" (10.5%) in adults and with similar results in adolescents. There were 68.0% adults withdrawal treatment, and 40.4% adolescents withdrawal treatment.
Conclusions In CHINA, the inadequate understanding of the asthma treatment target is the most important reason for non-adherence rather than the economic burden. Disease education should be pay more attention in chronic management.

OS109

A CLINICAL ANALYSIS TO COMPARE THE ANTI-INFLAMMATORY EFFECT ON PERIPHERAL AIRWAY BY SALMETEROL/FLUTICASONE COMBINATION INHALER BETWEEN DPI AND pMDI PRODUCTS

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Background and Aim of Study Salmeterol/Fluticasone combination inhaler (SFC) is currently most widely used inhaled drugs for the maintenance therapy against mild to moderate persistent asthmatics in the world. Although the usefulness of dry powder inhaler (DPI) product of SFC has been well documented, the evaluation for pressurized metered dose inhaler (pMDI) product of SFC, especially for its anti-inflammatory effect, is still lacking. Therefore, we conducted a clinical analysis to compare the anti-inflammatory effect on peripheral airway by SFC between DPI and pMDI products.
Method A randomized crossover controlled trial. Patients were randomized to receive the 12-week treatment by SFC DPI 250 2 puffs/day or SFC pMDI 125 4 puffs/day. After the 4 weeks of wash-out period, patients received another crossover treatment for 12 weeks. Respiratory resistance and reactance (R5-R20, Fres) were measured by FOT which was a primary outcome. FeNO, ACT score and side effects were also examined every 4 weeks.
Results Forty-eight subjects are enrolled. Mean age is 62.4 ± 16.9 years old, FEV1.0 is 68.4 ± 13.8%, and as for the previous treatment, SFC DPI was 27 cases, while Budesonide/Formoterol combination inhaler was 19 cases. Significant improvements were observed in R5, Fres and ACT score among both treatment groups, while significant improvement in R5-R20 (0.93 ± 0.54 to 0.79 ± 0.43 cm H_2O/L/s) and FeNO (34.9 ± 23.7 to 30.2 ± 14.9 ppb) were seen only in SFC pMDI treatment group.
Conclusions It was suggested that SFC pMDI might produce stronger anti-inflammatory effect on peripheral airway, even for the asthmatics who was well-controlled by SFC DPI.

OS110

DIFFERENTIAL EFFECTS OF ASYMPTOMATIC ALLERGIC AIRWAY DISEASE ON AIRWAY INFLAMMATION AND PHYSIOLOGY IN ADOLESCENTS

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Background Bronchial asthma and allergic rhinitis often develop from childhood to adolescence. In some patients, allergic airway diseases are outgrown. However, even in such patients, we hypothesized that history of allergic airway diseases affects airway physiology and inflammation.
Objective We evaluated the effects of asymptomatic allergic airway diseases on airway inflammation and physiology in young subjects.
Methods We recruited 101 students from Nagasaki University School of Medicine. History of bronchial asthma, allergic rhinitis, and smoking were taken. Students with smoking history and current treatment were excluded. Ultimately, data of 92 students (Female : Male = 36 : 56, mean age: 24.4 ± 2.7 years) were assessed. All asthma participants were asymptomatic and had required no medicine during >2 consecutive years before study entry. Even among the students with symptomatic allergic rhinitis, the study criteria required a status of no treatment for at least the past year. Fraction of exhaled nitric oxide (FeNO) level, respiratory function and static airway resistance were determined.
Results Approximately 20% and 50% of subjects had a history of bronchial asthma and allergic rhinitis, respectively. Males showed significantly higher FeNO levels than females. Asymptomatic asthma in males and allergic rhinitis in females significantly increased FeNO compared with subjects without those conditions. Similarly, asymptomatic asthma in females and allergic rhinitis in males significantly decreased respiratory function compared with subjects without those conditions. Static airway resistance did not show any significant differences irrespective of the presence of allergic airway diseases.
Conclusions Asymptomatic allergic airway diseases potentially affect airway inflammation and physiology in young people; the effects differ between males and females.

OS111

EXACERBATIONS AND SYMPTOMS REMAIN COMMON IN PATIENTS WITH ASTHMA CONTROL: A SURVEY OF 8000 PATIENTS IN EUROPE

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Background and Aim of Study Individuals with asthma may experience symptoms, despite achieving guideline-defined control. We report data on symptoms and exacerbations in patients with GINA-defined asthma control and those with perceived control from the largest European survey of asthma.
Methods Online surveys were conducted with 8000 patients with asthma (aged 18–50 years, ≥2 prescriptions in the past 2 years), recruited via validated consumer panels from 11 countries.
Results Mean age of respondents was 35 years; 61% were women. GINA-defined levels of controlled, partially controlled and uncontrolled asthma were 20%, 35% and 45%, respectively. No respondent with GINA-defined control reported symptoms or reliever inhaler use on ≥3 days, or night-time awakening on ≥1 day, in the past 7 days; however, 35% of those with controlled asthma and 64% of those with partially controlled asthma reported symptoms on 1 or 2 days in the previous week. Of those with GINA-defined control, 7% had been treated in A&E in the past year, compared with 13% of those with partially controlled and 40% with uncontrolled asthma. Notably, of those with controlled asthma, 24% had ≥1 acute asthma exacerbation (requiring oral steroid use) in the past year. Moreover, 43% of those who perceived their asthma as controlled had an exacerbation. Of those reporting exacerbations (n = 3516), 75% did not consider their asthma to be serious. There was not a strong correlation between control level and exacerbations (r = 0.332).
Conclusions Asthma control in Europe remains sub optimal. Patients with GINA-defined control continue to have symptoms and exacerbations, highlighting a need for initiatives to improve asthma management.

OS112

ASTHMA PHENOTYPES INTEGRATING LONGITUDINAL ASPECTS OF PULMONARY FUNCTION AND INFLAMMATION

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Background and Aim of Study Clustering approach has been used to classify heterogeneous asthma population into distinct phenotypes. However, longitudinal aspects of the phenotypes have been unclear. The aim of this study was to determine the phenotypes of patients with asthma and to examine whether the defined phenotypes integrate longitudinal aspects of pulmonary function and inflammation.
Methods Adults with asthma (n = 224) receiving inhaled corticosteroids were enrolled from a cohort study in the Kinki-Hokuriku Airway disease Conference. Cluster analysis was applied to determine the phenotypes. Annual decline in forced expiratory volume in one second (FEV_1) over 8 years and biomarkers were assessed.
Results Four distinct clusters were determined: Cluster 1 (n = 25), characterised by late onset, lack of atopy, pauci granulocytic inflammation (<250 eosinophil/μL and <5000 neutrophil/μL), and preserved lung function; Cluster 2 (n = 105), early onset, atopy, eosinophilia, and a small decline in FEV_1; Cluster 3 (n = 73), late onset, refractory eosinophilia, moderate decline in FEV_1, and the highest serum periostin level among the 4 clusters; and Cluster 4 (n = 21), the poorest asthma control, mixed granulocytic (eosinophilic and neutrophilic) or neutrophil predominance, the lowest FEV_1, the greatest decline in FEV1, and the highest serum interleukin-6 level among the 4 clusters. In subsets of patients, a distinct pattern of blood granulocytes in each cluster was observed before the initiation of treatment.
Conclusion These findings indicate that distinct asthma phenotypes may integrate longitudinal aspects of pulmonary function and inflammation.

OS113

ENDOGENOUS HYDROGEN SULFIDE IN SERUM AND SPUTUM AS NOVEL BIOMARKER OF ASTHMA

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Background Hydrogen sulfide (H_2S) is considered to be the third gasotransmitter along with nitric oxide (NO) and carbon oxide (CO). However little is known about the role. We examined whether H_2S in serum or sputum can be used as a biomarker of asthma.
Methods Forty asthmatic subjects and 15 healthy volunteers were recruited in this study. Subjects were asked to answer asthma control questionnaire and take bloods, sputum, lung function tests, and fractional exhaled nitric oxide (FeNO) measurements. H_2S concentrations in sputum and serum samples of patients with severe and non-severe asthma and of healthy subjects were measured using a sulfide-sensitive electrode and compared H_2S levels with other conventional parameters.
Results H_2S levels in induced sputum from severe and non-severe asthmatic patients (27.7 ± 14.6 and 26.7 ± 8.47 mM, respectively) were significantly higher than those from healthy subjects (11.4 ± 8.38 μM; $p < 0.001$) but there was no difference between the severe and non-severe group. Serum H_2S levels were 10 times higher than in sputum and these were also higher in severe and non-severe asthmatic subjects (283 ± 81.3 mM and 280 ± 179 mM, respectively) compared to healthy subjects (152.2 ± 84.0 μM; $p < 0.05$). There was a positive correlation between sputum and blood H_2S levels ($r = 0.418$, $P = 0.017$). Sputum H_2S levels were inversely correlated with FEV1 % predicted ($r = -0.422$, $P = 0.003$), and with reversibility to salbutamol ($r = -0.541$, $P = 0.002$). There was a correlation between sputum H_2S and sputum neutrophils and macrophages ($r = 0.487$ and $r = -0.475$, $P = 0.001$, respectively), and a negative correlation between sputum H_2S and FeNO levels ($r = -0.522$, $P = 0.002$).
Conclusions Sputum H_2S levels may represent a novel biomarker of asthma, particularly useful as a marker of neutrophilic inflammation, chronic airflow obstruction and b-adrenergic bronchodilator responsiveness. However, it is not an indicator of asthma severity.

OS20: RESPIRATORY STRUCTURE AND FUNCTION

OS114

SPIROMETRIC REFERENCE EQUATIONS FOR HEALTHY CHILDREN AGED 5–15 YEARS IN GUANGZHOU, SOUTHERN CHINA

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Background Establishing and updating reference values is imperative for interpreting spirometry result, but there were few reference values for Chinese children. The reference values currently in use were developed past decade ago and the secular trends were unclear.
Objectives To produce reference equations for forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), peak expiratory flow (PEF), and forced expiratory flow at 25 to 75% of expired volume (FEF 25–75%) among children aged 5–15 years in Guangzhou, Southern China, and to compare them with other reference equations.
Methods This cross-sectional study was conducted among 422 healthy children (226 boys and 196 girls) aged 5–15 years in Guangzhou. All subjects underwent spirometric measurements by experienced technicians. Reference equations for FVC, FEV1, PEF and FEF 25–75% were derived by using the Lambda-Mu-Sigma (LMS) method based on age, height and weight, and separated for both genders.
Results Height was the strongest predictor of all spirometric parameters in comparison to age and weight. Spirometric values increased with age and height, and were significantly higher in boys than girls except FEF 25–75%. Compared with data decade previously from the same population and of Chinese children in other studies, our study got the increased values, but lower than those of white population. The coefficients of variation (CoV) of all spirometric parameters were decreasing steadily with increasing age, and the variability of FEF 25–75% was noticeably larger than for FEV1 and FVC for both sexes.
Conclusions The new reference values and the lower limit of normal (LLN) of spirometric values derived by LMS method are recommended for evaluation of spirometry in children living in Guangzhou.

OS115

FACTORS THAT INFLUENCE LUNG FUNCTION OF TRAFFIC POLICEMEN IN EAST JAKARTA

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Background Air pollution from road traffic is a serious health hazard and thus the traffic policemen who are continuously exposed to pollutant, may be at an increased risk. Types of main pollutants in the outdoor air pollution will significantly influence lung function. This study determined the factors that affect pulmonary function of traffic policemen working in the area of East Jakarta.
Method This study is a part of the major research in the areas of Jakarta, Bogor, Depok, Tangerang and Bekasi (JABODETABEK). A cross sectional study was conducted among traffic policemen of East Jakarta Region from October-November 2012. This study has assessed respiratory clinical symptoms using questionnaires of Pneumobile Project Indonesia, examined spirometry lung function, chest x-ray, and expiratory CO measurement.
Results A total of 170 subjects were included in this study. Most of them aged 41 to 50 years (48.2%), were over weight (52.9%), active smokers (53.5%), had low Brinkman Index (31.2%), have worked more than 10 years (77.5%), did not use masker (65.3%), and had normal chest x ray (95.9%). Results of Spirometry examination showed mild restriction in 16 subjects (9.4%), mild obstruction in 8 subjects (4.7%) and mixed problems in 2 subjects (1.2%). This study showed that 11 policemen who did not use masker and 12 policemen with history of work more than 10 year had mild lung restriction. There are significant association between age, Brinkman Index with lung function ($p < 0.05$), but no significant association was found between nutritional status, smoking history, working history, chest x-ray, use a masker with pulmonary function of traffic policemen ($p > 0.05$).
Conclusion This study showed that age and Brinkman Index significantly affected lung function, but there was no significant association found between lung function with nutritional status, history of smoking, working history, chest x-ray abnormalities, and use of masker among traffic policemen.

OS116

NOVEL INTERPRETATIONS OF RESPIRATORY IMPEDANCE MEASURED BY FORCED OSCILLATION TECHNIQUE BASED ON COMPUTATIONAL FLUID DYNAMICS

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Rationale Respiratory impedance measured by forced oscillation technique (FOT) in pulmonary emphysema has two significant features during expiration; negative frequency dependence of respiratory resistance and deep decline of respiratory reactance. Although the conventional interpretation has been based on phase constant models, none of them includes convective acceleration of airflow which plays important role when the air velocity is large as in the trachea and generates much larger resistance than viscous resistance.
Methods We constructed a 4D finite element lung model in which the lung displacement due to forced oscillation was superimposed on the breathing motion. Forced oscillation was given as a continuous sine wave with the amplitude of the lung volume change rate of 0.05 L/s. In addition, dynamic airway constriction during expiration was simulated. Airflow was computed by solving incompressible Navier-Stokes' equation under moving boundary condition. Then, the airflow impedance was calculated from obtained flow rate and the average lung pressure.
Results The simulation successfully reproduced the air flow resistance and inertia. We found the resistance and reactance changed according to the air volume acceleration. We also found that decrease in reactance occurred during dynamic tracheal contraction due to the increase of convective acceleration. We furthermore found that when the contracted trachea is oscillated by the forced oscillation of 20 Hz, the value of R20 reduced but R5 did not changed. We measured respiratory impedance for fifteen normal volunteers during 1 Hz rapid breathing, and obtained significant decrease in X5 and significant increase of R5-R20 in comparison with usual breath.
Conclusion It was revealed that acceleration of the breath airflow acted as an apparent negative force on the oscillation and decreased the value of reactance. It was also revealed that not only cheek but also tracheal membranous part is the cause of frequency dependence of resistance.

OS117

THE EFFECTS OF THE REGULATING RESPIRATORY RATE ON FORCED OSCILLATION TECHNIQUE PARAMETERS MEASURED BY USING A MOSTGRAPH MACHINE

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Background The forced oscillation technique (FOT) can detect impairment of lung function by measuring lung impedance during normal tidal breathing. The FOT has a disadvantage that is variability of data in each measure. The FOT parameters can fluctuate due to the change of patients' ordinary breathing. We investigated the effect of frequency of respiratory rate to measure FOT parameters in the fixing respiratory rate states.
Methods We examined 30 normal volunteers (male 13, female 17: 32.0 ± 7.8 years old) had get tested FOT parameters in the regulating the respiratory rate as 5, 10, 15 and 30/min. We measured resistance at 5 Hz (R5), resistance at 20 Hz (R20), R5-R20, reactance at 5 Hz (X5), 20 Hz (X20) and frequency of resonance (Fres) by using a MostGraph FOT machine.
Results In the each fixed respiratory rate, the mean Rrs (R5, R20, R5-R20) values and Fres increased due to the respiratory rate. The reactance parameters (X5 and X20) decreased to the respiratory rate.
Conclusion These results suggest that the FOT parameters using a MostGraph machine fluctuate due to respiratory rate.

OS118

EFFECTS OF RESPIRATORY PATTERN INTERVENTION ON DYSPNEA DURING INSPIRATORY RESISTIVE LOADING IN HEALTHY SUBJECTS

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Breathing training is one of basic programs of pulmonary rehabilitation. Generally, to alleviate dyspnea, some respiratory patterns which are known as common and general techniques such as pursed lip breathing instructed to patients with chronic respiratory disease. In this study, we focused on beneficial strategy of respiratory pattern against inspiratory resistance. We hypothesized that respiratory pattern in which expiration is deeper than inspiration might be beneficial than the opposite one. Therefore, effects of respiratory pattern intervention on dyspnea during inspiratory resistive loading were examined. Inspiratory resistance of 0, 10, 20, 30 cm H_2O/l/sec was loaded in random order in ten healthy male volunteers (age 21.6 ± 1.9 yrs). Inspiratory capacity (IC) was measured at the end of each loading. Before and during the loading, the respiration was monitored by a flow sensor, and modified Borg scale (BS) was recorded. The loading was performed 4 times. The first two were simple loading without any instruction about breathing. The latter two were performed after the instruction of the deep inspiration or expiration. Enough long times for a rest were taken between each loading. No significant changes in minute ventilation and respiratory frequency were observed during the loading without the instruction. Instead, with resistance dependent fashion, mean inspiratory flow (V_TT_I) decreased ($p < 0.05$), duty cycle (T_I/T_{TOT}) and BS increased ($p < 0.05$). Instruction of the deeper expiration significantly decreased BS (0, 10, 20, 30 cm H_2O/l/sec: 2.8 ± 1.1 vs 1.9 ± 1.3, 3.0 ± 1.2 vs 2.3 ± 1.0, 3.9 ± 1.4 vs 2.6 ± 1.1, 4.0 ± 1.4 vs 3.2 ± 1.3, respectively, $p < 0.05$). BS was linearly correlated with (T_I/T_{TOT}) and (V_TT_I). The changes in the individual BS were correlated with the changes in IC. In conclusion, the instruction of the deeper expiration was beneficial compared to the breathing without any instruction or with the instruction of the deeper inspiration. Mechanisms of those might involve the physiological significance of IC.

OS119

RELATIVE CONTRIBUTION OF CT-BASED EMPHYSEMA AND AIRWAY WALL AREA IN PREDICTING AIRFLOW LIMITATION IN COPD

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Background and Aim of Study Airflow limitation in COPD is resulted from the combination of emphysema and airway remodeling. However, the relative contribution of each component to the decline of lung functions is still unclear. The aim of this study was to determine the relative contribution of CT-based emphysema and airway wall area in predicting the airflow limitation in patients with COPD.
Methods Pulmonary function tests and volumetric chest CT were performed in 145 male smokers with COPD. CT-based emphysema was estimated as the ratio of lung volume with attenuation less than –910 Hounsfield unit to total lung volume (LAV%). CT-based airway wall area was estimated as the square root of wall area of a hypothetical airway with internal perimeter of 10 mm ($Aaw^{1/2}$ at Pi10). The estimates of effect size of LAV% and $Aaw^{1/2}$ at Pi10 in predicting the airflow limitation were presented as standardized coefficients in the multiple regression analyses in which FEV_1/FVC or FEV_1 was outcome variable; LAV% and $Aaw^{1/2}$ at Pi10 were predictors.
Results Of 145 patients, 13 (9.0%) was in stage I, 63 (43.4%) stage II, 53 (36.6%) stage III, and 16 (11.0%) stage IV. Mean (SD) LAV% was 22.8% (16.0%). Mean (SD) $Aaw^{1/2}$ at Pi10 was 3.78 mm (0.13 mm). Both LAV% and $Aaw^{1/2}$ at Pi10 independently predicted FEV_1/FVC (adjusted $R^2 = 0.385$) or FEV_1 (adjusted $R^2 = 0.305$). However, the standardized coefficient of LAV% was twice as big as that of $Aaw^{1/2}$ at Pi10 in predicting FEV_1/FVC (–0.63 versus –0.31) or FEV_1 (–0.56 versus –0.29).
Conclusion In patients with COPD, CT-based emphysema has a greater contribution in predicting airflow limitation than CT-based airway wall area.

OS120

ROLES OF VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR –1 SIGNALING IN COMPENSATORY CONTRALATERAL LUNG GROWTH AFTER UNILATERAL PNEUMONECTOMY

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Compensatory lung growth has been widely used to investigate processes and programs of alveolization because the remaining lung can be kept intact and volume loss is controlled. Vascular endothelial growth factor (VEGF) has been reported as one of the important factors for blood formation during lung growth and repair, but the precise mechanism is not well understood. When mice underwent left pneumonectomy, the right lung was increased in VEGF transgenic mice compared to that in wild type mice (WT mice). Compensatory lung growth was significantly suppressed in VEGF neutralizing antibody treated mice and VEGF receptor 1 tyrosine kinase deficient mice (TK–/– mice) but not in ZD6474, VEGFR2 tyrosine kinase inhibitor treated mice. In TK–/– mice, the mobilization of progenitor cells expressing VEGFR1+ cells from bone marrow, and the recruitment of these cells to lung tissue, were suppressed. WT mice transplanted with TK–/– mice/green fluorescent protein (GFP)+ bone marrow cells (BM cells) exhibited a significantly decreased expression of GFP+/Aquaporin 5 (AQA), GFP+ Surfactant protein A (SPA), and GFP + VEGFR1+ cells compared to those in WT mice transplanted with WT/GFP+ BM cells. GFP+/VEGFR1+ cells co-stained with SPA and AQA. These results suggested that VEGFR1-TK signaling contributes to compensatory lung growth through mobilizing VEGFR1+ cells that differentiated to alveolar type I and II cells.

OS121

4D MODEL GENERATOR OF THE HUMAN LUNG; LUNG4CER

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We have developed free software application which generates 4D (= 3D + time) lung models for the purpose of studying lung anatomy, physiology, and pathophysiology. The application is named Lung CataChiCalaCli-er, alias Lung4Cer, which consists of two Japanese words, Catachi (= shape, structure) and Calacli (= machine, function). Furthermore, Cata means space, Chi means energy, Cala means direction or relation, and Cli means cyclic time. Indeed, these four words, 4C, are the most basic concepts of physics, and represent cyclic living activity in the 4D world. Lung4Cer generates a text file which is visualized by a free software application, ParaView. It is one of the most popular visualization software for science, and easily obtained via internet. Users can observe how the lung structures including the airway tree and alveoli move during breathing. In addition, origami models for the trachea and for the alveolar system are added in the manual. There are several versions of Lung4Cer from basic lung morphology to advanced airflow computations simulating clinical pulmonary function tests. They can be downloaded through the first author's personal homepage (http://www7b.biglobe.ne.jp/~lung4cer). All versions are designed so as to be operated on a common PC. Users can select model types according to their purposes and available computer resources. Pathologic Lung4Cer (PL4Cer) is for simulating histologic sections of the diseased lung parenchyma such as emphysema and interstitial pneumonia. CFD4Cer is designed so as to output a file set for simulating airflow during breathing by the use of computational fluid dynamics (CFD). PFT4Cer is an advanced version of CFD4Cer for simulating clinical pulmonary function tests. At present, spirometry, single-breath nitrogen washout test, and respiratory impedance measurement by forced oscillation technique are available.

OS21: OTHERS 1

OS122

CLINICAL CHARACTERISTICS OF SECONDARY PULMONARY ALVEOLAR PROTEINOSIS COMPLICATED WITH MYELODYSPLASTIC SYNDROME IN JAPAN

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Subject Secondary pulmonary alveolar proteinosis (SPAP) consists of approximately 10% of acquired PAP. We have reported that hematological disorders are the most common underlying disease, of which 74% cases demonstrated myelodysplastic syndrome (MDS). However, there is little information for SPAP complicated with MDS (SPAP/MDS). The aim of this study is to define the clinical characteristics of those cases.
Methods We have collected thirty one cases of SPAP/MDS since 1999 to 2013 in Japan. SPAP/MDS has been diagnosed by both pathological findings of PAP and negative GM-CSF autoantibody in patients with MDS. This study is retrospective chart study.
Results Median age at diagnosis of SPAP/MDS was fifty one years old and M/F ratio was 1.58. Duration from onset of MDS to diagnosis of SPAP/MDS was 23 months at median value. Refractory anemia was the frequent subtype of MDS according to WHO criteria. Interestingly, a karyotype with trisomy 8 had been found in 13 cases (42%). The majority of those cases had any clinical symptoms. Median value of serum KL-6, SP-D, and SP-A were higher than normal range. 10 cases had already been worse status with respiratory failure at diagnosis of PAP. Both the median value of % VC and FEV1% were normal range at diagnosis of PAP, whereas those of % DLCO was remarkable lower than 80%. The prognosis of SPAP/MDS was poor survival rate with 85.6%, 64.7%, 54.8% for 24, 48, 72 months, respectively.
Conclusion Complication with PAP passively exacerbates the prognosis of MDS. For the reason, it is suggested that the complication increases the risk for respiratory failure and/or pulmonary infections. To evaluate the prognosis of MDS/SPAP accurately, we think that the number of 31 cases is still small. Future international collaboration may overcome this difficulty.

OS123

RELATIONSHIP BETWEEN SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR-D LEVELS AND DISEASE SEVERITY IN LYMPHANGIOLEIOMYOMATOSIS

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Backgrounds Lymphangioleiomyomatosis (LAM) is a rare and progressive cystic lung disease found in women of childbearing age. Serum vascular endothelial growth factor-D (VEGF-D) is a useful marker for distinguishing LAM from other cystic lung diseases, but the relationship with disease severity remains unclear.
Methods We measured serum VEGF-D in 199 LAM patients (all females, 179 sporadic and 20 TSC-associated), and classified them as follows; Group A, patients with pulmonary LAM alone (n = 120); Group B, patients with chylous effusion (n = 30); and Group C, patients with extrapulmonary LAM, but without chylous effusion (n = 49). We also determined VEGF-D in LAM-associated chylous effusion (n = 11), and examined the relationship between its levels and clinical characteristics.
Results Mean serum VEGF-D level was 2,480 pg/ml (range 260–16,800) and median was 1,603 pg/ml. 158 patients (79.4%) were pathologically diagnosed, while 41 patients had the clinical diagnosis from a combination of characteristic computed tomography findings and an elevated serum VEGF-D. In Groups A and B, DLCO negatively correlated with serum VEGF-D (Group A, $r = -0.250$, $p = 0.020$ and Group B, $r = -0.380$, $p = 0.073$), but no significant correlation was evident in Group C ($r = -0.129$, $p = 0.398$). In Group B, serum VEGF-D were significantly greater than other Groups, and VEGF-D levels in chylous effusion were further increased as compared with serum levels (mean, 10,839 vs. 5,098 pg/ml, $p < 0.001$).
Conclusion Serum VEGF-D levels at the diagnosis are correlated with the disease severity in patients with lone pulmonary LAM. As reported in the precedent studies, LAM patients with lymphatic involvement showed the highest serum VEGF-D level among the entire LAM patients. Serum VEGF-D which LAM cells produce is released in the lymphatic fluid and it's also considered to be involved in the formation of LAM lesions.

OS124

MPO-ANCA POSITIVE GRANULOMATOSIS WITH POLYANGITIS (WEGENER'S) MAY BE EQUATED TO PR3-ANCA POSITIVE CASES: COMPARATIVE INVESTIGATION OF CLINICAL AND RADIOLOGICAL FINDINGS

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Background It's necessary for pulmonologists to know profoundly about granulomatosis with polyangiitis (GPA) because of high frequency of upper respiratory tract and pulmonary manifestation. Altough PR3-ANCA (C-ANCA) is usually found in GPA, MPO-ANCA (P-ANCA) positive GPA is also known to exist. However, sufficient investigation has not been conducted for P-ANCA positive GPA.
Objectives To retrospectively review GPA positive for P-ANCA or C-ANCA, document any differences in clinical features and outcomes.
Methods From December 2000 to March 2013, 14 patients (pts) were newly diagnosed with GPA based on the European Medicine Agency algorithm at Kurashiki central hospital. The comparison of clinical presentation was conducted for the C-ANCA group and P-ANCA group.
Results <Characteristics> ANCA was detected in all pts. Positive rate was 50% for both C-ANCA and P-ANCA (7 pts each). C-ANCA group included 71% of male, whereas P-ANCA group included 71% of female. In C-ANCA group, most common symptoms were exudative otitis media, hematuria and proteinuria (57% each). In P-ANCA group, purulent rhinorrhea and cough was most common (86% each). The incidence of common symptoms mostly resemble between two groups. <CT Findings> Pulmonary manifestations were found in all pts. In both groups, nodular shadow was most common (86% each), followed by thickening of tracheal and bronchial walls (57% each). The median number of nodules was greater for P-ANCA group. The incidence of cavitation was only 2.6%. <Treatment and Outcome> All pts were administered steroids, and cyclophosphamide was used concomitantly at 87% in both groups. Relapse was observed in 2 pts of C-ANCA group. Only 1 pts of C-ANCA group died from infection.
Conclusions High detection rate of P-ANCA in GPA pts was noteworthy. No marked difference was observed in clinical presentation between C-ANCA group and P-ANCA group. Search for granulomatous finding in the upper and lower respiratory tract is important even in P-ANCA positive cases.

OS125

MYASTHENIA GRAVIS WITH THYMOMA IN OUR HOSPITAL

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Background and Aim of Study Thymoma is most common anterior mediastinal tumor in the middle-aged population. Thymoma patient sometimes present myasthenia gravis symptoms such as ptosis, dysphagia and dyspnea. We had 52-year-old man who presented with ptosis, double vision, dysphagia and dysarthria. Later, we recognized he had mediastinal mass. Our aim of this study is to clarify clinical characteristics of thymoma with myasthenia gravis at out hospital.
Methods We reviewed medical records of thymoma patients including age, gender, clinical symptoms, symptom duration, laboratory data, treatment and pathology from January 2002 to June 2013 retrospectively.
Results We identified 21 thymoma patients over a decade. Among them, five patients had myasthenia gravis. Median age was 52.8 (47–63). Two were men and three were woman. Only one patient was smoker. Median disease duration was 4.5 months (0.25–7). In terms of clinical symptoms, all five patients had ptosis and four patients developed dysphasia. In laboratory findings, all patients had positive for anti-acetylchorine receptor antibody. Median value of serum anti-acetylchorine receptor antibody was 21.6 (15–29.2). All patients had positive for edrophonium test. In pathology of thymectomy, patients had Type A or Type B2 according to WHO staging. Regarding treatment, only one patient received plasma exchange two times for severe symptoms during acute phase and all patient's clinical symptoms in remission with prednisolone and pyridostigmine.
Conclusion Approximately a quarter of our thymoma patients had myasthenia gravis at our hospital. These patients main symptoms were ptosis and dysphasia. Combination of thymectomy with prednisolone and pyridostigmine are effective for our cohort.

OS126

STEROIDS FOR PULMONARY INVOLVEMENT IN LEPTOSPIROSIS: A META-ANALYSIS

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Background Pulmonary involvement in leptospirosis is associated with rapid clinical deterioration and high mortality. The role of steroids in treating the immunologic and toxin mediated pulmonary insult in leptospirosis has been described in literature albeit in anecdotal reports. A meta-analysis of studies using steroids as adjunct to standard care among leptopsirosis patients with pulmonary manifestations of the disease was done with reduction in mortality as the primary outcome.
Methods Authors included all available randomized and nonrandomized studies on patients ages 15 and above, with pulmonary symptoms of leptospirosis, who were given steroids of any type in addition to standard care. Medline, Cochrane, reference lists of articles and local journals were searched. Contact with authors and experts in pulmonary medicine and infectious diseases were done. Three reviewers independently did trial selection and assessed methodologic quality of randomized studies using the Cochrane Collaboration Criteria and the Downs and Black Tool for nonrandomized studies. Disagreements were resolved by consensus. Data were extracted and analysed using Review Manager Version 5.
Results Three nonrandomized prospective cohorts and one randomized controlled trial were reviewed after appropriate selection. Nonrandomized studies showed that intravenous methylprednisolone 500–1000 mg/day or dexamethasone 200 mg/day for 3 days followed by 1 mg/kg/day oral prednisolone for 7 days or methylprednisolone 8 mg/day for 5 days decreased mortality among patients with pulmonary leptospirosis (OR 0.20 95% CI 0.09–0.45; $chi^2 = 0.44$, $I^2 = 0\%$). The randomized trial showed no mortality benefit with addition of dexamethasone to standard care. Methylprednisolone decreased the need for mechanical ventilation in one study.
Conclusion Data from nonrandomized studies suggest a mortality benefit of steroids in pulmonary leptospirosis. Randomized trials are needed to investigate the therapeutic effects of steroids and to evaluate outcomes including safety and tolerability.

OS127

PREMATURE EJACULATION WITH ANTI-TUBERCULOSIS DRUGS

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Aim To Study the incidence of Premature Ejaculation (PE) in adult male patients on anti-tuberculosis treatment (ATT) under Category I from RNTCP.
Methods 150 adult males with no previous history of Diabetes and sexual dysfunction, who were started on ATT, were enrolled in the study. These patients were followed during the course of therapy and 6 months after completion of ATT, for sexual function and PE. PE was diagnosed when the patients on self assessment had intra vaginal discharge time of less than 1 minute. Patients were questioned at 2 months, 6 months of treatment and 3 months and 6 months after completion of treatment regarding their libido and PE.
Results Of the 150 patients enrolled into the study, 12 patients dropped out before the completion and could not be traced. The remaining 138 patients were followed and assessed at 2, 6, 9 12 after start of treatment. During the course of treatment, 31 patients complained of loss of libido after starting treatment.14 patients complained of PE at months of ATT. Of these, 10 patients still complained of PE at the end of 6 months. At the end of 12 months, 4 of them were satisfied with their sexual performance and the remaining 6 had to be referred for counseling. At the end of 12 months, 23 patients complained of loss of libido.
Conclusion There appears a definite relation between ATT and sexual function as 31 of 138 (22.46%) complained of loss of libido. PE was complained by 14 patients during Intensive phase (10.14%). Most of the patients recovered their sexual function and by the end of 6 months after treatment only 6 still complained of PE (4.37%) and 23 had loss of libido (16.6%).

OS128

END-OF-LIFE DECISION MAKING; ETHICS AND PRACTICES OF THE RESPIRATORY SPECIALISTS: A FILIPINO PERSPECTIVE

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Background Advances in medicine have greatly improved the ability to treat seriously ill patients and prolong life but with increasing recognition that extension of life might not always be an appropriate goal. In these cases, the objective is to provide guidance for end-of-life decision-making.
Methods A web-based, cross-sectional study was performed involving the members of the Philippine College of Chest Physicians using a validated 38-item questionnaire covering the current knowledge, behaviour and practices of Filipino respiratory specialists over an 8-week period.
Results A total of 116 (28%) respiratory specialists sent their responses and 48.3% is from the National Capital Region. Majority (88.8%) were general pulmonary medicine specialists from private hospitals (69.0%). Most common conditions with end-of-life issues were lung malignancy (64.7%) and COPD (47.4%). Majority (83.2%) usually advise a Do not attempt resuscitation/Do not intubate (DNAR/DNI) order. Patient's decision (38.8%) is the most important factor influencing withholding of therapy advise. Futility (60%) is the most common criteria in initiating end-of-life decisions. Almost 60% of physicians consider opiods to relieve dyspnea. More than half (54.8%) of patients opt to receive non-invasive ventilation as a ceiling of ventilatory care. All physicians involves the patient's family in the decision-making process. The most frequent assistance is sought from the ethics committee (47.5%) and 90% of the patients seek religious advice. More than 80% of terminally-ill patients do not have an advanced written directives.
Conclusion This national survey of Filipino respiratory specialists with response rate of 28%, showed that terminally-ill Filipino patients are still not used to written advanced directives. Patient and family are the most important end-of-life decision-makers with religion as an important influence. Non-invasive ventilation as well as use of opiates are underutilized. Futility, physical suffering and quality of life more than medical economics are considered the most important crieria for end-of-life decisions.

OS22: INTERSTITIAL LUNG DISEASE 2

OS129

POOR PROGNOSTIC FACTORS FOR INTERSTITIAL LUNG DISEASE (ILD)-RELATED DEATH IN JAPANESE NON-SMALL-CELL LUNG CANCER (NSCLC) PATIENTS IN THE POLARSTAR STUDY

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Background A large-scale surveillance study (POLARSTAR) was implemented to investigate erlotinib safety and efficacy in Japanese patients, focusing on factors that may contribute to the onset of ILD in patients receiving erlotinib. Primary risk factors for erlotinib-induced ILD are reported as: concurrent/previous ILD, existing emphysema/chronic obstructive pulmonary disease or lung infection, smoking status and ECOG performance status 2–4.
Methods All NSCLC patients in Japan receiving erlotinib between December 2007 and October 2009 were enrolled; observation period: 12 months. "ILD-like" events were assessed by an independent ILD review committee. ILD was defined as all "ILD-like" events excluding those events deemed non-ILD by the review committee. Risk factors for poor prognosis concerning ILD death were analyzed by multivariate analysis using a logistic regression model.
Results A total of 10,708 patients were enrolled by the data cut-off of 12 October 2009, with data available for 9,909 patients. Of the 491 patients who experienced "ILD-like" events, 93 were not evaluated by the review committee due to lack of imaging data. A total of 310 patients (125 of whom had died) with confirmed ILD were assessed by multivariate analysis. Sixty-two events were deemed non-ILD and 26 events could not be definitively categorized as ILD by the review committee using image evaluation. The multivariate analysis identified ECOG performance status 2–4 (adjusted odds ratio: [OR] = 2.5), remaining normal lung area (OR = 3.1) and interstitial pneumonia with concomitant honeycomb lung (OR = 6.7) as poor prognostic factors for ILD-related death. However, pre-existing interstitial pneumonia by grade of severity was not identified as one of these factors, which could be attributed to practical bias in this surveillance study.
Conclusions Patients with these poor prognostic factors may need to be carefully selected for therapy, with close monitoring of lung function during treatment with erlotinib.

OS130

ANTI-ARS ANTIBODY POSITIVE INTERSTITIAL LUNG DISEASE: A COMPARISON OF CLINICAL CHARACTERISTICS IN AUTOANTIBODY SUBTYPES

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Background and Aim of Study Autoantibodies against aminoacyl-tRNA synthetases (ARS) are highly associated with interstitial lung disease (ILD) and inflammatory myositis. They has been classified into eight subtypes; anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, anti-OJ, anti-KS, anti-Zo, and anti-Ha. Although ILD with anti-ARS antibodies has been increasingly recognized, the clinical characteristics according to the antibody specificity remain unknown. The aim of this study was to investigate common and different features between the subtypes of anti-ARS antibodies.
Methods We reviewed 54 patients with anti-ARS antibody positive interstitial lung disease. At their first visit, we examined patient characteristics, symptoms, chest computed tomography (CT) findings, hematological and bronchoalveolar lavage fluid (BALF) test results, and pulmonary function test results. We compared the features among anti-ARS-based subgroups.
Results Of 54 patients, anti-ARS antibodies included anti-EJ (n = 19), anti-Jo-1 (n = 13), anti-PL-7 (n = 7), anti-PL-12 (n = 6), anti-KS (n = 6), and anti-OJ (n = 3). At the initial visit, polymyositis and dermatomyositis (PM/DM) was associated with anti-Jo-1 (78%), anti-PL-7 (71%), and anti-EJ (60%). On the other hand, idiopathic ILD was associated with anti-PL-12 (83%), anti-KS (71%), and anti-OJ (66%). Total lung capacity % predicted was slightly decreased in the patients with anti-PL-12, anti-KS, and anti-OJ. Common features among the subgroups included volume loss in lower lobes, ground-glass opacities, reticular shadows, and traction bronchiectasis on chest CT, and high percentage of lymphocytes in BALF.
Conclusion Patients with anti-ARS antibody-positive ILD have similar pulmonary manifestations according to anti-ARS specificity, except for the different frequency of PM/DM.

OS131

COMPARISON OF NSIP WITH OR WITHOUT ANTI-ARS ANTIBODY IN IDIOPATHIC INTERSTITIAL PNEUMONIA

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Background Autoantibodies against aminoacyl-tRNA synthetases (ARS) are highly specific for polymyositis and dermatomyositis (PM/DM). Recently, we reported that the patients with anti-ARS antibody-positive interstitial pneumonia had common pulmonary manifestations regardless of the presence of PM/DM. However, the common and different features between idiopathic NSIP patients with and without anti-ARS antibodies are unknown.
Method We reviewed 54 patients with idiopathic NSIP who screened for the detection of anti-ARS antibodies from Jan 2003 to Dec 2009. At their first visit, clinical manifestations in the patients with anti-ARS antibodies (ARS+ group) were compared with those in the patients without anti-ARS antibodies (ARS- group).
Result Of 54 patients, 22 patients had anti-ARS antibodies, and most patients were female (16/22 patients). More patients with anti-ARS antibodies had dyspnea on exertion, nail fold bleedings, and finger swellings than the patients without anti-ARS antibodies ($p < 0.05$). The ARS+ group had lower PaO_2 (80.2 mmHg vs 84.4 mmHg), FRC % predicted (76.9% vs 86.6%), TLC % predicted (73.9% vs 90.2%), and higher RV/TLC (31.6% vs 28.7) than the ARS- group. The cell fractionation of BALF showed higher neutrophils in the ARS+ group (8.9% vs 5.8%). Lung involvements in the ARS+ group have a good response to immunosuppressive therapy and a chronic clinical course.
Conclusion The ARS+ group had some different clinical features in comparison with the ARS- group, and had lower lung volume at their first visit regardless of good response to treatment.

OS132

ANTI-CADM-140/MDA5 AUTOANTIBODY TITER PREDICTS DISEASE OUTCOME IN PATIENTS WITH DERMATOMYOSITIS AND RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE

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Anti-CADM-140/MDA5 antibody titer could predict outcomes of interstitial lung disease (ILD) as well as monitor disease activity in patients with dermatomyositis (DM) and ILD. However, that may be controversial because the disease is heterogeneous and therefore, the choice of therapy is often individualized. We examined clinical records of patients with DM and ILD to confirm whether the antibody titer predicts outcomes in a different cohort of patients with the disease. We reviewed clinical records of patients with ILD associated with DM treated in the Niigata University Medical and Dental Hospital. Anti-CADM-140/MDA5 antibody titer was kindly measured by Dr. Sato, Tokai University School of Medicine using preserved serum from the patients before treatment. We compared results of laboratory tests between responders and non-responders. In total, 13 patients were enrolled into the study. All of them were diagnosed as amyopathic DM. Among them, 4 patients did not respond to intensive immunosuppressive therapy including intravenous methylprednisolone, followed by oral prednisolone and cyclosporine. In 3 of them, the third immunosuppressive agents were also added: intravenous cyclophosphamide for two and mycophenolate mofetil for one patient. Nine patients responded to immunosuppressive therapy. Although two of them had high titer of the autoantibody, one was successfully treated by triple immunosuppressive agents, and the other with direct hemoperfusion with polymyxin B-immobilized fiber column (PMX-DHP). In comparison between responders and non-responders, although we found no statistical differences in white blood cell counts, CRP, AST, ALT, LDH, CK, Alb, KL-6, or P/F ratio, anti-CADM-140/MDA5 antibody titer of non-responders was significantly higher than that of responders. Anti-CADM-140/MDA5 autoantibody titer can predict outcomes in patients with ILD associated with CADM. Intensive immunosuppressive therapy with PMX-DHP may be effective to even those who have high titer of the autoantibody.

OS133

IS THERE A DIFFERENCE BETWEEN IDIOPATHIC PULMONARY FIBROSIS AND AUTOIMMUNE/CONNECTIVE TISSUE DISORDER RELATED PULMONARY FIBROSIS?

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Introduction Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause and until now there is no proven pharmacologic therapy.
Objective To compare the demographics and lung function tests between IPF group and autoimmune/connective tissue disoreder related pulmonary fibrosis group.
Methods Data were retrieved from CGH MRO (Medical Record Office) from 1990 till 2012. All patients with a confirmed diagnosis of IPF and autoimmune/connective tissue disorder related pulmonary fibrosis were included in the study. Patients who did not have complete spirometry, lung volumes and DLCO were excluded.
Results 7 patients with confirmed diagnosis of IPF and 10 patients with confirmed autoimmune/connective tissue disorder related pulmonary fibrosis were included in the study. IPF group were older (67.57 ± 16.76) compared to autoimmune/connective tissue disorder related pulmonary fibrosis group (56.60 ± 15.09). IPF group were all males [7/7 (100%)] whereas autoimmune/connective tissue disorder related pulmonary fibrosis group were mainly females [7/10 (70%)]. Both IPF [6/7 (85.71%)] and autoimmune/connective tissue disorder related pulmonary fibrosis [9/10 (90%)] groups were mainly Chinese. IPF group had lower BMI (21.73 ± 3.42) compared to autoimmune/connective tissue diorder related pulmonary fibrosis group (22.46 ± 2.40). More patients in the IPF group had co-morbidity [4/7 (57.14%)], smoking history [4/7 (57.14%)] than in the autoimmune/connective tissue disorder related pulmonary fibrosis group [co-morbidity 2/10 (20%) and smoking 1/10 (10%)]. IPF group had lower FVC (70.57 ± 26.80%), FEV1 (81.57 ± 23.71%), TLC (75.71 ± 20.20%), RV (64.00 ± 10.41%), RV/TLC (35.14 ± 7.90%) as compared to autoimmune/connective tissue disorder related pulmonary fibrosis group [FVC (75.40 ± 20.29%), FEV1 (87.10 ± 24.11%), TLC (88.20 ± 23.54%), RV (89.40 ± 37.64%) and RV/TLC (36.20 ± 12.31%)]. Autoimmune/connective tissue disorder related pulmonary fibrosis had lower DLCO (52.80 ± 13.86%) than IPF group (65.71 ± 39.30%).
Conclusion IPF group were older, predominantly male, had lower BMI, more co-morbidity and smoking history compared to autoimmune/connective tissue disorder related pulmonary fibrosis group in our study. IPF group had worse lung function tests than autoimmune/connective tissue disorder related pulmonary fibrosis group.

OS134

PROGNOSTIC SIGNIFICANCE OF LUNG-DOMINANT CTD ON USUAL INTERSTITIAL PNEUMONIA

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Rationale Fisher et al proposed a new disease concept of lung-dominant connective tissue disease (LD-CTD) which has positive autoimmune antibodies for CTD with falling short of allowing a clear diagnosis of CTD. However, the prognostic significance of LD-CTD still remains uncertain.
Objective The aim of this study was to evaluate the prognostic significance of LD-CTD among idiopathic usual interstitial pneumonia (UIP).
Methods We retrospectively reviewed 191 patients with interstitial lung disease who underwent surgical lung biopsy and multidimensional analysis at Tosei General Hospital between 2008 and 2011, and patients with idiopathic UIP were recruited. Among idiopathic UIP, LD-CTD was diagnosed serologically based on the criteria proposed by Fischer et al. (Chest 2010;138;251–256). Cox's proportional hazards regression analysis was used to determine predictors of mortality among idiopathic UIP. In an effort to evaluate LD-CTD as an independent prognostic predictor, stepwise method was used.
Results Seventy-three patients with idiopathic UIP (55, men; mean age, 64.3 ± 0.88 years; FVC % predicted, 81.3 ± 2.23%, DLco % predicted 55.8 ± 1.89%) were studied. Idiopathic UIP consisted of 28 patients with LD-CTD/UIP and 45 patients with IPF/UIP. Univariate Cox's proportional hazards regression analysis showed that initial FVC (hazard ratio = 0.488; 95% CI, 0.280–0.848; P = 0.011), the lowest SpO2 during a 6-Minute Walk Test (6MWT) (hazard ratio = 0.998; 95% CI, 0.996–1.000; P = 0.033), Initial Borg Dyspnea Index (hazard ratio = 0.874; 95% CI, 0.773–0.988; p = 0.032), and LD-CTD/UIP (hazard ratio = 0.471; 95% CI, 0.156–1.118; p = 0.082) were significant prognostic factors. Stepwise multivariate analysis showed that LD-CTD/UIP (hazard ratio = 0.341; 95% CI, 0.126–0.925; p = 0.035) along with initial FVC (hazard ratio = 0.335; 95% CI, 0.179–0.628; p = 0.001) and the lowest SpO2 during a 6MWT (hazard ratio = 0.976; 95% CI, 0.961–0.990; P = 0.001) were independently associated with better survival inidiopathic UIP.
Conclusion Our study revealed that LD-CTD/UIP, initial FVC and the lowest SpO2 during a 6MWT were independent predictors of mortality in the studied UIP patients. LD-CTD/UIP might be a distinct clinical phenotype in UIP.

OS23: RESPIRATORY INFECTIONS (NON-TUBERCULOSIS) 1

OS135

CLINICAL CHARACTERISTICS OF PATIENTS WITH CHRONIC PULMONARY ASPERGILLOSIS; RETROSPECTIVE ANALYSIS OF PATIENTS WITH ISOLATION OF ASPERGUILLUS SPECIES FROM RESPIRATORY SAMPLES

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With the advancement of anti-fungal drugs, it becomes more important to diagnose chronic pulmonary aspergillosis (CPA). When Aspergillus species are isolated from respiratory samples, it is not easy to distinguish CPA from colonization. The aim of this study is to clarify the clinical characteristics of CPA and colonization.
Methods We retrospectively extracted one hundred twenty-five patients with isolation of Aspergillus species from respiratory samples (sputum or bronchioloalveolar lavage fluid) between 01/2001–12/2011 at our hospital. Patients diagnosed with CPA were analyzed of its clinical characteristics, compared with patients with isolation of Aspergillus species as colonization.
Results Median age of patients was 72 years-old (range 32–92). Fifty four (43%) were women. The most frequent Aspergillus species isolated was Aspergillus fumigatus (68 patients), followed by Aspergillus niger with 36 patients, Aspergillus flavus 10, Aspergillus terreus 4, Aspergillus nidulans 1, and Aspergillus spp 16. Thirty-one (25%) were diagnosed with CPA, whereas eighty-nine (71%) with colonization and five (4%) with ABPA. When compared with colonization, CPA included more men (CPA vs colonization; 86.7% vs 49.3%), with low BMI (18.45 kg/m^2 vs 21.09 kg/m^2). As to underlying pulmonary diseases, CPA patients had a significantly higher prevalence of sequalae of pulmonary tuberculosis (40% vs 8%) and a history of thoracic surgery (43% vs 13%) than colonization. On the other hand, bronchial asthma is less frequent in CPA group than colonization (0% vs 15%). We found no significantly important underlying extra-pulmonary diseases. Positivity of Aspergillus antigen is 64% in CPA group and 14% in colonization. CPA patients have significantly shorter survival than colonization (median survival time from isolation: CPA, 1126 days; colonization, not reached; p = 0.007).
Conclusion CPA shows distinct clinical characteristics from colonization.

OS136

LOOP-MEDIATED ISOTHERMA AMPLIFICATION METHOD FOR DIAGNOSING PNEUMOCYSTIS PNEUMONIA IN NON-HIV PATIENTS WITH PULMONARY INFILTRATES

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Background A new specific DNA amplification technique called loop-mediated isothermal amplification (LAMP) was developed recently. LAMP method for diagnosing pneumocystis pneumonia (PCP) was administered in our hospital from April 2010.
Method We reviewed the medical records of 134 non-HIV patients who underwent either polymerase chain reaction (PCR) or LAMP for the diagnosis of PCP from December 2008 to June 2013. Patients were divided into two groups; 63 patients with conventional outsoursing PCR (non-LAMP group) and 71 patients with in-hospital LAMP (LAMP group). PCP was diagnosed on the basis of the following: A. microbiological analysis of respiratory samples by use of PCR, LAMP, conventional staining with Grocott methenamine silver stain and Diff-Quick. B. radiographic findings on chest image compatible with PCP. C. compatible clinical findings, including dyspnea, cough, and fever.
Results Final diagnoses were as follows; 28 patients of PCP, 82 patients of non-PCP and 23 patients of undetermined diagnosis. About underlying disease, 46 patients have connective tissue disease and 30 patients have hematologic disorder. In non-LAMP group, induced sputum (IS) was obtained in 42 patients and bronchoalveolar lavage (BAL) fluid in 21 patients. In LAMP group, IS was obtained in 51 patients and BAL fluid in 20 patients. Sensitivity were 71.4% in PCR and 94.4% in LAMP ($p = 0.06$). Specificity were 96.3% in PCR and 95.2 % in LAMP. Average lag from admission to PCP diagnosis were 6.9 days in non-LAMP group and 3.4 days in LAMP group ($p = 0.001$). Among 14 non-PCP patients who underwent unnecessary PCP treatment, the median duration of PCP treatment were 7 days in non-LAMP groups and 2 days in LAMP group ($P = 0.005$).
Conclusion LAMP method for diagnosing PCP is a rapid nucleic acid amplification method with high specificity and sensitivity. Early diagnosis of PCP in non-HIV patients is possible by in-hospital LAMP method.

OS137

USEFULNESS OF THE ANTI- GLYCOPEPTIDOLIPID-CORE ANTIBODY TO MAC LUNG DISEASE (CONTRAST WITH CLINICAL SYMPTOMS, BACTERIOLOGICAL EXAMINATION AND A PICTURE VIEW)

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Contrast of an antibody test to MAC disease, a picture view, a bacteriological examination were performed. Eighty patients who suspect Mac lung disease by picture findings were tested. Control examinations were performed at other five anti-acid fungus diseases and 21 healthy adults. Chest computed tomography (CCT) were checked and the number of pulmonary segments with focuses were calculated. All of an antibody test of a healthy person and other anti-acid fungus diseases are negative, and 36 patients showed the positivity of 0.7 or more U/mL of Cut-off values. Forty patients were antibody-positive in 19 patients (73.7% of sensitivity). By 16 in 25 patients of one positive culture, the antibodies were positive and seven among nine negative patients showed the low antibody level. Three among 30 patients indicated the high values near a Cut-off level, Other 27 patients showed the low antibody level. By the CCT findings, Patients who have positive antibodies and bacteriological examination were observed more cavitary opacities change. Correlation of the picture range and antibody value was slightly. ($R = 0.236$)

OS138

PREDICTORS OF MORTALITY IN INDONESIAN PATIENTS WITH HOSPITAL ACQUIRED PNEUMONIA

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Background and Aim Mortality and morbidity due to Hospital Acquired Pneumonia (HAP) are high. Mortality rate reaches up to 50%, but currently there is no local Indonesian data about the issue. Predictors of mortality are also not yet identified. The aim of this study were to recognize the mortality proportion in Internal Medicine Ward of Cipto Mangunkusumo Hospital (CMH) and identify factors that can be used to predict mortality in HAP patients.
Methods This was a prognostic study with the design of retrospective cohort. Subject's data were taken from medical records from January 2006 to December 2012. For univariate analysis, we used Chi-square and Fisher test and for multivariate analysis the logistic regression test.
Results There were 204 patients included. The mortality proportion of HAP was 44.1%. Patients were mostly men, 109 subjects (53.4%) with age ranging between 18 to 88 years old (mean age 50.78 years). The most common co morbidity was hypertension (17.22%). Microorganism isolated from sputum culture most frequently was Klebsiella pneumonia. Univariate analysis revealed that decrease of consciousness, shock, sepsis, immune-compromised and hypoalbuminemia as statistically significant predictors of mortality. Multivariate analysis showed independent statistically significant predictors of mortality included decrease of consciousness ($p < 0.0001$ OR 7.9 95% CI 3.3 to 18.3), shock ($P = 0.012$ OR 3.8 95% CI 1.3 to 10.7), immune-compromised ($p < 0.0001$ OR 3.4 95% CI 1.7 to 6.4) and hypoalbuminemia ($P = 0.009$ OR 2.8 95% CI 1.2 to 5.9).
Conclusion Mortality of Indonesian patients with HAP was high. Significant predictors of mortality of HAP were decrease of consciousness, shock, immune-compromised and hypoalbuminemia.
Key Words Hospital Acquired Pneumonia, mortality, predictors.

OS139

THE CLINICAL ASPECTS OF PULMONARY CRYPTOCOCCOSIS IN NON-HIV/AIDS PATIENTS IN TOKYO METROPOLITAN AREA

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Introduction Pulmonary cryptococcosis (PC) is common in the patients with human immunodeficiency virus-1 infection or acquired immunodeficiency syndrome (HIV/AIDS). It is also seen in non-HIV/AIDS patients: However, the clinical features of PC in non-HIV/AIDS patients are poorly understood due to only a few case reports and small-scale studies available.
Objectives & Methods To clarify the clinical features of PC in non-HIV/AIDS patients, we retrospectively reviewed 16 cases from 1987–2012 at Nippon Medical School Hospital. The criteria for diagnosis of PC were (a) histopathological confirmation of the Cryptococcus neoformans or (b) positive culture or positive cryptococcal antigen test (CRAG) using latex agglutination with clinical and radiographic evidences consistent with PC. The time required from the first visit to the final diagnostic procedure is also evaluated in each patient.
Results Eleven out of 16 patients were asymptomatic. Fourteen out of 16 patients had underlying diseases: malignancy (6 cases), autoimmune connective tissue disease with corticosteroid therapy (4) and diabetes mellitus (4). None of the patients had clinical cryptococcal meningitis. The most common radiographic finding was pulmonary nodule or mass (14/16 cases). Diagnostic approach was made by computed tomography-guided percutaneous needle biopsy (CTNB, 7 cases), bronchoscopy (4), surgical biopsy (3) and serum CRAG (2). Only 2 cases showed positive culture (sputum and blood, respectively). Average time to confirm diagnosis was 54 days (serum CRAG: 9 days, bronchoscopy: 20 days, CTNB: 51 days, additional CTNB after bronchoscopy: 71 days, surgical biopsy: 172 days). The time to confirm the diagnosis longer than 30 days was observed in 7 patients.
Conclusion Non-HIV/AIDS patients might be susceptible to PC. CTNB is a reliable and rapid approach for diagnosis because solitary nodule or mass is often seen in the patients with PC in non-HIV/AIDS.

OS140

RELATIONSHIP BETWEEN PULMONARY NON-TUBERCULOUS MYCOBACTERIAL INFECTION AND AUTOANTIBODY

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Backgrounds Non-tuberculous mycobacteria (NTM) are the opportunistic pathogens, which can be frequently isolated from the patients with chronic pulmonary diseases in Japan. Although many of these pathogens are considered to be colonized in immuno-competent hosts, some species have the ability to deteriorate lung function with future risk of fatal outcome. In addition to the virulence properties of these bacteria, susceptibility to the host is also known to contribute to the pathogenesis of this disease. Autoimmune diseases such as rheumatoid arthritis and Sjogren's syndrome often associate with chronic airway infection including NTM.
Objective Based on these backgrounds, we investigated the frequency of the patients that autoantibody is positive, and the relationship between the types of autoantibody and the clinical features including the findings of Computed Tomography (CT) in the patients suffering from NTM infection in this study.
Methods 51 patients (female/male: 35/16, avium/intracellulare/unknown/gordonae/kansasii/abscessus: 30/13/3/2/2/1) were enrolled in this study. Under the informed consents, chest CT and blood sampling was underwent in all of the patients to analyze the types of lung involvement including bronchiectasis, cavity, granular and nodular shadows, and to detect autoantibody, respectively.
Results More than one kind of autoantibody was positive in 25 patients (49%). Rheumatoid factor was most frequently detected (31.4%). Antinuclear antibody (23.5%), anti-Sjogren's syndrome A (15.7%), anti-Sjogren's syndrome B (5.9%), matrix metalloproteinase-3 (3.9%), and anti-cyclic citrullinated peptide (3.9%) were also positive in these patients, respectively. There were no significant differences in positive rate of autoantibody between avium and intracellulare. Positive rate of autoantibody was significantly higher in the patients with bronchiectasis and cavity (62.8%) than those with granular and nodular shadows (18.7%).
Conclusion These data suggest that autoimmunity may play some roles in the pathogenesis of pulmonary NTM.

OS24: LUNG CANCER 5

OS141

PROGESTERONE INHIBITS THE MIGRATION AND INVASION OF A549 LUNG CANCER CELLS THROUGH MEMBRANE PROGESTERONE RECEPTOR ALPHA-MEDIATED MECHANISMS

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Lung cancer is the leading cause of cancer morbidity and mortality in the world. The incidence of lung cancer, particularly lung adenocarcinoma, is increasingly in women compared to men. The role of sex hormones in the development of lung cancer has attracted substantial interest, but remains unknown. In this study, we demonstrated that membrane progesterone receptor alpha (mPRalpha) was expressed in a lung adenocarcinoma cell line, A549, and was located on the cell membrane. In additional experiments, we found that mPRalpha functioned as an essential mediator for progesterone (P4)-induced inhibitory effects on cell migration and invasion of A549 cells. Furthermore, PP1 (a Src pathway inhibitor), when co-incubated with P4, synchronously enhaced the inhibitory effects of P4 on cell migration and invasion. To explore the mechanisms of inhibition, we found that P4 and PP1 induced a cascade of molecular signalling events, such as dephosphorylation of focal adhesion kinase (FAK) and down-regulation of matrix metalloproteinase 9 (MMP-9). Our study provides a mechanistic view on the effects of P4 through mPRalpha/Src/FAK relevant pathways in human lung adenocarcinoma cells and may aid in development of novel therapeutic tools for the treatment of lung cancer.

OS142

ABSTRACT WITHDRAWN

OS143

HUMAN LUNG EPITHELIAL CELLS PROGRESSED TO MALIGNANCY THROUGH SPECIFIC ONCOGENIC MANIPULATIONS

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Background Lung cancer develops as a multistep process from normal lung epithelial cells to overt malignant cells, involving accumulation of multiple genetic and epigenetic changes. To evaluate the importance of these changes, we have developed a model human lung epithelial cell system (cdk4/hTERT-immortalized normal human bronchial epithelial cells (HBECs)).
Methods We used CDK4/hTERT-immortalized normal human bronchial epithelial cells (HBEC) from several individuals to study lung cancer pathogenesis by introducing combinations of common lung cancer oncogenic changes (p53, KRAS, and MYC) and followed the stepwise transformation of HBECs to full malignancy.
Results This model showed that: (i) the combination of five genetic alterations (CDK4, hTERT, sh-p53, KRAS (V12), and c-MYC) is sufficient for full tumorigenic conversion of HBECs; (ii) genetically identical clones of transformed HBECs exhibit pronounced differences in tumor growth, histology, and differentiation; (iii) HBECs from different individuals vary in their sensitivity to transformation by these oncogenic manipulations; (iv) high levels of KRAS (V12) are required for full malignant transformation of HBECs, however, prior loss of p53 function is required to prevent oncogene-induced senescence; (v) overexpression of c-MYC greatly enhances malignancy but only in the context of sh-p53 + KRAS (V12); (vi) growth of parental HBECs in serum-containing medium induces differentiation, whereas growth of oncogenically manipulated HBECs in serum increases in vivo tumorigenicity, decreases tumor latency, produces more undifferentiated tumors, and induces epithelial-to-mesenchymal transition (EMT); (vii) oncogenic transformation of HBECs leads to increased sensitivity to standard chemotherapy doublets; (viii) an mRNA signature derived by comparing tumorigenic versus nontumorigenic clones was predictive of outcome in patients with lung cancer.
Conclusion Our findings show that this HBEC model system can be used to study the effect of oncogenic mutations, their expression levels, and serum-derived environmental effects in malignant transformation, while also providing clinically translatable applications such as development of prognostic signatures and drug response phenotypes.

OS144

DUAL MET/VEGFR-2 INHIBITOR FORETINIB OVERCOMES ACQUIRED RESISTANCE TO BEVACIZUMAB IN LUNG CANCER

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Background and Aim of Study Bevacizumab, a monoclonal antibody targeting vascular endothelial growth factor (VEGF), had promising therapeutic efficacy in lung cancer. However, acquired resistance is common in the clinic. The purpose of this study was to generate bevacizumab-resistant lung cancer in vivo model to characterize mechanisms of acquired resistance.
Methods We generated Bevacizumab-resistance clones from a Bevacizumab-sensitive lung cancer cell line in vivo by exposing Bevacizumab-sensitive xenografts to increasing concentrations of Bevacizumab, followed by validation of resistant phenotype in vivo.
Results We generated a novel lung cancer xenograft model of bevacizumab resistance and identified increased c-Met phosphorylation, Notch-1 and STAT3. Foretinib, an oral multikinase inhibitor targeting Met, VEGF, RON, AXL, and TIE-2 receptors, significantly inhibited tumor cell growth in bevacizumab-acquired resistance cell lines derived from xenograft models. Western blot analyses showed that foretinib effectively decreased the phosphorylation of Met, VEGFR-2 in these cells. Combinating foretinib with bevacizumab enhanced tumor growth retardation in bevacizumab resistance xenograft model compared with foretinib alone.
Conclusion These data suggest that dual Met/VEGFR-2 inhibitor foretinib can enhance response to bevacizumab, partly due to down-regulation of c-Met. This novel in vivo model provides rationale for phase I clinical trials using combination treatment of foretinib and bevacizumab in metastatic lung cancer patients.

OS145

THE EFFECT OF RE-EXPRESSION OF RASSF1A INDUCED BY 5-AZA-CDR ON PROLIFERATION AND APOPTOSIS OF A549 CELL LINE

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Background and Aim of Study Inactivation of tumor suppressor genes (TGS) plays an important role in tumorigenesis, and promoter hypermethylation is the main causes for silencing TSGs. Ras associated domain family protein 1A (RASSF1A) is a novel TSG, and has defective expression in many cancers due to promoter hyper-methylation, including lung cancer. This study was designed to induced the re-expression of RASSF1A in the lung adenocarcinoma A549 cells by treatment of demethylating agent 5-Aza-2-deoxycytidin (5-Aza-CdR), and explore the effect of restored RASSF1A on A549 cells.
Methods A549 cells were treated with $5*10^{-5}$ mol/L, $5*10^{-6}$ mol/L, $5*10^{-7}$ mol/L of 5-Aza-CdR. The control group was treated with PBS. Expression of RASSF1A gene was observed by RT-PCR. MTT was used to detect the growth of A549 cells. Cell cycle and apoptosis were analyzed by flow cytometry before and after treatment of 5-Aza-CdR.
Results There was no expression of RASSF1A mRNA in control group; RASSF1A gene was re-expressed after treatment of 5-Aza-CdR, and the higher concentration of 5-Aza-CdR induced the more expression of RASSF1A and the difference between the relative level of RASSF1A mRNA expression induced by the three concentration of 5-Aza-CdR was significant ($p\alpha 0.05$). A549 cells treated with 5-Aza-CdR showed a slower growth velocity in contrast to the control group ($p\alpha 0.05$). There was no difference in the rate of G1 phase among 5-Aza-CdR treated groups and the control group ($p > 0.05$). The apoptotic rates in the 5-Aza-CdR treated groups were higher than the control group, the rates were $19.5 \pm 2.1\%$ in $5*10^{-5}$ mol/L group, $15.9 \pm 0.8\%$ in $5*10^{-6}$ mol/L group, $12.3 \pm 1.5\%$ in $5*10^{-7}$ mol/L group and $4.2 \pm 0.8\%$ in control group ($p\alpha 0.05$). There was a positive correlation between RASSF1A expression and apoptosis rate ($p\alpha 0.05$).
Conclusions According to our study, RASSF1A expression was restored by 5-Aza-CdR treatment in a concentration-dependent manner, and re-expression of RASSF1A gene could promote apoptosis of A549 cell line.

OS146

ABILITY OF THE MET KINASE INHIBITOR CRIZOTINIB AND NEW GENERATION EGFR INHIBITORS TO OVERCOME RESISTANCE TO EGFR INHIBITORS

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Background Although EGF receptor tyrosine kinase inhibitors (EGFR-TKI) have shown dramatic effects against EGFR mutant lung cancer, patients ultimately develop resistance by multiple mechanisms. We therefore assessed the ability of combined treatment with the Met inhibitor crizotinib and new generation EGFR-TKIs to overcome resistance to first-generation EGFR-TKIs.
Methods Lung cancer cell lines made resistant to EGFR-TKIs by the gatekeeper EGFR-T790M mutation, Met amplification, and HGF overexpression and mice with tumors induced by these cells were treated with crizotinib and a new generation EGFR-TKI.
Results The new generation EGFR-TKI inhibited the growth of lung cancer cells containing the gatekeeper EGFR-T790M mutation, but did not inhibit the growth of cells with Met amplification or HGF overexpression. In contrast, combined therapy with crizotinib plus afatinib or WZ4002 was effective against all three types of cells, inhibiting EGFR and Met phosphorylation and their downstream molecules. Crizotinib combined with afatinib or WZ4002 potently inhibited the growth of mouse tumors induced by these lung cancer cell lines. However, the combination of high dose crizotinib and afatinib, but not WZ4002, triggered severe adverse events.
Conclusions Our results suggest that the dual blockade of mutant EGFR and Met by crizotinib and a new generation EGFR-TKI may be promising for overcoming resistance to reversible EGFR-TKIs but careful assessment is warranted clinically.

OS25: BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES 1

OS147

FIBREOPTIC ENDOSCOPY EXAMINATION OF SWALLOWING (FEES) IS AN EFFECTIVE DIAGNOSTIC EXAMINATION IN ASPIRATION PNEUMONIA

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Aspiration pneumonia accounts for up to 68% of patients hospitalized for pneumonia, and is commonly underdiagnosed even among high risk patients including those with neurological and upper airway disorders including head and neck malignancy. The traditional assessment of dysphagia, thus risks of aspiration pneumonia entails the use of Videoflurouscopic study of Swallowing (VFSS) although there is considerable risks of barium contrast aspiration in the process without the benefits to retrieve it. Fibreoptic Endoscopy Examination of Swallowing (FEES), employs the use of a bronchoscope positioned at the oropharynx to observe swallowing, overcomes such although there are still limited data to show its efficacy. We have, therefore, performed a case-controlled study between 2006 to 2012, recruiting consecutive dysphagic patients, with matched age, gender and medical diagnoses, with and without pneumonia. Swallowing performance of these patients, the pneumonia PG group and non-pneumonia group NPG, using FEES and the Rosenbek 8-point Penetration-Aspiration Scale. Thirty-three pairs of patients with neurological and head and neck malignancywere assessed using FEES from 2006 to 2012. Independent samples t-test showed that PG and NPG patients were similar in gender, age (74.8 ± 13.8; 74 ± 12.6 yr) and medical diagnosis [sex: $p = 1.00$; age: $p = 0.80$; medical diagnosis: $p = 0.93$]. When comparing the two groups' performance in swallowing thin liquid, puree and solid food using the Rosenbek Penetration-aspiration scale, PG patients had significantly poorer performance than NPG patients in all three food consistencies [thin liquid: $p = 0.02$; puree: $p = 0.01$; solid: $p = 0.03$]. Our data, for the first time, show that FEES is an effective diagnostic method to differentiate patients with and without aspiration pneumonia. Further research on this poorly understood area should follow.

OS148

PROSPECTIVE STUDY OF THE OPTIMAL SEQUENCE FOR BRONCHIAL BRUSHING AND BIOPSY IN LUNG CANCER DIAGNOSIS

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Background and Objective Optimizing basic techniques in diagnostic bronchoscopy is important for improving medical services in developing countries. In this study, the optimal sequence of bronchial brushing relative to bronchial biopsy for lung cancer diagnosis was evaluated.
Methods A total of 314 patients with visible endobronchial tumours were prospectively enrolled in two groups: a pre + post-biopsy brushing group, receiving two brushings before biopsy and two afterwards; and a post-biopsy brushing group, receiving two brushings after biopsy. Diagnostic yield of brushing was compared before and after biopsy, and as well as for different tumour pathologies and bronchoscopic morphologies.
Results A total of 262 patients who met the inclusion criteria were analysed. Diagnostic yield for pre-biopsy brushing (48.3%, 56/116) was significantly higher than for post-biopsy brushing within the same pre + post brushing group (31.0%, 36/116) ($P = 0.007$), and significantly higher than for post-biopsy brushing in the post group (30.1%, 44/146) ($P = 0.003$). Subgroup analysis stratified by bronchial morphology revealed that the superiority of pre-biopsy brushing was limited to exophytic tumours: for this tumour type, pre-biopsy brushing gave a diagnostic yield of 56.7% (38/67), while post-biopsy brushing gave yields of 32.8% (22/67) in the pre + post group ($P = 0.005$) and 30.0% (24/80) in the post group ($P = 0.001$). Pre- and post-biopsy brushings were associated with similar diagnostic yields for other tumour types and bronchoscopic abnormalities.
Conclusions Supplementing bronchoscopic biopsy with brushing improves diagnostic yield in lung cancer. In cases of endobronchial exophytic tumours, pre-biopsy brushing appears to be superior to post-biopsy brushing.

OS149

COMBINED EFFECT OF UROKINASE INTRATHORACIC INFUSION THERAPY AND DEBRIDEMENT WITH THORACOSCOPY UNDER LOCAL ANESTHESIA FOR ACUTE EMPYEMA

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Backgrounds In patients with acute empyema and pneumonia associated pleurisy, the usefulness of urokinase intrathoracic infusion therapy and debridement with thoracoscopy has been reported. We examined combined effect of urokinase intrathoracic infusion therapy and debridement with thoracoscopy under local anesthesia for acute empyema.
Materials and Methods We reviewed 20 cases with acute empyema in our hospital between 2008 and 2011, retrospectively. The periods of hospitalization, receiving antibiotics and drainage were compared between thoracoscopic treatment group ($n = 10$, age 75.4 ± 10.4, M : F = 7 : 3) who received antibiotic therapy and underwent urokinase intrathoracic infusion therapy following debridement with thoracoscopy and medical treatment group ($n = 10$, age 72.9 ± 8.9, M : F = 8 : 2) who received antibiotic therapy and closed-tube thoracostomy alone.
Results The average period of hospitalization and drainage in thoracoscopic treatment group was 34.2 ± 20.9 days and 9.3 ± 6.0 days, shorter than the period in medical group (44.2 ± 18.4 days and 15.2 ± 9.7 days), but not significantly. The period of receiving antibiotics in thoracoscopic treatment group was 24.3 ± 13.8 days, shorter than the period in medical group (72.7 ± 62.1 days), significantly.
Conclusions The combined therapy, urokinase intrathoracic infusion therapy and debridement with thoracoscopy under local anesthesia for acute empyema contributes to shorten the treatment period.

OS150

THORACIC ULTRASOUND VERSUS CT FOR IMAGING PRE-ASSESSMENT PRIOR TO MEDICAL THORACOSCOPY

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Background and Aim of the Work To assess the concordance between thoracic ultrasound (TUS) and chest CT findings prior to medical thoracoscopy (MT), and whether US alone or in combination with chest X-ray (CXR) can omit routine pre- assessment chest CT.
Methods The study was conducted prospectively on 52 patients referred with unexplained pleural exudate for MT during 2012 (28 males and 24 females; 56 ± 14 years old). All patients received CXR, TUS and chest CT prior to the procedure. Images were evaluated for effusion, loculation, fibrin strands, pleural masses, nodules and thickening and lung parenchymal lesions. Imaging findings were correlated with thoracoscopic findings.
Results TUS findings were *discordant* with CT findings regarding consistency, septation and loculation of effusion in 24/52 patients, with TUS detecting the findings in 24/24 patients (thick fibrous septation with multiloculations in 17/24 and few fibrin strands in 7/24). None of these findings was detectable in CT ($P < 0.001$). The TUS findings prevented MT in12/52 cases, and led to prolongation of MT in 6/40 and to change in port of entry in 2/40 and they were associated with failure to achieve post-MT full lung expansion in7/40 cases. TUS findings were consistent with MT findings in all cases who underwent the procedure except for one case with morbid obesity and thick septation undetectable in TUS and CT. TUS findings were *concordant* with CT findings regarding site and size of effusion, butTUS missed tiny nodules in 10/52, consolidation in 2/52, mediastinal lymphadenopathy in 6/52, and mediastinal shift in 42/52 cases. CXR could identify mediastinal shift but none of other CT findings missed by TUS. None of TUS-missed abnormalities directly altered MT management.
Conclusion Pre-MT imaging workup can be limited to CXR and TUS, reserving chest CT for cases in which TUS is technically unrevealing.

OS151

FEBRILE COMPLICATIONS AFTER ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION FOR INTRA-PULMONARY MASS LESIONS OF LUNG CANCER

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Background Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is an effective and dependable, minimally invasive procedure to investigate mediastinal and hilar lymphadenopathy. However, recent case reports have shown that endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for mediastinal lesions is sometimes accompanied by severe infectious complications.
Method We analyzed three cases with refractory febrile complications following EBUS-TBNA for intra-pulmonary large mass lesion of lung cancer (squamous cell carcinoma in two cases and adenocarcinoma in one).
Results After the EBUS-TBNA, all cases showed prolonged fever and systemic inflammation in spite of a sufficient dose of broad-spectrum antibiotics. Blood cultures taken early at the onset of fever did not demonstrate bacteraemia. Needle washing, bronchial secretion, or biopsy tissue culture was also negative in all 3 patients. It is important to recognize and identify patients who may be at high risk for developing EBUS-TBNA related febrile complications. We experienced these 3 cases of febrile complications from the 48 consecutive cases of EBUS-TBNA in a rather short period of 9 months. Among these 48 cases, 5 had intra-pulmonary mass lesions and 43 had mediastinal lesions. No febrile complications occurred after EBUS-TBNA for mediastinal lesions.
Conclusion We speculate that patients who undergo EBUS-TBNA for intra-pulmonary tumors may have a higher risk of developing febrile complications as compared to those with mediastinal lesions. The presence of a low-density area inside of masses on CT examination, suggesting necrosis, could be a predictive sign of febrile complication associated with EBUS-TBNA.

OS152

USE OF HOURGLASS STENT FOR UPPER TRACHEAL STENOSIS

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Background Migration of airway stents often occurs, especially when they are placed in the upper trachea. An hourglass stent (DUMON™ ST, Novatech, France), designed to avoid the risk of migration, is now available, but only a few studies on its efficacy and safety have been reported.
Methods Patients with tracheal stenosis who underwent ST stent placement from March 2006 to September 2011 at Nagoya Medical Center were retrospectively reviewed. All stenting procedures were performed using rigid and flexible bronchoscopes under general anesthesia.
Results During the study duration, 7 patients underwent ST stent placement for the treatment of upper tracheal stenosis. Three had malignant stenoses due to esophageal cancer, and 4 had post-intubation/tracheostomy stenoses. An ST stent 16-14-16 mm in outer diameter was used in 6 cases, and 14-12-14 mm in 1. All 7 patients were relieved of dyspnea immediately after the procedure. Migration occurred in 2 patients; one required stent replacement and the other was due to tumor reduction after chemoradiotherapy. Granulation tissue formation occurred in 2 patients.
Conclusions Stent placement using a ST stent is effective for the treatment of upper tracheal stenosis, and seems to have a low risk of migration.

OS26: INTERSTITIAL LUNG DISEASE 3

OS153

IS EMPHYSEMA A PROGNOSITIC FACTOR IN ACUTE EXACERBATION OF IDIOPATHIC PULMONARY FIBROSIS?

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Background and Aim of Study Acute exacerbation of idiopathic pulmonary fibrosis (IPF) is a fatal condition of unknown etiology and very poor prognosis. These days, IPF has been considered as a component of various different phenotypes of parenchymal lung disease, such as combined pulmonary fibrosis and emphysema (CPFE). CPFE patients may have different clinical course, and acute exacerbation of this entity may have different prognosis, too. The objective of this study was to retrospectively analyze treatment outcome and identify prognostic factors of acute exacerbation of IPF, including IPF patients with emphysema.
Methods We retrospectively analyzed medical records of 57 patients diagnosed with acute exacerbation of IPF. Clinical presentation, radiographic emphysema score, pulmonary function tests, laboratory data, treatment, and outcome were analyzed. A logistic regression analysis was used to identify prognostic factors of 90-day survival of acute exacerbation of IPF.
Results The mean survival time after the onset of acute exacerbation of IPF was 69 days, and the mortality rate was 56.1% at 90-day. For acute exacerbation of IPF, all patients were treated with methylprednisolone pulse therapy and broad-spectrum antibiotics. In addition, 21 patients (37%) received cyclophosphamide pulse therapy, 38 (67%) received cyclosporin A, 20 (35%) received neutrophil elastase inhibitor, and 17 (29.8%) received Direct hemoperfusion with Polymixin B-immobilized fiber column. The patients who had multimodal treatment were likely to have long-term survival, although without statistical significance. A logistic multivariate analysis showed that, patients with obvious emphysematous change on chest high-resolution computed tomography (Odds ratio = 0.101, P = 0.044), and PaO2/FIO2 ratio over 200 (Odds ratio = 0.004, P = 0.022) have significant better prognosis in 90-day survival of acute exacerbation of IPF patients.
Conclusion IPF patients with obvious emphysema have better prognosis in acute exacerbation than without emphysema.

OS154

CLINICAL SIGNIFICANCE OF SERUM MARKER OF INTERSTITIAL PNEUMONIA IN COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Background Recently, it was reported that about 28–51% of idiopathic pulmonary fibrosis (IPF) is accompanied by emphysema, whose pathology and clinical features are different from those of IPF without emphysema. Furthermore, the clinical features of combined pulmonary fibrosis and emphysema (CPFE) vary in individual cases.
Purpose Using an interstitial pneumonia marker and the pulmonary diffusion capacity as clinical indicators, we divided CPFE patients into three groups, and compared their clinical features.
Subjects Subjects were 30 CPFE patients treated in our hospital over the last five years. There were 29 males and 1 female. The mean age range was 69.4 ± 5.9 years.
Results Based on %DLco – %DLco/VA values, we divided patients into three groups: Group 1: >= 10 (10 cases), Group 2: –10 to 10 (15 cases), and Group 3: <–10 (5 cases). The KL-6 value was 739 ± 550 U/ml in Group 1, 1,114 ± 549 U/ml in Group 2, and 1,035 ± 312 U/ml in Group 3, with no significant differences between the three groups. Based on KL-6 values, we again divided patients into three groups: Group A: <500 U/ml (8 cases), Group B: 500–1,000 U/ml (10 cases), and Group C: >= 1,000 U/ml (12 cases). The %DLco value was 78.6 ± 20.8% in Group A, 69.2 ± 16.3% in Group B, and 58.0 ± 20.0% in Group C, with a significant difference between Groups A and C ($p < 0.05$). The %DLco – %DLco/VA value was 12.2 ± 12.1 in Group A, 2.7 ± 10.8 in Group B, and –2.1 ± 13.6 in Group C, with a significant difference between Groups A and B and between Groups A and C ($p < 0.05$). There was a negative correlation between KL-6 and %DLco – %DLco/VA values ($r = 0.28$, $p = 0.13$).
Conclusion CPFE was noted in various patient groups, and, in the subgrouping of CPFE patients, we suggest that KL-6 and %DLco are important clinical indicators.

OS155

IS PLEUROPARENCHYMAL FIBROELASTOSIS WITH USUAL INTERSTITIAL PNEUMONIA PATTERN A DISEASE DISTINCT FROM IDIOPATHIC PULMONARY FIBROSIS?

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Background and Aim of Study Pleuroparenchymal fibroelastosis (PPFE) is a rare disease entity with unique changes in the upper lobes, sometimes coexisting with usual interstitial pneumonia (UIP) pattern in the lower lobes. PPFE may be potentially diagnosed as idiopathic pulmonary fibrosis (IPF), although upper predominant distribution is a negative finding in IPF diagnosis according to the recent guideline. The aims of this study are to distinguish PPFE with UIP pattern from hitherto diagnosed as IPF, and to compare the characteristics of PPFE with UIP pattern with the other IPF.
Methods We retrospectively reviewed the medical records of 110 consecutive IPF patients diagnosed by surgical lung biopsy and multidisciplinary discussion in Kanagawa Cardiovascular and Respiratory Center between 2001 and 2011. From the all IPF patients, two radiologists extracted patients with upper predominant distribution on high-resolution CT (HRCT), and independently, two pathologists identified those with PPFE in the upper lobes. We assessed the coincidence rate between the radiologically selected patients and pathologically evidenced patients. Clinical and radiological findings were compared between patients with PPFE with UIP pattern and the other IPF patients.
Results Eleven patients had upper predominant distribution on HRCT. Nine patients were pathologically identified with PPFE. The PPFE patients were all with the upper predominance. The remaining two of the 11 upper predominant patients did not fulfill the criteria of PPFE. The PPFE patients showed significantly higher residual volume, PaCO2, and complication rate of pneumothorax than the other IPF patients. Bilateral apical consolidation on HRCT was more common, and the survival time tended to be shorter in the PPFE patients.
Conclusion In comparison with IPF, PPFE with UIP pattern showed distinct clinical and radiological features. This disease entity is an important differential diagnosis of IPF, when the patients have not only UIP pattern but also upper lobe predominant distribution.

OS156

FORCED VITAL CAPACITY AND DLCO RAPIDLY DETERIORATE IN PATIENTS WITH PULMONARY UPPER-LOBE FIBROSIS

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Background and Aim of Study Pulmonary upper-lobe fibrosis (PULF) or pleuroparenchymal fibroelastosis (PPFE) is a unique but rare pulmonary fibrosis. Its clinical, pathological, and physiological characteristics are not fully understood. Respiratory function characteristcs were retrospectively examined in patients with biopsy- or autopsy-proven PPFE.
Methods Fifteen patients with PULF admitted in our hospitals were enrolled in the study. Respiratory function at the first visit and annual decrease in FVC and DLco were examined. FVC data in 9 of 15 patients were already reported in Respir Investig 50: 88–97, 2012.
Results Patients consisted of 7 males and 8 female with 57.3 ± 3.5 years old. Follow-up periods were 5.71 ± 1.0 years in which ten patients passed away. Four patients had underlying diseases or conditions such as ulcerative colitis, post-irradiated state for esophageal cancer, post-lung transplantation state, and pulmonary mycobacterial disease by *Mycobacterium avium-complex*. FVC % pred, FEV1/FVC%, TLC % pred, and RV/TLC % pred at first visit were 60.73 ± 6.03%, 92.59 ± 1.52%, 68.29 ± 6.16% and 163.6 ± 14.17%, respectively. DLco % pred and DLco/VA % pred at first visit were 66.36 ± 7.20% and 84.48 ± 7.09% (n = 12). Annual decrease in FVC was –295.8 ± 73.1 mL (–16.25 ± 2.73%) (n = 13), and annual decrease in DLco was –20.28 ± 6.95% (n = 6).
Conclusion PULF or PPFE has a poor prognosis with rapid decline in FVC and DLco.

OS157

THE USE OF NIPPV IN ACUTE RESPIRATORY FAILURE INCLUDING INTERSTITIAL PNEUMONIA (JOSS STICK LUNG): 3 CASES

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We experienced three cases of acute respiratory interstitial pneumonia managed by non-invasive positive pressure ventilation (NIPPV). The first case was a 44-year-old woman. She had metastatic lung tumors from a pelvic tumor complicated with CO_2 retention (ABG: pH 7.21, PO_2 33.1 torr, PCO_2 66.5 torr) after pneumonia. NIPPV and dopram were introduced. She was successfully extruded by NIPPV in one day (ABG: pH 7.46, PO_2 156.0 torr, PCO_2 35.7 torr). The second case was a 64-year-old man. He had small-cell lung cancer (stage IV, T2bN1M1) complicated with interstitial pneumonia after chemotherapy (Amrubicin). Lung function was recovered by NIPPV using prednisolone and antibiotics. The third case was a 61-year-old woman. She had been engaged in manufacturing incence sticks for many years. She had chronic pneumothorax complicated with interstitial pneumonia (Joss stick lung) (ABG: pH 7.40, PO_2 127.0 torr, PCO_2 59.3 torr). When she fell into acute respiratory failure, the family did not wish to maintain IPPV, which requires tracheal intubation, so we performed NIPPV and administered dopram. Unfortunately, NIPPV did not recover this type II respiratory failure completely. In any case, rapid care using NIPPV for acute respiratory failure including interstitial pneumonia was worth performing to put off the patient's demise.

OS158

THE PROGNOSTIC INFLUENCE OF CIGARETTE SMOKING IN IDIOPATHIC NONSPECIFIC INTERSTITIAL PNEUMONIA

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Background and Aim of Study The recent Report of an American Thoracic Society project has suggested that idiopathic NSIP does represent a distinct clinical entity, showing a good prognosis and middle-aged woman who are never smokers. Though a recent report suggested that cigarette smoking is a prognostic factor of patients with NSIP, the correlation between the cigarette smoking status and idiopathic NSIP is not known well. To clarify the correlation between smoking status and mortality in idiopathic NSIP, we performed a retrospective analysis.
Methods Patient selection was made on a review of the medical records of 123 patients who had received a histological diagnosis of NSIP on the basis of surgical lung biopsy between 2000 and 2009. Seventy-three cases of idiopathic NSIP were excluded because surgical lung biopsy, HRCT examination or clinical records were incomplete. The remaining 50 NSIP cases had clinical, radiologic and pathologic consensus acceptable for inclusion in the study. The correlation between cigarette smoking status and mortality was evaluated using the Kaplan -Meier method.
Results The 5-year survival was 90% in idiopathic NSIP. The patients studied consisted of 26 men and 24 women. Mean age was 61 years, 48% were female (current and former smokers 6 cases (25%), never smokers 18 cases (75%)). The current and former smokers tended to have acute exacerbation of idiopathic NSIP or cancer. Never smokers had a lower mortality than former smokers and current smokers ($p = 0.037$). Emphysema and cystic formation were higher instances in idiopathic NSIP with smoking than that of never smokers. % DLco levels ($p = 0.02$) were lower in current and former smokers than in nonsmokers.
Conclusion Never smokers had lower mortality than former and current smokers in idiopathic NSIP. Although idiopathic NSIP has a very good prognosis, cigarette smoking may have an impact on a prognosis.

OS27: RESPIRATORY INFECTIONS (NON-TUBERCULOSIS) 2

OS159

EVALUATION OF INITIAL ANTIMICROBIAL THERAPY FOR PNEUMOCOCCAL RESPIRATORY INFECTIONS

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Background Pneumococcus (*Streptococcus pneumoniae*) is one of the most common pathogens that cause community-acquired pneumonia (CAP). Since pneumococcal infection (PIx) may get seriously ill, appropriate antimicrobial therapy should be required.
Aim of Study The aim of this study is to evaluate the clinical factors that affect initial antimicrobial therapy of PIx.
Methods A total of 40 patients (27 men and 13 women) were enrolled in this study if they were diagnosed with PIx in Yamagata University Hospital from 2010 through 2012. PIx was diagnosed by either of the following criteria: isolation of *S. pneumoniae* from sputum or blood culture, or positive result for urinary antigen test of *S. pneumoniae*. Initial antimicrobial therapy was to be succeed if 3 or more of the following parameters were improved: symptoms; consolidates on chest X-ray; peripheral blood leukocytes; C-reactive protein (CRP). The patients were divided into two groups based on the efficacy of initial antimicrobial therapy (26 of the success group vs. 14 of the failure group), and clinical parameters were analyzed.
Results The median age of the patients was 73 years (49 to 93 years). Of these 40 patients, 26 were CAP, 7 were respiratory tract infection, and 7 were sepsis. Performance status (PS) of the patients were significantly poor (3 or more) in the failure group ($p < 0.05$, Chi-square test). Following antimicrobials were initially administered: Ampicillin/Sulbactam (ABPC/SBT, $n = 14$); Ceftriaxone (CTRX, $n = 10$); Fluoroquinolones (FQs, $n = 6$); Carbapenems (CPs, $n = 6$); others ($n = 4$). Clinical efficacies of ABPC/SBT, CTRX, FQs, CPs were 71.4%, 70%, 100%, 16.7%, respectively ($p < 0.05$, Chi-square test). Multivariate analysis indicated that administration of CPs was an independent risk factor for the failure of initial antimicrobial therapy (odds ratio 12.45, 95% C.I. 1.49–280.54).
Conclusion CPs might be inadequate for initial antimicrobial therapy of PIx.

OS160

ASSOCIATION BETWEEN MYCOBACTERIAL GENOTYPES AND THE TREATMENT RESPONSE OF *M. AVIUM* LUNG DISEASE

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Background and Aim of Study For *Mycobacterium avium* lung infection, factors that can affect the successful treatment have been not fully studied. We sought to define a potent predictor for the therapeutic response.
Methods We assessed variable numbers of tandem repeats (VNTR) at 16 minisatellite loci of *M. avium* clinical isolates from 59 subjects.
Results Among them, 30 subjects were defined as responsive to clarithromycin-containing treatments for the microbiologic and radiographic improvement, and the remaining 29 subjects were defined as refractory. When the genotypic distance was assessed by the Manhattan distance aggregated over VNTR data from 16 minisatellite loci, 59 *M. avium* isolates were distributed and divided into 3 clusters in neighbor-joining phylogenetic tree, which showed the nearly significant association with therapeutic responses ($P = 0.06$). The association was further clarified in principal component analysis using the raw VNTR data without the distance calculation ($P < 0.05$). In analysis by logistic regression, we could construct the highest likelihood multivariate model to predict the therapeutic response of *M. avium* lung infections with a sensitivity and specificity both greater than 70%.
Conclusion Genotyping *M. avium* isolates may be a useful strategy for predicting the clinical outcome of the lung infection.

OS161

EVALUATION OF HBZ AND FOXP3 MRNA EXPRESSION IN BRONCHOALVEOLAR LAVAGE CELLS FROM HUMAN T-LYMPHOTROPIC VIRUS TYPE 1-ASSOCIATED LUNG DISORDER PATIENTS

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Back Ground and Aim of Study Human T-lymphotropic virus type 1 (HTLV-I) is the etiological agent of adult T-cell leukemia (ATL), and also associated with chronic inflammatory diseases including inflammatory pulmonary diseases. Among the HTLV-I viral genes, tax has been considered as a critical player in HTLV-1 pathogenesis. Tax expression is frequently lost in ATL cells, other HTLV-1 pX gene HTLV-I bZIP factor (HBZ) is consititutively expressed in ATL cells. Recent study shows that HBZ play a critical role in the development of lymphoma and systemic inflammation. It is also known that HTLV-I is harbored by CD4+ T cells that express forkhead box P3 (Foxp3), and HBZ interacts with Foxp3. The purpose of this study was to investigate the manifestations of chest computed tomography (CT) findings and expression of HBZ and Foxp3 in bronchoalveolar lavage (BAL) cells from patients of HTLV-I-associated lung disorders.
Methods CT scans from 37 patients (10 males and 27 females, aged 37–77 years) with HTLV-I-associated lung disorders were retrospectively reviewed. And the expressions of HBZ and Foxp3 mRNAs in BAL cells and the levels of inflammatory cytokines of BAL fluid (BALF) from patients were compared with control subject.
Results In CT findings, diffuse panbronchiolitis (DPB)-like pattern was observed most frequently (45.9%, 17/37), followed by nonspecific interstitial pneumonia (NSIP) pattern (29.7%, 11/37). BALF cells of HTLV-1 carrier patients showed lymphocytosis and expression of *HBZ* mRNA. Expression of *Foxp3* mRNA tended to be positively correlated with the percentages of lymphocytes presented in BALF. Inflammatory cytokine and IL-10 levels were significantly increased in the BALF from HTLV-1 carrier patients compared with control subjects.
Conclusion On CT, NSIP pattern could be one manifestation of pulmonary involvement in HTLV-I-infected patients as well as DPB-like pattern. And HBZ and Foxp3 likely have a role in the development of lung inflammation.

OS162

ADVANTAGES AND DISADVANTAGES OF GRAM STAINING IN THE INITIAL APPROACH TO PLEURAL EFFUSIONS

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Background and Aim of Study Gram staining is the simplest and most rapid test for the diagnosis of infectious diseases, but the significance of gram staining of pleural effusions is not fully investigated. The aim of this study is to evaluate the benefits versus the problems of gram staining in the initial approach to pleural effusions.
Methods We reviewed 705 pleural effusions evaluated by both gram staining and culture at the clinical microbiology laboratory of Juntendo University Hospital from September 2010 through August 2012.
Results The sensitivity of gram staining was 35.1%, specificity 99.8% and accuracy 89.4% compared to culture. We identified 63 pleural effusions (8.9% of total) diagnosed with empyema according to the modified ACCP classification. The sensitivity, specificity and accuracy of gram staining for the diagnosis of empyema were 33.3%, 100% and 94%. In contrast, the sensitivity, specificity and accuracy of culture were 77.8%, 98.8% and 96.9% respectively. The low sensitivity of gram staining for the diagnosis of empyema was mainly due to the amount of pathogen present. Interestingly, the administration of antimicrobials prior to laboratory testing did not influence the positive rate of the gram staining.
Conclusion Gram staining is useful in the initial approach to pleural effusions with high specificity and accuracy for the diagnosis of empyema. However, gram staining of pleural effusion should be assessed carefully because of its low sensitivity.

OS163

RESPIRATORY VIRAL INFECTION IN ADMITTED ADULT PATIENTS

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Background and Aim of Study Respiratory viral infections are common and usually self-limiting disease in adult patients. These infections may be serious in fragile patients with comorbid illness. There were few data about respiratory viruses associated with diverse respiratory diseases in adult. Thus, we prospectively investigate those respiratory viruses in various respiratory diseases.
Methods Prospective observational cohort studyAdmitted adult patients who suffered from acute or progressive respiratory diseases from 1 August to 10 December were enrolled. Respiratory samples such as nasal discharge, sputum, and bronchioalveolar lavage fluid were collected and assessed. Human rhinovirus (HRV), respiratory syncytial virus (RSV), human metapneumovirus (HMPV), parainfluenza virus, influenza virus, and bocavirus were examined by (reverse transcription) polymerase chain reaction. Clinical data, such as age, sex, comorbidities, and mortality, were also collected.
Results Seventy subjects (male 37 vs female 33, mean 68.5 y), were consisted of pneumonia (n = 26), asthma (n = 8), COPD (n = 8), IIPs (n = 6), collagen vascular disease (n = 8), and others (n = 14) were enrolled. Seven cases (10%) had positive viral PCR and identified viruses were HRV (n = 3), RSV (n = 3), and HMPV (n = 1). All viral detected patients were asthma or COPD on exacerbative status. Both five of eight (63%) patients with asthma attack and two of eight (25%) patients with COPD exacerbation were viral positive. There was no viral detection in patients with chest x-ray proven pneumonia and IIPs. However, chest computed tomography demonstrated bronchopneumonia in patients with COPD exacerbation. A patient with RSV detection died of COPD exacerbation and HMPV positive patient with asthma attack transferred to her local hospital because of a decline of ADL.
Conclusion Respiratory viruses were detected in 10% of admitted patients. In particular, respiratory virus infections appeared to be a life threatening event in some patients with asthma or COPD.

OS164

BACTERIAL LOAD AND MULTIPLE-SEROTYPE COLONIZATION OF PNEUMOCOCCUS IN A CASE-CONTROL STUDY OF PNEUMONIA IN VIETNAM

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Background and Aim of Study Effects of bacterial load and multiple serotype colonization of pneumococcus in the development of pneumonia need to be elucidated. By applying the nanofluidic real time PCR system, we aimed to measure the serotype-specific pneumococcal bacterial load and detect multiple serotype colonization among under-5 children in pneumonia cases and healthy controls in Vietnam.
Methods A hospital-based case-control study was conducted: 576 nasopharyngeal samples were collected from 226 chest x-ray confirmed pneumonia cases in the pediatric ward, Khan Hoa General Hospital and 350 randomly selected healthy children in Vietnam. Samples were screened for the presence of *Streptococcus pneumoniae* by *lytA* primer in the Light Cycler 480 PCR system, prior to the nanofluidic real time PCR system (Fluidigm Biomark HD System) that can identify 50 serotypes and quantify the serotype specific bacterial loads.
Results Pneumococcal load was high in all the age groups. The median bacterial load was 100 times higher in the pneumonia cases than the controls (6 log 10/μL versus 4 log 10/μL; $p < 0.001$). The prevalence of multiple serotype colonization was two times higher in the pneumonia cases (19% versus 8%; OR 2.5, 95% CI 1.2–5.2; $p < 0.01$); among these serotypes only a single serotype dominated the other serotypes by contributing more than 99% of the total pneumococcal load ($p < 0.001$). Thirteen-valent pneumococcal conjugate vaccine (PCV13) covered 70% of the prevalent serotypes in the pneumonia cases and 50% in the healthy children.
Conclusion Higher pneumococcal bacterial load and multiple serotypes were associated with pneumonia. The dominant serotype, with a higher bacterial load, seems to be the causal pathogen in pneumonia cases. Introduction of PCV will reduce the burden of pneumonia in Vietnam.

OS28: LUNG CANCER 6

OS165

VASCULAR NORMALIZATION IN HUMAN LUNG ADENOCARCINOMA INDUCED BY EGCG AND THE EFFICACY OF COMBINE CHEMOTHERAPY IN NORMALIZATION TIME WINDOW

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Background and Aim Microvasculature and microenvironment play important roles in proliferation, metastasis and prognosis in human lung adenocarcinoma, which might be altered by many anti-angiogenic drugs and cause "vessel normalization". Epigallocatechin-3-gallate (EGCG), a natural anti-angiogenesis agent refined from green tea, was defined to have multiple effects on angiogenesis factors. So we hypothesizing that EGCG might cause "vessel normalization", and in addition combined chemotherapy exert a synergistic effect in the tumor vessel normalization window caused by EGCG.
Methods Build nude mice xenograft tumor model (A549 cell line). Randomly divided them into three groups (treated with saline, EGCG, bevacizumab). Test following indexes at day of 0, 2, 4, 6, 9, 12: Vessel structure: MVD, MPI; vessel GBM; Transmission-electron-microscope of microvessles; Vessel functional: perfusion function, vessel permeability; Microenvironment effect: IFP, PO2. Test cisplatin concentration in tumor tissues with different combination of EGCG and cisplatin. Treated mice with saline, cisplatin, EGCG, EGCG+ cisplatin on day0 and EGCG+ cisplatin on day5 and record growth delay.
Results EGCG treated group undergoing a persisting decrease of MVD, a gradual decrease of MPI, a transient elevation of vessel perfusion function, permeability and PO2, transient decrease of IFP in tumor tissue. Full-dose cisplatin at day5 had a concentration significantly higher than Full-dose at day0 and half-dose at d5. Statistical analysis shows EGCG and cisplatin had synergistic effect as a combined anti-tumor chemotherapy. Combined treatment groups had significantly lower xenograft tumor growth rates than other three groups, and tumor growth rate in combining cisplatin on day5 was significantly lower than on day0.
Conclusion EGCG causes vessel normalization in human lung adenocarcinoma tumor, the window is between Day 4 to Day 9. Combined therapy in this window period can escalate drug concentration in local tumor tissue, and leads to anti-tumor synergistic effect, providing a new strategy for EGCG applying as a complementary chemotherapy drug.

OS166

INHIBITION OF H446 GROWTH BY BCL-XL ANTISENSE OLIGONUCLEOTIDE (ASON) LOADED CYCLODEXTRIN HYBRID NANOSYSTEM

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Background and Aim Study The absence of safe, efficient, cost-effective, and easily scalable delivery platforms is one of the most significant hurdles and critical issues that limit the bench to bedside translation of oligonucleotides-based therapeutics. In this study, a nanovector was designed by integrating a pH-responsive cyclodextrin material and low molecular weight polyethylenimine (PEI). To investigate the effect of Bcl-xl antisense oligonucleotide (ASON) loaded these nanomaterials on H446 cells.
Methods FT-IR spectrum was recorded on a PerkineElmer FT-IR spectrometer (100 S), 1H NMR spectrum was recorded on a Varian INOVA-400 spectrometer operating at 400 MHz. Dynamic light scattering (DLS) and potential measurements of various Third Military Medical University. RPMI-1640 medium, trypsin, and fetal bovine NPs in a queous solution were performed on a Malvern Zetasizer Nano ZS instrument at 25 centigrade. Transmission electron microscopy (TEM) observation was carried out on a ECNAI-10 microscope operating at an acceleration voltage of 80 kV. Scanning electron microscopy images were taken on an S-3400N II electron microscope. Intracellular uptake study was performed by confocal laser scanning microscope. Cell transfection efficiency was evaluated by flow cytometry. H446 cell viability was analysed by MTT method. Cell apoptosis analysis was conducted using the Annexin V-FITC (Annexin V) and propidiumiodide (PI) detection kit (BD PharMingen, SanDiego, CA) according to the manufacture's protocol.
Results The developed pH-responsive ASON nanotherapeutics could be efficiently transfected into human lung carcinoma cells H446 in a time- and dose-dependent manner, resulting in effective cell growth inhibition, significant suppression on the expression of Bcl-xl mRNA/protein, and efficient cell apoptosis. Ac-aCD showed drastically higher efficacy and lower cytotoxicity, compared with PLGA, PEI (25,000 Da) and Lipofectamine 2000.
Conclusion This pH-responsive hybrid nanosystem Ac-aCD may serve as a safe and efficient nonviral vector that may find wide applications in gene therapy.

OS167

EFFECT OF BCL-XL ANTISENSE OLIGONUCLEOTIDE LOADED CYCLODEXTRIN HYBRID NANOSYSTEM ON THE PROLIFERATION OF VASCULAR SMOOTH MUSCLE CELLS

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Background and Aim Study It is well known that abnormal growth of pulmonary vascular smooth muscle cells (PASMCs) cause the pulmonary hypertension. To investigate the effect of Bcl-xl antisense oligonucleotide (ASON) loaded these nanomaterials on PASMCs proliferation.
Methods Intracellular uptake study was performed by confocal laser scanning microscope. Cell transfection efficiency was evaluated by flow cytometry. H446 cell viability was analysed by MTT method. Cell apoptosis analysis was conducted using the Annexin V-FITC and propidiumiodide detection kit according to the manufacture's protocol. The mRNA expression of Bcl-xl was tested by two-step RT-PCR. The levels of Bcl-xl protein was determined by western blot.
Results Bcl-xl ASON loaded Ac-aCD/PEI nanoaystem could be efficiently transfected into rat PASMCs in dose-dependent manner, and take the inhibition effect on the cell proliferation. It could significantly decrease the expression of Bcl-xl mRNA/protein, and enhance PASMCs apoptosis. Ac-aCD showed drastically higher efficacy and lower cytotoxicity, compared with PEI (25,000 Da) and Lipofectamine 2000.
Conclusion This pH-responsive hybrid nanosystem Ac-aCD, as a safe and efficient nonviral vector, that can load Bcl-xl ASON, which induce PASMCs apoptosis and suppress the cell proliferation.

OS168

SURFACTANT PROTEINS A AND D SUPPRESS EPIDERMAL GROWTH FACTOR SIGNALING THROUGH INTERACTIONS WITH N-GLYCANS OF RECEPTOR

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Background and Aim of Study Surfactant proteins A and D (SP-A and SP-D) play important roles in innate immunity of the lung. Although it has been suggested that SP-A and SP-D expression levels are inversely correlated with lung cancer progression, the particular mechanisms have not been fully elucidated. In this study, we examined whether SP-A and SP-D suppressed lung cancer progression by downregulation of epidermal growth factor (EGF) signaling.
Methods Effects of SP-A and SP-D on EGF signaling in A549, H441 and human EGF receptor (EGFR) stable expressing CHO-K1 cells were examined by Western blotting. Cell proliferation, migration and invasion were examined by WST-1 assay and the transwell double chamber assay. EGF to EGFR binding was analyzed by using ^{125}I-EGF. We purified the recombinant extracellular domain of EGFR (soluble EGFR = sEGFR). The binding of SP-D to sEGFR was examined by ELISA, ligand blotting and surface plasmon resonance analysis. The structures of N-glycans of sEGFR were analyzed by mass spectrometry.
Result SP-A and SP-D suppressed EGF-induced phosphorylation of EGFR, Akt and Erk. SP-A and SP-D also inhibited the proliferation, migration and invasion of A549 cells. SP-D downregulated the binding of EGF to high affinity EGFR. SP-D directly bound to sEGFR in a Ca^{2+} dependent manner. In the presence of EDTA or mannose, the binding of SP-D to sEGFR was suppressed and N-glycans cleavage of sEGFR also suppressed the binding. Mass spectrometric analysis indicated that N-glycans on Asn328 and Asn337 of EGFR were of a high-mannose type.
Conclusion We found that SP-A and SP-D inhibit EGF signaling in A549 and H441 cells. SP-D directly binds to the extracellular domain of EGFR, probably via a high mannose type of N-glycans in domain III. It is assumed that SP-D competes with EGF to bind EGFR, downregulates EGFR activation and suppresses lung cancer progression.

OS169

THERAPEUTIC EFFICACY OF ENDOTHELIN RECEPTOR BLOCKADE ON EXPERIMENTAL BRAIN METASTASES OF HUMAN NON-SMALL CELL LUNG CANCER

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Background and Aim of Study Treatment of patients with lung cancer brain metastases remains a major challenge due to the limited availability of standard therapy. Thus, the development of successful treatment options for these patients is mandatory. Recently, the endothelin axis was reported to be involved in cancer progression through its pleiotropic biological effects on cell survival, proliferation, invasion, and metastasis. In this study, we evaluated both the in vitro and in vivo effects of macitentan, an orally bioavailable, dual endothelin A receptor and endothelin B receptor antagonist, as monotherapy, and in combination with paclitaxel.
Methods In vitro cell proliferation was determined by MTT assay. To produce experimental brain metastasis human lung adenocarcinoma, PC-14 cells were injected into the internal carotid artery of male athymic nude mice.
Results In human non-small cell lung cancer PC-14 cells, macitentan treatment inhibited cell proliferation, corresponding with inhibition of Akt and p42/44 mitogen-activated protein kinase phosphorylation, and increased apoptosis. The combination of macitentan and paclitaxel resulted in the potentiation of all of these effects, suggesting that macitentan could enhance sensitivity to paclitaxel. Moreover, macitentan completely abrogated astrocyte-mediated protection of tumor cells against paclitaxel. In an experimental brain metastasis model of human lung cancer, the combination of macitentan and paclitaxel significantly inhibited the growth of brain metastasis and produced a striking survival prolongation of tumor-bearing mice.
Conclusions The endothelin A and B receptor blockade by macitentan could be a promising therapeutic strategy for brain metastases of non-small cell lung cancer.

OS170

POSSIBLE ROLE OF TOCILIZUMAB FOR CACHECTIC PATIENTS WITH INTERLEUKIN-6 EXPRESSING LUNG CANCER

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Background and Aim of Study IL-6 is a key mediator of cancer cachexia. We currently reported a case that tocilizumab, anti-IL-6 receptor antibody, had the dramatic effect on cachexia induced by IL-6 over-expressing lung cancer (J Clin Oncol 31; e69, 2013), and are currently planning a clinical trial of tocilizumab. As preliminary step, we executed evaluation of serum IL-6 level in patients with lung cancer and the experiment of murine cachexia model.
Methods First, we measured serum IL-6 levels in patients with lung cancer, and analyzed its association with cachexia and survival. Next, we examined the effect of a murine analogue of tocilizumab (MR16-1) in the experimental cachexia model.
Results Serum IL-6 levels were higher in patients with cachexia than those without cachexia. In patients with chemotherapy-resistant lung cancer, serum IL-6 was strongly correlated with the survival. Its cut-off level for affecting their prognosis was 21 pg/mL. Meanwhile, transplantation of IL-6 expressing Lewis Lung Carcinoma cells caused cachexia in mice, and we administered MR16-1 (MR16-1 group) or 0.9% saline (control). Tumor growth was not significantly different between two groups, but the decrease of body weight, and food and water intakes were significantly improved in MR16-1 group. Weights of the extremities muscles, fat tissue around testes, and values of hematocrit, triglyceride, and glucose in the blood were significantly higher in MR16-1 group than those in control group.
Conclusion Serum IL-6 level was a surrogate marker for evaluating the prognosis in patients with chemotherapy-resistant lung cancer and tocilizumab could be a promising treatment option for patients with IL-6 overexpressing lung cancer.

OS29: BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES 2

OS171

ENDOBRONCHIAL ULTRASONOGRAPHY WITH A GUIDE SHEATH IN THE DIAGNOSIS OF BENIGN PERIPHERAL LESIONS

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Background Transbronchial biopsy (TBBX) using Endobronchial ultrasonography with a guide sheath (EBUS-GS) can achieve a sensitivity of 73% and a specificity of 100% for diagnosing malignant peripheral lesions. For benign peripheral lesions, however, the role of EBUS-GS is not well established.
Methods Retrospective analysis for cases of peripheral lung lesions, for which we conducted EBUS-GS TBBX for diagnosis from October 2012 to March 2013 in Hokkaido University Hospital.
Results During this period, we conducted EBUS-GS-TBBX for 59 patients, of whom 5 were diagnosed to have benign lung disease with help EBUS-GS-TBBX, 48 with malignancy, and the other 6 could not be diagnosed. The role of EBUS-GS-TBBX in the diagnostic process for the 5 benign cases was analyzed. They included 3 cases of mycobacterium infection and 2 cases of sarcoidosis. CT findings included consolidation in 1 case, mass-like lesions in 2 and cavity-containing lesions in the remaining 2. The EBUS probe was successfully positioned within the lesion in 4 cases and adjacent-to the lesion in 1 case. One patient presented with a mass-like lesion was diagnosed as mycobacterium infection with help of typical bronchoscopic finding and positive PCR for mycobacterium avium. Two patients with sarcoidosis, who had high clinical suspicions of the disease because of cervical lymph node involvement in one and bilateral hilar lymphadenopathy in the other, could reach the definite diagnosis with help of the lung pathology of epithelial granuloma obtained by EBUS-GS-TBBX. The remaining two patients with mycobacterium infection also reached the final diagnosis with help of the lung pathology in addition to clinical and/or radiological features suggestive of mycobacterium infection. There were no significant complications associated with EBUS-GS TBBX for all patients.
Conclusion From our experience, TBBX with EBUS-GS is a potential diagnostic modality for benign peripheral lung lesions. Further prospective study is warranted.

OS172

BRONCHOSCOPY FOR THE DIAGNOSIS OF LUNG LESIONS IN HEMATOLOGIC DISEASES

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Background and Aim of Study Patients with hematologic diseases may complicate with various lung lesions, but diagnosis was sometimes difficult as transbronchial lung biopsy (TBLB) was not performed due to thrombocytopenia or bleeding tendency. To clarify the usefulness and complications during bronchoscopy for the diagnosis of lung lesions in hematologic diseases.
Methods Medical records of 49 patients with hematologic diseases, who underwent bronchoscopy at our hospital since Jun 2008 to May 2013, were reviewed and analyzed retrospectively.
Results Patients with malignant lymphoma (n = 25), leukemia (n = 10), multiple myeloma (n = 9), and others (n = 5) underwent bronchoscopy for the diagnosis of diffuse ground glass opacities (n = 18), focal consolidation (n = 13), focal nodules or masses (n = 9), diffuse consolidation (n = 4), and others (n = 5) on chest computed tomography. Cytology and bacteriology was performed in all patients but only 12.2% and 38.8% was diagnostic, respectively. TBLB with average 3 specimens and bronchoalveolar lavage (BAL) was performed in 34 patients (69.4%) and 31 patients (63.3%), and 58.8% and 83.9% was diagnostic, respectively. Lymphoma antigen was analyzed by flow cytometry in 9 patients with malignant lymphoma and 77.7% was diagnostic. Platelets were less than 50,000/μL in 8 patients whom TBLB was not done. Lacking of TBLB was associated with failure to definite diagnosis, but BAL was useful even without TBLB in cases with ground glass opacities on chest computed tomography or suspected lung involvement of malignant lymphoma. Complications included transient hypoxia (n = 26), transient fever (n = 15), bleeding required endobronchial epinephrine or thrombin administration (n = 7), and 1 patients required transient endobronchial intubation due to massive bleeding after curetting.
Conclusion Combination of bronchial wash, BAL, TBLB was the best way to the definite diagnosis, however BAL was useful for the diagnosis of pulmonary hemorrhage, interstitial pneumonia, or lung involvement of malignant lymphoma even in cases without TBLB due to thrombocytopenia.

OS173

FACTORS INFLUENCING DIAGNOSTIC YIELD OF TRANSBRONCHIAL BIOPSY USING ENDOBRONCHIAL ULTRASONOGRAPHY WITH A GUIDE SHEATH (EBUS-GS) IN PERIPHERAL PULMONARY LESIONS

KAZUYOSHI IMAIZUMI, TOMOYUKI MINESAWA, SUMITO ISOGAI, TAKUYA OKAMURA, SAYAKO MORIKAWA, YOSHIKAZU NIWA, TOMOKO TAKEYAMA, YUKI MIENO, MARIKO MORISHITA, SAKURAKO UOZU, TAMI HOSHINO, MASAMICHI HAYASHI, TORU NAKANISHI, MITSUSHI OKAZAWA
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Background Recent evidences have shown endobronchial ultrasonography with a guide sheath (EBUS-GS) improves diagnostic yield of transbronchial biopsy (TBB) for peripheral pulmonary lesion (PPL). However, factors related to diagnostic yield of transbronchial biopsy using EBUS-GS are not fully understood.
Methods We retrospectively reviewed 120 consecutive patients with PPLs (7.7–75.0 mm: median 22.0 mm) who underwent TBB with EBUS-GS in our institute from April 2012 to March 2013.
Results The ultimate diagnosis included 68 cases of lung cancer, 15 cases of other tumor and 37 cases with benign or inflammatory lesions. The definite diagnosis was established by bronchoscopy in 90 cases (75%), and the pathological diagnostic yield of tissue biopsy was 70%. The diagnostic yield of malignant lesion (78%) was significantly higher than that of benign or inflammatory lesions (42%). In the multivariate analysis, position of the EBUS probe (within to the PPL), malignant lesion, and visibility on fluoroscopy were determined to be significant factors predicting diagnostic yield.
Conclusion Although TBB using EBUS-GS is a useful approach for diagnosis of PPL, it should be noticed that the diagnostic yield of benign lesions or fluoroscopic invisible lesions is not so high. The position of EBUS-probe (within to the lesion) is essential for higher diagnostic yield.

OS174

DIAGNOSTIC PERFORMANCE AND SAFETY OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION IN SUSPECTED MEDIASTINAL LYMPH NODE METASTASIS

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Introduction Most lung cancers are in locally advanced or metastatic stages upon diagnosis and proper staging is critical in assessment of operability. Mediastinal lymph node staging remains one of the most important factors determining the overall staging in the absence of distant metastasis. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) had been shown to be a highly accurate and safe procedure for diagnosis and staging in patients with confirmed or suspected lung cancer.
Methodology Consecutive patients with suspected mediastinal lymph node metastasis underwent EBUS-TBNA between January 2011 and September 2012 were recruited and followed up.
Results A total of 58 EBUS-TBNA procedures were performed in 57 patients (M : F = 43 : 14, mean age = 62, range = 28–84). Seventy-nine lymph node stations (67 mediastinal and 12 hilar lymph nodes) and four para-tracheal masses were targeted for tissue sampling with average of 4.1 needle passes per site. Thirty-five patients with lung cancer (85.4% of all lung cancer patients) were accurately staged by EBUS-TBNA. The procedure diagnosed 31 cases of mediastinal metastasis from carcinoma of lung, 4 cases of metastasis from extrathoracic malignancy and 6 cases of tuberculosis (11 true negative cases). The overall diagnostic accuracy was 89.7%. Regarding diagnosing malignancy, the sensitivity, specificity and negative predictive value were 85.4%, 100% and 64.7% respectively. Only two patients (3.4%) had significant desaturation during the procedure and there are no major procedure-related complications.
Conclusion EBUS-TBNA is a safe, promising and accurate diagnostic modality for patients with suspected mediastinal metastasis.

OS175

UTILIZATION OF THORACIC ULTRASONOGRAPHY (USG) BY PULMONOLOGISTS: A PROSPECTIVE EVALUATION

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Introduction Thoracic ultrasonography (USG) is increasingly by pulmonologists in Hong Kong.
Objective To prospectively evaluate the performance and outcomes of thoracic USG in a public general hospital in Hong Kong.
Method Between 6th March to 6th June 2013, all consecutive thoracic USG performed were prospectively evaluated, with follow-up information at 2 weeks after the procedure. Information collected includes indications, procedure performed, diagnostic yields and complications.
Results Seventy-two thoracic USG were performed by the 7 pulmonologists during the 3-month period. Sixty-five procedures (90.2%) were done in hospitalized patients. The commonest indication was pleural effusion (68, 94.4%), with only 16.7% being "large" (more than mid-thorax posteriorly) effusions. USG alone were performed in 13 (18.1%), with another 7 (9.7%) done prior to pleuroscopy to determine the entry site. Diagnostic pleural aspiration (PA) alone was performed in 28 (38.9%), closed pleural biopsies (PB) in 7 (9.7%), transcutaneous lung fine needle aspiration cytology (FNAC) in 2 (2.8%), and pleural drainage (PD) in 15 (20.8%). Diagnostic yields of PA, PB and FNAC were 75% (all malignancies), 100% (all tuberculosis) and 100% (all malignancies) respectively. PD was successful in all cases, with small-bore catheter insertion in 93.3% (80% under Seldinger technique). In the 59 USG-guided interventions, only 2 cases of vagovagal syncope were noted (3.4%) as complications. Procedures performed within "safety triangle" for PA, PB and PD were 21%, 43% and 36% respectively.
Conclusions USG was shown to be a useful aid for pulmonologists. In addition to a superior diagnostic and therapeutic performance, the safety profiles were excellent even with interventions in small effusions and outside "safety triangle".

OS176

DIAGNOSIS OF PERIPHERAL PULMONARY LESIONS WITH RADIAL ENDOBRONCHIAL ULTRASOUND-GUIDED BRONCHOSCOPY

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Background and Aim of Study The diagnosis of peripheral pulmonary lesions (PPLs) is a challenging task for pulmonologists. Radial endobronchial ultrasound (EBUS) has been developed to enhance the diagnostic yield. The aim of this study was to evaluate the effectiveness of radial EBUS in the diagnosis of PPLs.
Methods A retrospective study was conducted on 174 patients who were diagnosed with PPLs and underwent EBUS-guided bronchoscopy between July 2009 and May 2013. Histological examination of specimens obtained by transbronchial lung biopsy (TBLB) and cytological examinations of brushing smear, rinsed fluid of brushing, and bronchoalveolar lavage fluid (BALF) were evaluated for the diagnosis.
Results The mean diameter of the PPLs was 25.1 ± 10.7 mm. The final diagnosis included 129 malignancies and 45 benign lesions. The overall diagnostic yield of EBUS-guided bronchoscopy was 79.9%. Both size and etiology of the PPLs had no influence on the diagnostic yield of EBUS-guided bronchoscopy (82.9% vs 74.6% for PPLs > 20 mm and PPLs < 20 mm; $p = 0.19$ and 82.9% vs 71.1% for malignancy and benign diseases; $p = 0.09$). The performance of TBLB rendered the highest diagnostic yield among these specimens (69.0%, 50.6%, 42.0%, and 44.3% for TBLB, brushing smear, rinsed brushing fluid, and BALF, respectively; $p < 0.001$). Combination of TBLB, brushing smear, and BALF provided the highest diagnostic yield, while rinsed brushing fluid did not add benefits on the outcomes.
Conclusion EBUS-guided bronchoscopy is a useful technique in the diagnosis of PPLs. To achieve the highest diagnostic performance, TBLB, brushing smear and BAL should be performed altogether.

OS30: INTERSTITIAL LUNG DISEASE 4

OS177

SERUM HEAT SHOCK PROTEIN 47 LEVELS ARE ELEVATED IN ACUTE INTERSTITIAL PNEUMONIA

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Background and Aim of Study Heat shock protein (HSP) 47, a collagen-specific molecular chaperone, is involved in the processing and/or secretion of procollagen. We hypothesized that HSP47 could be a useful marker for fibrotic lung disease. The aim of this study was to evaluate serum levels of HSP47 in patients with various idiopathic interstitial pneumonias (IIPs).
Methods Subjects comprised 9 patients with acute interstitial pneumonia (AIP), 12 with cryptogenic organizing pneumonia (COP), 16 with nonspecific interstitial pneumonia (NSIP), 19 with idiopathic pulmonary fibrosis (IPF), and 19 healthy adult volunteers.
Results Patients with AIP had serum HSP47 levels that were significantly higher than those of COP, NSIP or IPF patients and those of healthy volunteers. In contrast, serum levels of HSP47 among patients with COP, NSIP, IPF, and healthy volunteers did not differ significantly. Receiver operating characteristic curves revealed that the cut-off level for HSP47 that resulted in the highest diagnostic accuracy for discriminating between AIP and COP, NSIP, IPF, and healthy controls was 859.3 pg/mL. The sensitivity, specificity, and diagnostic accuracy were 100.0%, 98.5%, and 98.7%, respectively.
Conclusion The present results demonstrate that, among patients with various IIPs, serum levels of HSP47 were elevated specifically in patients with AIP.

OS178

ETHNIC DIFFERENCE AND SERUM KL-6 AS PREDICTORS FOR ACUTE EXACERBATION OF IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study Acute exacerbation (AE) is a major cause of death in idiopathic pulmonary fibrosis (IPF). Ethnic difference and several biomarkers may be associated with the incidence of AE of IPF (AE-IPF). However, little is known about sensitive predictors for the risk of AE-IPF. The aim of our study was to investigate the significance of ethnic difference and biomarkers as predictors for AE-IPF.
Methods We have prospectively collected a total of 79 Caucasian patients and 49 Japanese patients with IPF. Serum samples were obtained from every patient at the enrollment. Serum level of KL-6 was measured by ECLIA. The correlation between ethnicity, baseline serum KL-6 level, pulmonary function and the incidence of AE-IPF was evaluated.
Results There were 60 males and 19 females in the German population (age, 69 ± 8) and 37 males and 12 females in the Japanese population (age, 67 ± 10). Median follow-up period was 3.4 ± 3.2 years. Although there was no significant difference in the clinical backgrounds and pulmonary function variables between the groups, combined therapy of steroids, immunosuppressants and oral N-acetylcysteine were more frequently used in the German cohort, and inhaled N-acetylcysteine or pirfenidone were more frequently used in Japanese cohort. In the univariate analysis, Japanese ethnicity, baseline serum KL-6 ≥1300 U/mL, lower baseline vital capacity (VC) % predicted and the non-use of immunosuppressants or oral N-acetylcysteine were risk factors for AE-IPF. In the multivariate analysis, Japanese ethnicity (hazard ratio (HR), 4.44; p-value, 0.027), baseline serum KL-6 ≥1300 U/mL (HR, 2.76; p-value, 0.023) and lower baseline VC % predicted (HR, 1.04; p-value, 0.001) were independent risk factors for AE-IPF.
Conclusion Japanese ethnicity, baseline serum KL-6 level ≥1300 U/mL and lower baseline VC % predicted seem to be independent risk factors for AE-IPF.

OS179

HIGHER SERUM CCL17 MAY BE A PROMISING PREDICTOR OF ACUTE EXACERBATIONS IN CHRONIC HYPERSENSITIVITY PNEUMONITIS

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Background Recent research has suggested that the Th1 and Th2 chemokine/cytokine axis contributes to the development of chronic hypersensitivity pneumonitis (HP). Acute exacerbations (AE) are significant factors in the prognosis of chronic HP. Little is known, however, about these biomarkers in association with AE in chronic HP patients.
Methods Fifty-six patients with chronic HP were evaluated, including 14 patients during episodes of AE. Th1 mediators (C-X-C chemokine ligand [CXCL]10 and interferon [IFN]-γ), Th2 mediators (C-C chemokine ligand [CCL]17, interleukin-4, and interleukin-13), and pro-fibrotic mediator (transforming growth factor [TGF]-β) were measured to evaluate the mediators as predictors of AE. C-C chemokine receptor (CCR) 4 (receptor for CCL17)-positive lymphocytes were quantified in lung specimens.
Results Serum CCL17 levels at baseline independently predicted the first episode of AE (HR, 72.0; 95% CI, 5.03–1030.23; $p = 0.002$). AE was significantly more frequent in the higher-CCL17 group (>285 pg/ml) than in the lower-CCL17 group (<285 pg/ml) (log-rank test, $p = 0.0006$; 1-year incidence: higher CCL17 vs. lower CCL17, 14.3% vs. 0.0%). Serum CCL17 levels and CCR4-positive cells during episodes of AE were increased from the baseline ($P = 0.01$ and 0.031).
Conclusions Higher serum concentrations of CCL17 at baseline may be predictive of AE in patients with chronic HP, and CCL17 may contribute to the pathology of AE by inducing the accumulation of CCR4-positive lymphocytes in the lungs.

OS180

COMPARISON OF KL-6, SP-A, SP-D, 8-ISOPROSTANE, MMP-9, AND TIMP-1 AS SERUM BIOMARKERS FOR PATIENTS WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Introduction Combined pulmonary fibrosis and emphysema (CPFE) is characterized by severe dyspnea on exertion, preserved lung volume, severely impaired diffusing capacity for carbon monoxide (DLCO), and hypertension, and has poor survival rates. Krebs von den Lungen-6 (KL-6), surfactant proteins (SP), 8-isoprostane, and matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) have been linked to cigarette smoke-induced lung remodeling, idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD). However, the significance of these proteins has not been well studied in patients with CPFE.
Aims The aim of this study was to investigate the clinical significance of biomarkers in serum obtained from patients with CPFE, IPF, and COPD.
Methods The concentrations of KL-6, SP-A, SP-D, 8-isoprostane, MMP-9, and TIMP-1 in the serum of 21 patients with CPFE, 24 patients with IPF, and 32 patients with COPD were measured using enzyme-linked immunosorbent assay/electrochemiluminescence immunoassay (ELISA/ECLIA). The correlation between the results of a pulmonary function test and the levels of these biomarkers was evaluated.
Results Serum levels of KL-6 and SP-D were elevated in the majority of patients with CPFE or IPF, compared with those with COPD, and correlated with lung impairment. The ratio of MMP-9 to TIMP-1 was higher in CPFE and IPF than in COPD, indicating a significant protease/anti-protease imbalance, in favor of proteases.
Conclusion The results of this study show that KL-6 and SP-D are potential diagnostic biomarkers for CPFE. A protease/anti-protease imbalance may play and important role in the pathogenesis of CPFE.

OS181

BRONCHOALVEOLAR LAVAGE NEUTROPHILIA PREDICTS MORTALITY IN ACUTE EXACERBATION OF INTERSTITIAL PNEUMONIA

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Background and Aim of Study Acute exacerbation of interstitial pneumonia (AE-IP) is now identified as a life-threatening complication of interstitial pneumonia. The purpose of the present study was to evaluate the prognostic factors of in-hospital mortality in terms of clinical findings including bronchoalveolar lavage (BAL) fluid analysis in AE-IP.
Methods We retrospectively evaluated the patients with AE-IP admitted between April 2010 and March 2013. Clinical presentation, laboratory data, treatment, and outcome were analyzed.
Results We identified 37 consecutive episodes of AE-IP in the medical records of 34 patients. All patients received BAL. The in-hospital mortality rate was 29.7% (11/37). The multivariate logistic regression analysis revealed that only BAL fluid neutrophil percentage was a significant prognostic factor determining in-hospital mortality. The log-rank test showed that patients with increased BAL fluid neutrophil percentage (>30%) had significantly lower survival rates than others ($p < 0.001$).
Conclusions BAL fluid neutrophilia is an independent predictor of in-hospital mortality among patients with AE-IP. This finding highlights the prognostic significance of performing BAL in those patients.

OS31: PAEDIATRIC LUNG DISEASE

OS182

LUNG FLUTE IN THE MANAGEMENT OF PNEUMONIA IN CHILDREN

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Background According the WHO pneumonia is the leading cause of death in children worldwide. Pneumonia is an inflammation of the lung parenchyma resulting in obliteration of alveolar air space by purulent exudates, due to an infectious agent most of the time. Lung flute is a device available; indicated for positive expiratory pressure therapy which is part of the bronchial hygiene therapy.
Objective To determine the effectiveness of lung flute in the management of pneumonia in pediatric patients.
Design Open labeled randomized controlled trial.
Setting Philippine Heart Center from February 1, 2012 to December 31, 2012.
Materials and Methods Patients were randomized either to the standard therapy or the lung flute group. The standard therapy received antibiotics and bronchodilator if needed, sputum induction was done. Quality and quantity of sputum was assessed. In the lung flute group, same procedure was done with the use of lung flute. Assessments were based on resolution of fever, disappearance of crackles, improvement on chest x-ray, and removal of oxygen support and hospital stay. Adverse events were noted.
Results A total of 60 subjects were enrolled in the study. Thirty one under the standard therapy group and 29 under the lung flute group. Among the factors analyzed, only the quality of sputum showed significant result, standard therapy yielded 7 subjects (22.6%) with good quality sputum compared the lung flute group of 18 subjects (62.1%). No significant difference comparing the resolution of fever, disappearance of crackles, improvement on chest x-ray, number of hours oxygen removed and hospital stay.
Conclusion Lung flute can be used as an adjunct in the treatment of pneumonia, helping the patient to expectorate easily and can aid in the collection of sputum as a specimen for further diagnostic work-up.
Key Words Pneumonia, Lung Flute.

OS183

NON-TYPEABLE H. INFLUENZAE-SPECIFIC IMMUNE RESPONSES IN CHILDREN WITH CHRONIC SUPPURATIVE LUNG DISEASE

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Introduction Non-typeable *H. influenzae* (NTHi) is the most common bacterial pathogen associated with chronic suppurative lung disease (CSLD). Limited data exists regarding the adaptive immune response to NTHi and the role it may have in the aetiology of CSLD in children.
Aim To determine if children with CSLD have a suboptimal adaptive immune response to NTHi.
Method NTHi-stimulated cytokine (IFNg, IL-13 and IL-10) production from peripheral blood mononuclear cells (PBMC) were measured in 82 children with CSLD and 51 healthy control children (HC). Plasma antibody titres (IgG1, IgG4) to the *H. influenzae* outer membrane proteins P4 and P6 were also measured.
Results Compared to healthy controls, PBMC from children with CSLD produced significantly more IL-13 ($p = 0.030$) and significantly less IFNg ($p < 0.001$) and IL-10 ($p = 0.029$) in response to NTHi. CSLD was associated with significantly lower P4-specific IgG1 titres but there was no significant difference in P6-specific IgG1 between the two groups. The prevalence of detectable IgG4 to both P4 and P6 was low in both groups however the level of response to P6 was significantly lower in children with CSLD ($p < 0.001$). IL-10 was positively correlated with P4 and P6-specific IgG4 ($p = 0.022$ and $p = 0.003$ respectively).
Conclusion Cell mediated immunity, in particular the IFNg response, likely plays an important role in protective immunity against NTHi in children. The inability to elicit a strong IFNg response to NTHi may contribute to the pathogenesis of CSLD. Whilst the cell-mediated immune response in CSLD is TH2-skewed (high IL-13, low IFNg), low IL-10 production and low IgG4 titres suggest a more complex form of immune dysregulation in children with CSLD.

OS184

CARBON-MONOXIDE LEVEL AS INFLAMATORY MARKER OF SMOKE IN PREGNANCY WOMEN AND NEWBORN INFANTS

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Background Low birth weight (BW), small head circumference, reduced length, increased preterm births are among known consequences of smoking during pregnancy. Few studies have linked carbon-monoxide level as the predictor of the level of cigarette smoking. In this study we evaluate the level of maternal carbonmonoxyde in relation with smoking status and BW.
Methods This is a cross sectional study. Subjects were mother who gave birth in Persahabatan Hospital and grouped into three categories: active smokers, passive smokers, non smokers. The level of exhaled carbon-monoxide was measured by smoke analizer and analized were related to BW.
Results A total of 93 subjects were recruited in this study, which median age 30 (16–42) years. The distribution of active smokers was 24 (26.7%), passive smokers 36 (40.0%), and non smokers 30 (33.3%). Smoking was more frequent in younger mothers and from lower socio-economic groups. The mean birth weight of infants born to active smokers were lighter (2757 g) than passive smokers (2960 g) and non smokers (3238 g). The mean weight of the placenta were lighter (450 g) in active smokers, passive smokers (496 g) and non smokers (559 g). Carbon-monoxide exhale concentration was higher in smoker (mean 12.57 ppm), passive smoker (mean 7.82) and non smoker (mean 3.25 ppm) and statistically significant ($p = 0.001$). Birth weight was not associated with smoke exposure ($p = 0.111$).
Conclusion Exhaled CO monitoring in pregnant mother can predict the smoking status. Further studies are needed to determine the influence of smoking to low birth weight.
Key Words smoking; carbon-monoxide; pregnancy.

OS185

RUDHE SYNDROME: REVERSIBLE SHUNT RELATED LOBAR EMPHYSEMA- A REPORT OF CASES AND SYSTEMATIC REVIEW OF LITERATURE

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Rudhe syndrome was used to refer to reversible shunt related lobar emphysema (LE). Ulf Rudhe who made his first observation in 1971 that emphysema in children with congenital heart disease is secondary to the shunt thus surgical intervention be directed to the correction of the cardiac defect alone and not lobectomy. We reviewed the cases of four patients with concomitant LE and CHD. The medical records were evaluated with reference to age, type of CHD, pulmonary function, radiographic findings, pulmonary artery pressure, clinical signs and symptoms, surgical management and outcome after surgery. We also reviewed 21 literatures on LE with CHD. Among the four cases we had, 3 were left to right shunts and 1 is a case of Tetralogy of Fallot (TOF) with an absent pulmonary valve. The 3 underwent correction of the cardiac lesion and repeat chest radiograph and CT scan showed almost complete resolution of the lobar emphysema with complete resolution of clinical symptoms 6 months post cardiac surgery. The other one underwent TOF correction with lung tacking with radiographic resolution of the lobar emphysema however patient succumbed to sepsis. The most commonly affected lobes were the left upper and right middle lobes. The literature review consisted of 137 subjects with lobar emphysema with concomitant congenital heart disease. The three most common cardiac lesions associated with lobar emphysema are ventricular septal defect, patent ductus arterioles and TOF with absent pulmonary valve. One hundred out of the 137 underwent correction of the cardiac lesion without lobectomy. Resolution of airway obstruction as well as radiographic resolution of the emphysematous lung were noted as early as 3 months to 1 year post cardiac surgery. Earlier correction of cardiac lesion improves the prognosis in terms of reversibility of lobar emphysema and anatomic defects of the bronchus.

OS186

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 two 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 larygomalacia. 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 aryepigiottic 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.

OS32: RESPIRATORY NEUROBIOLOGY AND SLEEP

OS187

RISK FACTORS OF OBSTRUCTIVE SLEEP APNEA AMONG OVERWEIGHT AND OBESE TAXI DRIVERS IN JAKARTA, INDONESIA

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Introduction Obstructive sleep apnea (OSA) correlated with the increase risk in traffic accident. Study in developed countries has found a high prevalence of OSA in commercial drivers but its data in Indonesian taxi drivers is still unknown. Overweight and obese are known to be the most important risk factors for OSA. This study was conducted to know the magnitude of OSA in overweight and obese taxi drivers in Jakarta, Indonesia.
Method A cross sectional study was done in a population of taxi drivers with BMI 23 until 29.9 in Jakarta and ramdomly sample proportionally from 10 taxi pool/station. Study was done from 1 November 2011 until 31 September 2012. The diagnosis of OSA were based on clinical symptoms and portable polysomonography (PSG) home monitoring.
Result Among 62 from 118 drivers (52.5%) were diagnosed with OSA. Significant OSA symptoms were snoring (p 0.002), fatique (p 0.027), unrefreshing sleep (p 0.001), occasional sleep while a driving (p 0.003), and headache or nausea while woke up in the morning (p 0.038). Risk factors for OSA in overweight and obese subjects were increased of body mass index/BMI (adjusted OR 1.56, p 0.003, 95% CI 1.16–2.11), history of snoring in the family (adjusted OR 2.75, p 0.018, 95% CI 1.18–6.36) and sleep duration less than 6 hour within 24 hour (adjusted OR 2.56, p 0.028, 95% CI 1.11–5.94).
Conclusion Overweight and obese taxi driver have higher risk of developing OSA. The risk factors correlated with OSA were increased of body mass index, history of snoring in the family and sleep duration less than 6 hour within 24 hour.
Key Words Obstructive sleep apnea, risk factors, taxi driver, overweight.

OS188

SIGNIFICANT ASSOCIATIONS BETWEEN OBSTRUCTIVE SLEEP APNEA AND FAT ACCUMULATION IN THE LIVER IN MALE SUBJECTS WITHOUT VISCERAL OBESITY

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Background Non-alcoholic fatty liver disease (NAFLD), emerging as the most common chronic liver disease, has a strong relationship to visceral fat accumulation (VFA). Obstructive sleep apnea (OSA) is also associated with VFA, and recently the association between OSA and NAFLD has been reported. However, the interrelations between OSA, VFA and NFALD are not well understood.
Methods To investigate the gender-specific relationships among OSA, liver fat accumulation (LFA), and visceral obesity (VO; VFA > or = 100 cm^2), we surveyed consecutive 250 subjects (189 males, 61 females) with polysomnography and computed tomography (CT). LFA was quantitatively estimated by CT values of liver. Visceral fat area (VFA) and subcutaneous fat area (SFA) were also measured.
Results Among study subjects, average age, BMI and VFA were 57 years, 26.6 kg/m^2, and 145 cm^2, respectively. In males, VFA, 4% oxygen desaturation index, % sleep time of $SpO_2 < 90\%$ (% T < 90), and serum ALT, GGT, and triglyceride (TG) levels were significantly higher, and SFA and serum HDL-cholesterol levels were significantly lower than in females. Stepwise multiple regression analyses revealed that the variables independently correlated with LFA in males were age, BMI, VFA, TG, HDL-cholesterol and fasting plasma glucose levels, and those in females were BMI and TG. When multiple analyses were also performed in subgroups with and without VO respectively, % T < 90 ($R^2 = 15.1\%$, $P < 0.001$), in addition to BMI ($R^2 = 16.5\%$, $P = 0.004$), TG ($R^2 = 10.1\%$, $P = 0.022$) and HOMA-IR ($R^2 = 14.4\%$, $P = 0.005$), was independently correlated with LFA in only males without VO.
Conclusions OSA-related nocturnal hypoxia (% T < 90) was one of the important risk factors for LFA in male OSA patients without VO. Treatment of OSA might prevent or improve fatty liver disease in these patients.

OS189

THE ADDITIVE IMPACT OF PERIODIC LIMB MOVEMENTS DURING SLEEP ON INFLAMMATION IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Background Both periodic limb movements during sleep (PLMS) and obstructive sleep apnea (OSA) are major causes of sleep disorders and have been associated with systemic inflammation and cardiovascular events. However, it is uncertain whether in combination they promote a higher inflammatory response and greater risk of cardiovascular events than each condition alone.
Objectives To investigate whether the presence of PLMS is associated with increased inflammation in patients suspected of having OSA.
Methods In 342 patients who underwent polysomnography to diagnose OSA, plasma C-reactive protein (CRP) and fibrinogen levels were measured.
Results OSA was found in 254 patients, with 46 also having PLMS. Among the 88 patients who did not have OSA, 8 had PLMS. Plasma CRP and fibrinogen levels in the group with both PLMS and OSA were higher than in patients with neither OSA nor PLMS and in patients with OSA only (CRP: 0.20 ± 0.48 vs. 0.09 ± 0.15 vs. 0.13 ± 0.18 mg/dl, $p = 0.03$; fibrinogen: 298.2 ± 76.1 vs. 269.0 ± 57.1 vs. 270.0 ± 52.6 mg/dl, $p < 0.01$) Multivariate analysis showed that the presence of PLMS was associated with higher plasma CRP levels ($\beta = 0.1402$, $p < 0.01$) and fibrinogen levels ($\beta = 0.1359$, $p < 0.01$) independently from other clinical variables such as body mass index and the severity of OSA.
Conclusion PLMS were positively associated with plasma CRP and fibrinogen levels in patients suspected of having OSA. Since plasma levels of these proteins have been established as predictive factors of future cardiovascular events, the presence of PLMS may be a useful clinical sign to identify OSA patients at high risk of cardiovascular events.

OS190

THE ROLE OF CIH MEDIATED BY TNF-α-REGULATED FRACTALKINE IN LIVER INJURY

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Background Obstructive sleep apnea hypopnea syndrome has been increasingly linked to liver injury. Fractalkine is increased in the liver during times of injury. To tested the hypothesis that hepatic injury induced by CIH will be mediated by TNF-α-regulated fractalkine, we observe the expression of fractalkine in OSAHS style CIH HepG2 cells. The possible pathogenesis of liver injury induced by CIH will be approached in the research.
Methods HepG2 cells were randomly allocated into 5 groups: control group, 10% CIH group, 5% CIH group, 5% CIH + 10 mg/L TNF- α antibody group, 5% CIH + 20 mg/L TNF-α antibody group. Cell proliferation was observed by MTT analysis. Significant fat accumulation was documented by oil red O staining. Real-time PCR method was adopted to detect the fractalkine mRNA. Western-blotting method was adopted to detect the fractalkine protein.
Results 1. Compared with a negative control, CIH decreased growth of HepG2 cells in vitro, $P < 0.01$. There was statistically significant difference between the four CIH groups and CIH inhibition of the growth of HepG2 cells in a concentration-dependent manner. TNF-α antibody induced significant inreases in the ability of CIH HepG2 cells to grow in a concentration-dependent manner, $P < 0.05$. The intracellular lipid metabolism in HepG2 cells was strongly associated with the severity of CIH. TNF-α antibody decreased the lipid accumulation in HepG2 cells induced by CIH. 2. Fractalkine mRNA and protein expression stimulated by CIH was increased in a concentration-dependent manner. Fractalkine mRNA and protein expression stimulated by CIH was decreased by 10.20 mg/L TNF-α antibody in a dose-dependent manner.
Conclusion OSAHS style CIH might participate liver injury by effect on fractalkine though TNF-α.

OS191

THE ROLE OF RAPHE SEROTONERGIC NEURONS IN THE RESPONSES OF GENIOGLOSSUS CORTICOMOTOR AREA DURING INTERMITTENT HYPOXIA IN RATS

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Background Although serotonin (5-HT) plays an important role in the control of genioglossus (GG), little is known about the respective effect of raphe dorsal (DRN) and magnus nuclei (RMg) 5-HT neurons in the control of GG during intermittent hypoxia (IH). The objective is to evaluate the contribution of 5-HT neurons in DRN and RMg to the transcranial magnetic stimulation (TMS) responses of GG corticomotor area during IH.
Methods TMS were performed in the normoxia rats and IH rats. In the IH group, some rats were microinjected anti-SERT-SAP into DRN and RMg respectively to specificly kill 5-HT neurons, and the others were injected artificial cerebrospinal fluid (ACSF) in parallel. The comparisons of TMS responses were carried out between the specific lesion group and ACSF-injected group.
Results Compared with the normoxia group, the shorter latencies of GG TMS responses were observed on the day of 7.21 and 28 of IH, while the higher amplitudes were only found on the 28th day of IH ($P < 0.05$). Compared with the corresponding ACSF-injected groups, the longer TMS latency and lower amplitude were observed in the DRN Lesion group and RMg Lesion group during hypoxia from the 1st to the 28th day ($P < 0.05$). However, after 28-day IH, longer latency and lower amplitude only manifestated in DRN lesion group when compared with those in ACSF-injected DRN group ($P < 0.05$).
Conclusions The results indicated that DRN and RMg 5-HT neurons played different roles in the increased activities of GG corticomotor area during IH.

OS33: TUBERCULOSIS 3

OS192

AUDIT OF TURNAROUND TIME FOR SPUTUM MYCOBACTERIOLOGICAL LABORATORY TESTS IN PUBLIC HOSPITALS IN HONG KONG FROM CLINICIANS' PERSPECTIVE

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Background and Objective For public hospitals in Hong Kong, sputum for tuberculosis (TB) smear and culture are performed in 7 hospital TB laboratories while positive cultures are sent for identification and drug susceptibility tests (DST) in a central reference laboratory. This audit assessed the turnaround time (TAT) for these tests under such a system from the clinicians' perspective.
Patients and Methods This audit was conducted by clinicians with the laboratories totally uninformed. New smear-positive TB patients were identified by the clinicians with the TAT for microscopy recorded. Further reports of the subsequent culture, identification and DST were actively traced for their first appearance in the clinical management computer system. TAT was defined as the number of days from the sputum specimen sent to laboratory to the appearance of the reports. The expected upper limits of TAT for microscopy, culture and DST were arbitrarily set as 1 day, 60 days and 90 days respectively.
Results Seventy-seven cases were identified from seven hospitals. The median TAT for microscopy, culture, identification and DST were 1, 29, 43 and 81 days respectively. TAT was above the upper limit in 9.1% of microscopies, 0% of cultures and 14.3% of DST. When comparing the data from individual hospitals, TAT from one hospital laboratory was found to be significantly shorter than the rest (median TAT: 20 vs 30 days for culture; 33 vs 44.5 days for identification). On subsequent enquiry, this laboratory was actually routinely performing an additional broth culture for all smear positive cases as well as additional antigen-detection and DNA-probe tests for TB identification.
Conclusion TAT for mycobacteriology laboroatory tests in public hospitals in Hong Kong is satisfactory with most cases within the clinicians' expectations. A significant reduction in TAT could be achieved by addition of broth medium for culture and rapid TB identification tests.

OS193

TUBERCULOSIS TESTIS AND DIABETES MELLITUS

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Background Tuberculosis (TB) infectious disease caused by Mycobacterium tuberculosis, Incidence testicular Tuberculosis 3.2 per 100,000 patient. Diabetes mellitus is one of the important risk factors for worsening of TB Case: A 34-year-old male came to Soetomo Hospital with chief complaint wound in the left scrotum, patient complained of discharge like pus in left scrotal skin since 7 months ago, weight loss of 5 kg in 1 month, intermittent cough. Patient had been treated with anti tuberculosis drug, first category. Acid fast bacilli (AFB) smear and sputum culture negative. Chest X-ray examination showed normal, with FNAB suggested inflammation of tuberculosis. Patient treated with Antituberculosis drug (R450H300) continued until 9 months, continued anti diabetic drug and then re-evaluated. Routine monitoring of laboratory, AFB smear, sputum culture and radiology examination.
Results The patient's had ATD Ist category treatment for 9 months with anti diabetic drug.
Conclusions We already reported a patient with tuberculosis testis and diabetes mellitus.
Key Words Testis TB, Diabetic mellitus.

OS194

THE ROLE OF TLR-2, TNF-ALPHA, II-4 IN DIABETES MELLITUS PATIENTS WITH PULMONARY TUBERCULOSIS

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Background There is a high incidence of diabetes mellitus (DM) in the country, and sufferers of DM are also susceptible to a high incidence of tuberculosis (TB).
Objective The objective of this study was to analyze the role of TLR 2, TNF-alpha, IL-4 in DM patients with pulmonary TB.
Method This study used an observational-analytic research method, using a cross sectional design. The subject sample was comprised of two groups of thirty patients, distributed among the DM group with TB positive and TB negative conditions. Each group had their TLR-2 protein expression in PBMCs examined using the immunocytochemistry method. The patients' levels of TNF-alpha, IL-4 were examined using the ELISA technique. Statistical analysis used two tests and a regression-logistic analysis.
Result The results of the research showed a difference in TLR-2 between TB positive and TB negative patients. In TB positive patients, there was a lower value of TLR-2 (9.3 per 10 HPF) than in TB negative patients (19.3 per 10 HPF), ($P < 0.05$; $R = 0.358$). This means that the risk that a low TLR-2 expression carried of triggering TB was 35.8%. TNF-alpha examination showed a significant difference in each group with a higher value in TB positive patients (6.2 pg/ml) than TB negative patients (3.2 pg/ml). The level of IL-4 in TB positive patients was higher (6.7 pg/ml) than in TB negative patiens (4.5 pg/ml).
Conclusion TLR-2 expression influences TB in DM patients; TNF-alpha, IL-4 values were all higher in TB positive patients.
Key Words DM with TB, TLR-2, TNF-alpha, IL-4.

OS195

LYMPHOCYTE-PREDOMINANT EXUDATIVE PLEURAL EFFUSION WITH LOW ADA LEVELS AND NEGATIVE CYTOLOGY: WHAT IS THE FINAL DIAGNOSIS?

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Background and Aim of Study In Japan, exudative pleural fluid with lymphocyte predominance and high levels of adenosine deaminase (ADA) often suggests tuberculous effusion, while lymphocyte-predominant exudate with low levels of ADA is thought to be of little diagnostic value. Establishing the diagnosis in such cases, especially those with negative cytology, can be very difficult. We retrospectively investigated the final diagnoses in such cases.
Methods Among patients with pleural effusion who were referred to our department and underwent thoracentesis during the period between January 2008 and December 2012, we selected 182 who met Light's criteria for exudative pleural effusion, with ADA levels below 40 U/L, lymphocyte subset proportion exceeding 50%, and negative cytology.
Results One hundred fifty-three patients were male and 29 were female with a mean age of 72 years. Final diagnoses were pleural effusion associated with malignant tumors in 78 patients (53 with lung cancer, 9 with malignant lymphoma, 7 with mesothelioma, and 9 with other malignancies), postoperative pleural effusion in 19, infections in 17 (12 with common bacteria, 3 with nontuberculous mycobacteria, 1 with Mycobacterium tuberculosis, and 1 with Paragonimus), benign asbestos pleurisy in 14, rheumatoid arthritis in 5, other disorders in 14, and unknown causes in 35.
Conclusion Although 40% of the lymphocyte-predominant, ADA-low, cytology-negative exudative pleural effusions were related to malignant tumors, most of the other 60% were due to benign diseases or the cause was unknown. Tuberculosis was very rare in our series.

OS196

CLINICAL FEATURES AND OUTCOMES OF ISONIAZID MONO-RESISTANT PULMONARY TUBERCULOSIS

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Background and Objective Tuberculosis (TB) remains a major public health problem around the world and also in Thailand. Mycobacterium tuberculosis strain with isoniazid mono-resistant drug susceptibility pattern is one of the most common isolates from patients with pulmonary TB. This study aims to verify the characteristics of patients harbored this organism.
Methods A retrospective review of medical records for all culture-proven adult pulmonary TB patients in Siriraj Hospital between July 2009 and July 2011 was conducted. Demographic data, clinical presentations, radiological characteristics, and treatment regimens with outcome determination were verified.
Results Among 489 pulmonary TB patients during the study period, 28 were infected with isoniazid mono-resistant strain (5.7%). The mean age was 53.8 years, and 8% of them had a history of previous treatment in the past. Cavity was noted from an initial chest radiograph in only 8% of the patients. When compared with those infected with any other form of resistant strains, isoniazid mono-resistant pulmonary TB patients tended to have less radiographic cavitary lesion (8.3% vs. 26.7%, $p = 0.006$) but no significant difference was seen in term of demographic data and clinical presentations. All of them who had completed the treatment were cured. No difference in cure rate and relapse rate among patients treated with quinolone or non-quinolone containing regimens.
Conclusion Isoniazid mono-resistance shares common clinical features with other resistances TB, except for less cavitary lesion from chest radiograph. Appropriate drug susceptibility testing with prompt regimen adjustment can lead to a favorable treatment outcome.

OS197

ASSOCIATIONS BETWEEN RECURRENT PULMONARY TUBERCULOSIS AND MDR-TB INFECTION EVENT IN PATIENTS WITH HIV

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Background and Aim of the Study Tuberculosis is one of the most common presenting illness and the leading cause of death among HIV-infected patients. HIV infection increases the risk of pulmonary tuberculosis due to MDR-TB. It's still unknown whether the occurence of recurrent increase the event of MDR-TB infection in patients with HIV. The aim of this study is to find associations between pulmonary tuberculosis category and MDR-TB infection event in patients with HIV.
Methods We performed a cross-sectional study to HIV-infected patients with pulmonary tuberculosis within January 2012 to April 2013 in Cipto Mangunkusumo Hospital. MDR-TB was confirmed by phenotypic drug-susceptibility testing. We compared the proportion of MDR-TB event between new onset (Group-1) and recurrent (Group-2) pulmonary tuberculosis with Fisher's exact test.
Results A total of 79 patients were involved in this study, 47 patients were included in Group-1 and 32 patients were included in Group-2. MDR-TB was found in 11 patients, 4 patients in Group-1 and 7 patients in Group-2. Fisher's exact test showed no difference of MDR-TB infection event between groups ($p = 0.109$).
Conclusion Recurrence of pulmonary tuberculosis was not related to the increasing event of MDR-TB infection in patients with HIV.

OS34: OTHERS 2

OS198

SMOKING CESSATION WHEN HOW & WHOM TO BE APPROACH

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Background & Aims SMOKING IS INJURIOUS TO HEALTH-IS A STATUTORY warning which appears more as legal than social responsibility. Indian Government has banned smoking in public place imposed fine even the law didn't give positive impact over the reduction. Person indulged in smoking are not aware of it's effects Method 90 person 18–60 yrs were studied. They were in three groups Gr –1 BEGINER (smoking < one year) Gr –2 chronic smoker smoking yrs Gr 3 EXSMOKERS left smoking one year Gr- 1 40 persons younger age 18–30 yr started smoking because of isolation ignorance depression social exclusion unemployment away from parents motivation from cinema or MACHO MAN feeling. Gr –2 –30 persons, regular smoker from lower socioeconomic status family problem. Explained the bad quality of life and interaction was done with ill hospitalized patients of chronic smoking. Gr 3 20 person sex smokers restarted in late 50 because of temporary stress death of family member due to cancer even non-smoker leads to negative idea. Gradual cessation of smoking – seven step to give up (SrivastavaGN) method was applied & individual counseling was done in all three group. Observation- Gr I younger group there problem were discussed & counseled 20/40 (50%) stopped or reduced number easily. Gr II 10/30 (33%) person stopped/reduced, the difficult group to stop when interacted with chronic patient of COPD or Lung cancer responded. Gr III 8/20 (40%) responded were explained the benefit of their own experience during the period of non smoking and present status after restart.
Conclusion Reason of smoking is different in individual person so the individual counseling is more effective than mass teaching. A ONE SIZE FIT-ALL formula should not practice It is easy to stop or reduce the frequency of smoking in beginners.

OS199

ASSOCIATION BETWEEN LSNS-6 AND CAT IN PATIENTS UNDERGOING LONG-TERM OXYGEN THERAPY (LTOT) FOR CHRONIC RESPIRATORY FAILURE (CRF)

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Introduction Socialization is one of therapeutic goals in pulmonary rehabilitation and pharmacologic treatment, according to COPD guideline by Japanese Respiratory Society. Although it impacts on health related quality of life (HR-QOL), only a limited data on patients' socialization has been published so far. Lubben Social Network Scale (LSNS)-6 is a handy questionnaire to estimate social isolation of an individual by assessing friend and family components. LSNS-6 ranges from 0 to 30, and scores less 12 indicates the condition of social isolation. In order to elucidate the impact of social isolation on HR-QOL, the association between LSNS-6 and CAT were investigated.
Methods Participants who conducted both LSNS-6 and CAT LSNS-6 between 1st June 2012 and 31 October 2012 were retrospectively enrolled and their association was investigated. They consisted of outpatients from Kyorin University Hospital and Chofu Sanso no Kai, a regional patients' committee, and all of them underwent long term oxygen therapy (LTOT) for chronic respiratory failure (CRF). Statistic analyses were made by linear regression analysis, using Prism ver 5.0 (Graph Pad, SanDiego, USA) and statistical significance was defined as p value < 0.05.
Results LSNS-6 scores of 45% of participants ($n = 33$) were less than 12. Friend sub-scores of LSNS-6 were associated with CAT scores ($p < 0.05$), although total LSNS-6 scores were not. In detail, friend sub-scores were significantly associated with item 3, 4, 6 and 8 of CAT questionnaire ($p < 0.05$).
Discussion Higher rate of participants in this study were regarded as socially isolated, than that in previously published study over community dwelling elderly residents, indicating that LTOT was associated with social isolation. It is also demonstrated that breathlessness, deterioration in outdoor activity, and depression were associated with social isolation in terms of friend. These suggested that LSNS-6 is promising measure for the social isolation of patients with respiratory disease.

OS200

THE CORRELATION OF PEF AND FEV1 VALUES IN NORMAL SUBJECTS, PATIENTS WITH RESTRICTIVE AND OBSTRUCTIVE PULMONARY DISEASES IN PERSAHABATAN HOSPITAL

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Background and Aim of Study Peak expiratory flow (PEF) and forced expiratory volume in one second (FEV_1) parameters are widely used in diagnosing and monitoring pulmonary diseases. The FEV_1 value is a gold standard in measuring lung function, however spirometer is not always available. Peak expiratory flow equipment as an alternative in lung function measurement is cheaper, easy to operate and to maintain. The aim of this study is to evaluate correlation between PEF and FEV_1 in normal subjects, patients with restrictive and obstructive pulmonary diseases.
Methods We evaluated subjects visiting Lung Function Laboratory in Persahabatan Hospital during January-June 2012. Spirometry measurements were performed based on American Thoracic Society (ATS) recommendation. Lung function tests were done to get three acceptable results and at least two of them were reproducible. The best result was selected to evaluate. Participants were divided into four groups, normal subjects, restrictive pulmonary diseases, asthma and COPD. The correlation between PEF and FEV_1 were analyzed using Pearson and Spearman correlation test.
Results Among 587 subjects undergone spirometry, 356 were males (60.6%) and 231 females (39.4%) aged between 18–88 years old. Among them, 139 normal subjects (23.7%), 47 subjects with restrictive pulmonary diseases (8%), 202 subjects with asthma (34.4%) and 199 subjects with COPD (39.9%). The correlation between PEF and FEV_1 in normal subjects was not significant ($p > 0.05$). However, there were very strong correlation in restrictive pulmonary diseases ($r = 0.829$), asthma ($r = 0.822$) and COPD ($r = 0.828$). These correlations were statistically significant ($p < 0.05$).
Conclusion We concluded that PEF could be used as an alternative measurement to evaluate lung function in patients with restrictive and obstructive pulmonary diseases.

OS201

A COMPARATIVE STUDY BETWEEN PORTABLE POLYGRAPH AND FULL POLYSOMNOGRAPHY IN PATIENTS WITH SLEEP APNEA SYNDROME

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Background Over three million Japanese patients are suspected to have sleep apnea syndrome (SAS), however, many of them are still undiagnosed. Excessive daytime somnolence and the resulting problems impair the patient's social life. Suitable timely treatment such as nasal continuous positive air pressure (CPAP) improves not only the somatic but also the neuropsychological symptoms. In addition to subjective symptom scores and SpO_2 monitoring, portable polygraph with recent advances is useful to detect. The aim of this study was to compare two types of devices, portable polygraph and full polysomnography (PSG), for the diagnosis of SAS.
Patients and Methods The patients visited our hospital with a suspicion of SAS (daytime sleepiness and/or snoring, etc.) from October 2005 to September 2010 were eligible for this study. Portable overnight sleep polygraph (PulsleepLS-10) and full PSG (Alice 5) were performed around the same time.
Results Eighty-four patients (Male/female 61/23, average 58.1 years old) included in this study were a significant correlation was observed between AHI of portable polygraph (average AHI = 29.16, 1.8–71.8 (SD = 17.65)) and full PSG (average AHI = 30.62, 0.2–76.1 (SD = 19.09) ($r = 0.791$)). Thus, AHIs of these two modalities were similar, but the portable polygraph showed relatively lower indexes than full PSG.
Conclusion Our data shows that the portable polygraph is useful not only in detecting SAS but also in estimating the indexes of full PSG and adequate and timely treatment introduction such as nasal CPAP.

OS202

THE COMPARISON OF SUPRALARYNGEAL AIRWAY DEVICES: SLIPA VERSUS LMA: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aim of Study The purpose of the present study was to compare, in patient undergoing general anesthesia, the streamlined liner of pharyngeal airway (SLIPA) with the laryngeal mask airway (LMA) in the incidence of successful placement on the first attempt, airway sealing pressure, and incidence of sore throat and postoperative blood staining on devices.
Methods A systematic review of randomized controlled trials (RCTs) was done to compare SLIPA with LMA. MEDLINE, EMBASE, and the Cochrane databases were searched for RCTs. The relative risk (RR), mean difference (MD), and corresponding 95% confidence intervals (CIs) were calculated using the RevMan 5.2 statistical software for dichotomous and continuous outcomes respectively.
Results The incidence of successful placement on the first attempt did not differ between two devices (RR = 1.02, 95% CI = 0.95, 1.09). It was significantly higher in using SLIPA than in using LMA when insertion was performed by novice persons (RR = 1.17, 95% CI = 1.01, 1.35), and did not differed between two devices when performed by experienced persons (RR = 0.99, 95% CI = 0.93, 1.06). It was higher when SLIPA was used compared with when Classic LMA was used (RR = 1.13, 95% CI = 1.00, 1.27), but it did not differ between SLIPA and ProSeal LMA (RR = 0.96, 95% CI = 0.91, 1.01). The incidence of postoperative blood staining on devices was significantly higher in using SLIPA than in using LMA (RR = 2.35, 95% CI = 1.57, 3.51). The incidence of sore throat (RR = 0.96, 95% CI = 0.61, 1.50) and the airway sealing pressure (MD = –0.37, 95% CI = –1.38, 0.65) did not differ between two devices.
Conclusions The insertion of SLIPA on the first attempt is more successful for novice persons than that of LMA. There was a greater incidence of postoperative blood staining on SLIPA compared with LMA, but incidence of sore throat was no significant difference between two devices.

OS203

EVALUATION OF FIBRINOGEN LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction Risk of vascular disorders is increased in Obstructive Sleep Apnea Syndrome (OSAS) patients. The exact mechanism of development of vascular disease in patients with OSAS remains to be unknown. Fibrinogen has been shown to be an independent risk factor for coroner heart disease and stroke.
Aim Our aim in this study was to compare plasma fibrinogen levels between OSAS and control groups.
Material-Methods Fifty patients with newly diagnosed moderate and severe OSAS and thirty three nonapneic control subjects were included in this study. Full polysomnography was performed in all patients.
Results Plasma fibrinogen levels in the OSAS group (4.2 ± 0.14 g/L) were significantly higher than that in the control group ($p < 0.028$). Plasma fibrinogen levels were positively correlated with Epworth sleepiness scale (ESS) ($r = 0.301$, $p = 0.006$), age ($r = 0.327$, $p = 0.003$), body mass index (BMI) ($r = 0.388$, $p < 0.001$), average oxygen desaturation ($r = 0.258$, $p = 0.019$), oxygen desaturation index ($r = 0.281$, $p = 0.010$), length of time spent with an oxygen saturation <90% ($r = 0.248$, $p = 0.024$) and arousal index ($r = 0.220$, $P = 0.046$). Plasma fibrinogen levels were negatively correlated with average oxygen saturation during sleep ($r = –0.254$, $p = 0.029$). Multiple linear regression analysis showed that high ESS and body mass index were risk factors for elevated plasma fibrinogen levels, independent of apne hipopne index.
Conclusion We suggest that plasma fibrinogen levels correlate with BMI and ESS. The association between plasma fibrinogen levels and nocturnal desaturation supports the linkage between hypoxia and inflamation. We conclude that fibrinogen may be an important factor for the development of vascular disease in patients with OSAS.

OS204

THE PROTECTION EFFECT OF SODIUM AESCINATE VIA JAK-STAT IN RAT MODLES OF HIGH ALTITUDE PULMONARY EDEMA

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Background High altitude pulmonary edema was one of major threat to individuals when they rapidly elevated to high altitude (above 3000 m). Our previously study showed that sodium aescinate alleviated rat high altitude pulmonary edema, However, the underlying mechanism was still no clear.
Methods 448 male SD rats were randomly and evenly allocated to 6 groups, including HAPE group, SA group, anti IL-6 group, AG490 group, SA plus AG490 group and SA plus anti IL-6 antibodies group. Rats were exposed in simulated 6000 m altitude hypobaric hypoxia, while exercised consisted for 48 h walk with 20 m/min every 6 h. Rats are injected with sodium aescinate (5 mg/kg), anti IL-6 antibodies (30 mg/kg), AG490 (10 mg/kg), sodium aescinate (5 mg/kg) plus AG490 (30 mg/kg) and aescinate (5 mg/kg) plus anti IL-6 antibodies (30 mg/kg) with tail intravenous in SA group, anti IL-6 group, AG490 group, SA plus AG490 group and SA plus anti IL-6 antibodies group respectively. After 48 hrs, serum IL-6 was detected by ELISA. p-JAK3 and p-STAT2 protein expression of lung tissue was assayed by Western blot. Lung W/D ratio was recorded.
Results The result showed serum IL-6 levels were higher in HAPE group and AG490 group than those of other groups. Compared with SA, anti IL-6 group and SA plus AG490 group, serum IL-6 levels in SA plus anti IL-6 antibody group were significant low. p-JAK3 protein expression showed similar tendencies. Expression level of p-STAT2 protein in HAPE group was higher than other groups. Compared with SA, anti IL-6 and AG490 group, p- STAT2 protein expression level was significant suppressed in SA plus AG490 group and SA plus anti IL-6 group. Lung W/D ratio showed the similar tendencies and attenuated in other groups compared to HAPE groups.
Conclusion These data suggested that sodium aescinate inactivated JAK3-STAT2 pathways and leaded to attenuated High altitude pulmonary edema.

OS35: ENVIRONMENTAL & OCCUPATIONAL HEALTH AND EPIDEMIOLOGY

OS205

EFFICACY OF VARENICLINE, AN NICOTINIC ACETYLCHOLINE RECEPTOR PARTIAL AGONIST, VS PLACEBO FOR SMOKING CESSATION. A RANDOMIZED CONTROLLED TRIAL

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Introduction Smoking has increased risk of morbidity and mortality. World Health Organization predicts that by 2020, disease caused by smoking will result in the deaths of around 8.4 million people in the world and half of these deaths from Asia. Varenicline, a partial agonist at the nicotinic acetylcholine receptor, has the potential to aid smoking cessation by relieving nicotine withdrawal symptoms and reducing the rewarding properties of nicotine.
Method A randomized, single-blind, placebo controlled trial conducted between July 2012 and December 2012 with a 12 week treatment period and 12 week follow-up of smoking status. 80 adult smokers who volunteered for the study divide into Varenicline and placebo group. Varenicline titrated to 1 mg twice daily (n = 40) or placebo (n = 40) for 12 weeks, plus weekly smoking cessation counseling.
Result During 4 weeks (weeks 1–4) after 12 weeks of treatment, 55% of participants in the Vernicline group were continuously abstinent from smoking compared with 27.5% in the placebo group (Prevalence Ratio [PR] 2.0). For weeks 5 through 8, 52.5% of participants in the Varenicline group were continuously abstinent compared with 20% in the placebo group (PR, 2.6). For weeks 9–12, 47.5% of participants in the Varenicline group were continuously abstinent compared with 17.5% in the placebo group (PR, 2.7). Mean of first day free of smoking used Varenicline for smoking cessation was 40.63 days and mean of first day free of smoking used placebo was 56.43 days. The most adverse event with varenicline was nausea, which occurred in 9 Participants (22.5%). Mean of CO level was 18.46 ppm, mean of Fagerstrom score for nicotine dependence was 6.4.
Conclusion Varenicline is an efficacious, safe, and well-tolerated smoking cessation pharmacotherapy.
Key Words Varenicline, counseling, Smoking Cessation.

OS206

THE NEGLECTED RISK FOR COPD AND LUNG CANCER FROM CHINESE WATERPIPE SMOKING: A MULTICENTER CROSS-SECTIONAL STUDY

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Background Recent studies showed the incidence of chronic obstructive pulmonary disease (COPD) and lung cancer had remained high in southwest China since stoves with chimneys were introduced to improve indoor air quality in 1976. While Chinese waterpipe smoking, which had been known as improving lung function and rendering less harm under the assumption that water filter tobacco smoke, is popular in these areas. We undertook a multicenter cross-sectional study to investigate whether Chinese waterpipe use and exposure are of etiologic association with COPD and lung cancer.
Methods 1238 individuals were enrolled and completed analysis from 12 local hospitals covered areas in China. We also collected the water of Chinese waterpipes and detected the exposure to fine particles of smoke differences between Chinese waterpipe and cigarette. The study was registered with Chinese Clinical Study. org, number ChiCTR-CCH-12002235.
Results The prevalence rate of COPD was 57.1% (OR, 6.88; 95% CI, 2.40–10.78) and 39.3% (OR, 4.04; 95% CI, 2.54–6.44) in Chinese waterpipe smokers and Chinese waterpipe passive smokers. Five individuals were confirmed lung cancer cases by CT and pathology, including 3 in Chinese waterpipe smokers, 1 in Chinese waterpipe passive smoker, and 1 in cigarette smoker. Chinese waterpipe aggravates pulmonary damage and increases risk of malignancy by large volume smoking with toxic constituents compared to cigarette.
Conclusion Our study providing strong evidence that exposure to active and passive Chinese waterpipe is a significant risk factor for COPD and lung cancer. Continued strengthening of health education programs are of importance on smoking prevention and cessation.

OS207

EFFECT VOLCANIC ASH BROMO MOUNTAIN IN PULMONARY FUNCTION TEST OF NGADAS AND SUKAPURA VILLAGE POPULATION EAST JAVA INDONESIA

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Background Volcanic ash consists of fragments of pulverized rock, minerals and volcanic glass, created during volcanic eruptions, less than 2 mm in diameter. Volcanic ash could have serious impact for Pulmonary function. This study was to evaluate effect of volcano ash in pulmonary function test in population villages around Bromo Mountain.
Methods This study was observational analysis with cross-sectional design. Occupant aged 20–50 years old, male or female were enrolled in this study. Population of Ngadas village was defined a exposed group because its location was about 1 Km from mountain. Population of Sukapura village were defined as non exposed group because its location was 40 Km from mountain and contrary from wind direction. Subject was perform to fill questionnaire, physical examination and pulmonary function test. Descriptive analysis was characteristics population and independent T-test for difference between two groups.
Result There were each 30 subject in exposure-group and non-exposure-group follow this study. There were 7 (23.3%) subject with mild restriction and 23 (76.7%) subject with normal pulmonary function test in exposure-group. There was no abnormality of pulmonary function test in non-exposure-group ($P = 0.005$).
Conclusion There was a difference in pulmonary function test between subject was exposed by volcanic ash and nonexposed volacanic ash.
Key Words volcanic ash, mountain dust, pulmonary function test, sillicosis, occupational lung disease.

OS208

HEALTH IMPACT OF THE 2013 SOUTH EAST ASIAN HAZE IN SINGAPORE

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Peat forest fires, hot, dry weather and wind conditions caused a severe South East Asian trans-national air pollution event in June 2013. Thick smoke blew over Sumatra in Indonesia, Singapore, Malaysia and as far as south Thailand. In Singapore, during the first week, the concentrations of fine, aerosolized, harmful particulate matter (PM) of 2.5 um exceeded the usual safe levels by more than 10×, pushing the pollution standard index (PSI) into the hazardous category. This report describes the immediate effects of this haze episode on the people and health care system of Singapore. Moreover, this occurred in the midst of a dengue outbreak of unprecedented proportion and intensity. There was public anxiety and an initial rush for face masks. The government published hourly air quality indices and daily health advisories. For the public, a proscribed level of physical activity, unsafe location and need for personal protective respirators was related to the PSI and PM 2.5 levels. Primary care was enhanced with medical subsidies extended for haze related problems to the elderly and vulnerable population. In the first week, following the initial spikes in PSI and PM 2.5, there was an increase in haze related respiratory illnesses presenting to the polyclinics and emergency rooms. However, the overall out-patient, emergency room and in-patient case-loads were not affected. There was an increase in hospital admissions for acute asthma but this was within the capacity of the hospitals to cope. However, this episode is still unfolding. Our presentation will also evaluate the effectiveness of the steps undertaken within the health care system of Singapore in response to this exceptional environmental crisis. Lessons from this experience may help other health care systems cope with similar severe and unexpected air pollution events.

OS209

PULMONARY FUNCTION CHANGES ON SURABAYA CITY OF FIRE FIGHTERS DEPARTMENT

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Background Long term toxic gas inhalation exposure can cause negative effect to lung function. Firefighter workers have a higher risk for lung damage due to long term toxic gas exposure. Lung function test can detect pulmonary abnormality early, before the symptoms founded. This study analysed lung function changes on Firefighter who had exposed to toxic gases during their duty.
Methods The research was conducted at the Fire Fighter Departement Surabaya City Chapter Pasar Turi. The sample was 122 male and female workers, consisted of 61 firefighters as an exposed group and 61 administrative workers as the control group, with age range 20–50 years and have a 5 years minimum working period.
Result There were no differences in pulmonary ventilation physiology significant association between the field firefighter and administrative workers in all parameters pulmonary ventilation physiology (FVC, FEV1, FEV1/FVC and MBC). There were significant differences in pulmonary ventilation physiology among groups based on smoking status, the smoking workers have the parameter of avarage VC, FVC has lower than non smoking workers. The incidence of abnormal restriction and obstruction in the exposure group and only restriction in control group, whereas abnormality of restriction type more higher in exposure group (16.40%) than obstruction (3.30). The decline pattern in pulmonary ventilation physiology (FVC, FEV1, FEV1/FVC, MBC and PEFR) along with increasingly of the getting of duty from the exposure group, whereas only VC and FVC parameters have significant decline, but in generally avarage for five parameters showed the pulmonary ventilation physiology result in exposure workers better than the exposure workers who have longer time of duty.
Conclusion Exposure of toxic gases causes a decrease in pulmonary ventilation physiology on firefighters although not significant in statistically.
Key Words Lung function test, firefighter, toxic gas exposure, smoking habit.

OS210

OCCUPATIONAL TUBERCULOSIS INFECTION COMPENSATED WITH THE INDUSTRIAL ACCIDENT COMPENSATION INSURANCE FROM 2006 TO 2011

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Background and Aim of Study Infectious diseases are one of the most important public health issues, and the risk of encountering them through occupations are well-known, especially among health care and agricultural workers. To know the characteristics of tuberculosis infection in workplace is important for administrators or physician to provide information on prevention-strategies for occupational tuberculosis infection. The aims of the present study were to find general and occupational characteristics from 2006 to 2011 in Korea.
Methods Using the electronic database of Korea Workers' Compensation & Welfare Service (KCOMWEL), a total of 1062 cases with occupational infection receiving compensation between 2006 and 2011 were analyzed. The diagnoses of those cases were reviewed and confirmed by specialists majored in internal medicine and occupational medicine. Disproved cases were excluded from this study.
Results The approved number of tuberculosis cases during 6 years was 227; 42 cases in 2006, 58 cases in 2007, 40 cases in 2008, 29 cases in 2009, 31 cases in 2010, and 27 cases in 2011. The most common lesion of occupational tuberculosis was lung (n = 189), followed by lymph node (n = 20), and pleura (n = 17). Mean (standard deviation) age and work duration of 227 cases were 31.1 (9.0) years and 55.5 (56.8) months. The number of females (n = 200) were higher than males (n = 27). Health care workers accounted for over 91% of tuberculosis cases, and infection occurred while they contacted patients with tuberculosis. The most common occupation was nurse (n = 150, 66.1%), followed by medical laboratory technologist (n = 14, 6.2%), and doctor (n = 12, 5.3%).
Conclusion This study provided administrators with valuable information on prevention strategies for work-related tuberculosis for several vulnerable working groups such as HCWs. Infection control programs should be directed at preventing work-related tuberculosis among HCWs.

OS211

WEATHER AND RESPIRATORY DEATH

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Background and Aim of Study Low ambient temperature is known to be harmful to respiratory system. We evaluated the relation between respiratory death and weather of daily temperature, temperature difference, wind speed, humidity, and barometric pressure in South Korea.
Methods Daily weather information of the years from 2008 to 2011 including average temperature, highest and lowest temperature, wind speed, relative humidity, and barometric pressure was obtained from the Korean Meteorological Administration. The statistics of mortality of the years was obtained from the Korea National Statistical Office. The correlation between daily weather and death from all causes and from respiratory diseases was analyzed with the consideration of delayed effect of weather. A linear regression model for the prediction of daily respiratory death by weather was developed in the years 2008~2010 and validated by comparison between the predicted and observed respiratory daily death in the year 2011.
Results The daily number of death from all causes and also from respiratory diseases correlated negatively with the average temperature and humidity but correlated positively with temperature difference, wind speed, and barometric pressure ($p < 0.01$ for all correlation analyses). Prediction model for respiratory death was shown that the daily number of respiratory death equals [30.0 – 0.409 T + 1.328 D + 2.155 W + 0.118 H (T, temperature; D temperature difference; W, wind speed; H, humidity in the average of the past week)] excluding the barometric pressure because of a low statistical significance. The predicted and observed daily number of respiratory death in the year 2011 correlated with the correlation coefficient of 0.58 ($p < 0.001$).
Conclusion We found that all cause death and respiratory death were related with weather of average temperature, temperature difference, wind speed, and humidity in South Korea. (This study was supported by Obstructive Lung Disease Research Foundation, Seoul, Korea.)

OS212

SIMIAN VIRUS 40 IS PREVALENT IN MALIGNANT PLEURAL MESOTHELIOMA IN VIETNAM

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Background and Aim of Study Mesothelioma is a rare and fatal disease and associated with a history of heavy and long-term exposure to asbestos. However, it might also be related to the Simian Virus 40 (SV40). The relationship between SV40 and malignant pleural mesothelioma (MPM) is still unclear in Vietnam. This study was conducted to examine how often SV40 or the asbestos body exists in clinical specimens of patients with MPM in Vietnam.
Methods Available histological specimens of 45 patients (19 men, 26 women) with MPM at Pham Ngoc Thach hospital (a referral chest hospital) in Ho Chi Minh city, Vietnam were further processed and examined to detect the existence of asbestos body and SV40 Large T antigen (SV40 Tag) by histology and immunohistochemistry, respectively.
Results Of 45 patients, 23 (51%) was epithelioid, 7 (16%) biphasic, 6 (13%) sarcomatoid, 4 (9%) desmoplastic, 4 (9%) well-differentiated papillary, and 1 (2%) anaplastic malignant mesothelioma. SV40 Tag was positive in the specimens of 9 (20%) amongst 45 patients. Women were more likely to be positive with SV40 Tag than men (OR, 8; 95% CI, 0.8–42.9). Asbestos body was detected in 10 (45%) amongst 21 patients. Only one (2%) patient was positive with both SV40 Tag and asbestos body.
Conclusion One fifth of patients with MPM in Vietnam are related to SV40. Asbestos exposure is still the main cause of MPM in Vietnam.

OS36: COPD 3

OS213

EMPHYSEMATOUS CHANGE IN LOW-DOSE CT SCREENING IS AN EVIDENT RISK FACTOR OF FUTURE AIRFLOW OBSTRUCTION AMONG SMOKERS

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Background and Aim of Study The correlation of emphysematous change detected by low-dose CT screening (CT emphysema) and chronic obstructive pulmonary disease (COPD) has not been established. To investigate the incidence of airflow obstruction among participants with CT emphysema, longitudinal examination of pulmonary function test is desirable.
Methods Retrospective analysis of health examination records from April 1998 to March 2012 was performed. Low-dose CT screening and annual pulmonary function test (without a bronchodilator) had been performed as part of the health examination. The presence of low FEV1/FVC (<70%) with decreased FEV1 (% FEV1 predicted < 80%) in at least one test was defined as airflow obstruction. Whether CT emphysema existed in baseline screening images had been determined by visual evaluation. The cumulative incidences of airflow obstruction of a CT emphysema group (n = 285) and a control group (absence of CT emphysema, with a smoking history of more than 20 pack-years, n = 1.879) were calculated.
Result Male participants with a smoking history (on average, 51.4 years old and 33.4 pack-years) had been followed up for 12.1 years. The cumulative incidences of airflow obstruction by an average of 11.6 times in pulmonary function tests were 37.2% among the CT emphysema group and 14.8% among the control group. The odds ratio of airflow obstruction with CT emphysema adjusted by age and smoking history with a logistic-regression model was 3.753 (95% confidence interval 2.885–4.882).
Conclusion The presence of CT emphysema in low-dose CT screening images could be recognized as a risk factor of airway obstruction. Although smoking cessation is essential for all participants of cancer screening, stronger intervention to promote smoking cessation based on CT findings is reasonable.

OS214

DUAL BRONCHODILATION WITH QVA149 IN PATIENTS WITH MODERATE-TO-SEVERE COPD: IGNITE TRIALS OVERVIEW

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Aim The IGNITE program investigated the efficacy and safety of dual bronchodilation with once-daily QVA149 [fixed-dose combination of indacaterol (IND; long-acting β_2-agonist) and glycopyrronium (GLY; long-acting muscarinic antagonist)] for the treatment of patients with moderate-to-severe COPD.
Methods Here we present an overview from 5 IGNITE trials: ARISE (Japanese safety study), SHINE, ILLUMINATE, SPARK and BLAZE, reporting lung function, transitional dyspnea index (TDI), health status (via the SGRQ), exacerbations, and safety data in a population of 5298 patients with moderate-to-severe COPD.
Results QVA149 provided statistically significant and sustained bronchodilation ($p < 0.001$) versus all comparators. The mean change from baseline in pre-dose FEV_1 was 189 and 52 mL for the QVA149 and tiotropium group, respectively at Week 52 in the ARISE study. In the ILLUMINATE study, FEV_1 AUC_{0-12h} for QVA149 was significantly higher vs. salmeterol/fluticasone, with a significant and clinically meaningful treatment difference of 0.138 L (95% confidence interval [CI] 0.100–0.176; $p < 0.0001$). In the BLAZE study, the LSM treatment difference in TDI score was 0.49 (95% CI 0.07, 0.91; $P = 0.021$) and 1.37 (95% CI 0.95, 1.79; $p < 0.001$) for QVA149 vs. tiotropium and placebo, respectively. QVA149 decreased the rate of overall COPD exacerbations by 15% (RR 0.85; 95% CI 0.77, 0.94; $P = 0.001$) and 14% (RR 0.86; 95% CI 0.78, 0.94; $P = 0.002$), versus GLY and tiotropium, respectively in the SPARK study. Moreover, QVA149 significantly improved SGRQ total score versus GLY (treatment difference: –2.07; $P = 0.07$) and tiotropium (–2.69; $p < 0.001$). In all studies QVA149 was safe and well tolerated.
Conclusion These results demonstrate that dual bronchodilation with once-daily QVA149 provides therapeutic benefits for patients with COPD as demonstrated by improved lung function, dyspnea, health status, reduced exacerbations, along with a favorable safety profile.

OS215

GLYCOPYRRONIUM AND TIOTROPIUM DEMONSTRATE SIMILAR IMPROVEMENTS IN LUNG FUNCTION AND REDUCTIONS IN EXACERBATIONS IN SEVERE-TO-VERY SEVERE COPD: THE SPARK STUDY

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Introduction Glycopyrronium (NVA237) and tiotropium are the approved once-daily (OD) inhaled long-acting muscarinic antagonists for the maintenance treatment of COPD. Long-acting bronchodilators are effective in preventing both moderate and severe exacerbations.[1]
Methods In this 64-week, multicenter, parallel-group, active-controlled SPARK study, patients ≥40 yrs with severe-to-very severe COPD (post-bronchodilator forced expiratory volume in 1 second [FEV_1] < 50% of the predicted normal value) and a history of exacerbations were randomized to receive double-blind QVA149 110/50 μg or glycopyrronium 50 μg (both via the Breezhaler® device) or open-label tiotropium 18 μg (via the Handihaler® device) once daily. COPD exacerbations, lung function (trough FEV_1), St. George's Respiratory Questionnaire (SGRQ) scores, rescue medication use, and safety were analyzed after 64 weeks treatment. Here we present the efficacy and safety results of glycopyrronium versus tiotropium in patients with COPD from the SPARK study.
Results 1483 patients were randomized, 99.5% analyzed (glycopyrronium = 739, tiotropium = 737); male: 74%. The reduction in the rate of all COPD exacerbations in the glycopyrronium group was comparable to tiotropium (Rate ratio [RR]: 1.01, 95% confidence interval [CI]: 0.913, 1.107, $P = 0.919$). At Week 64, trough FEV_1 and SGRQ total score (LS Mean [SE], L) was similar for glycopyrronium (trough FEV_1: 0.98 [0.011]; SGRQ: 45.46 [0.780]) and tiotropium (trough FEV_1: 0.99 [0.011]; SGRQ: 46.08 [0.778]). The reduction in daily rescue medication usage was comparable for both treatments (1.5 puffs/day). Glycopyrronium showed an overall safety and tolerability profile similar to tiotropium.
Conclusion In patients with severe-to-very severe COPD, once-daily glycopyrronium showed similar efficacy to tiotropium in reducing exacerbations, improving lung function and health status, and reducing rescue medication use, with a similar safety profile.
Reference
1. Wedzicha et al. Eur Respir J. 2012;40(6):1545–54.

OS216

CANNABIS LUNG CAUSING PRECOCIOUS EMPHYSEMA- ON THE VERGE OF AN EPIDEMIC

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Background The use of cannabis has increased dramatically in Worldwide over the last 20 years with a UN Drug Report 2009 quoting a prevalence in Europe of 7%, and Australia as high as 14%. It is particularly prevalent amongst adolescents and young adults. In a rural region of North Wales we have noticed an increasing amount of young patients presenting with precocious emphysema with a very high tobacco and cannabis usage. We postulate that the addition of cannabis to the tobacco, and high usage at a young age is leading to increase young patients with COPD, and we are concerned that over the next ten to twenty years this may reach epidemic proportions.
Method A series of four patients presented through the ED with exacerbations were noted to have precocious COPD associated with high cannabis use. The age was 38–48, and all had both physiological and radiological signs of advanced emphysema. All had at least 20 years of regular cannabis usage smoking more than 5 'joints' per day. Of these 3 patients were significantly impaired to require Long term oxygen therapy, and one is actively listed for a single lung transplant. All had normal levels of alpha 1 anti trypsin and chymo trypsin.
Conclusion We postulate that with the increasing early age and prevalence of cannabis smoking this is likely to lead to a profound affect on the presentation of COPD. We would predict that we will see a younger cohort requiring services such as oxygen, pulmonary rehabilitation and lung transplantation. We are concerned that the dangers of cannabis inhalation and these risks are 'under the radar' and not being appreciated by the wider health community. We would also support the need for basic science research to look at the mechanisms of the inflammatory response secondary to cannabis smoking.

OS217

DUAL BRONCHODILATION WITH QVA149 REDUCES COPD EXACERBATIONS: RESULTS FROM THE IGNITE PROGRAM

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Background and Aim of Study Combinations of long-acting bronchodilators maximize bronchodilation and may reduce the risk of exacerbations. QVA149 is a novel dual bronchodilator containing a fixed-dose combination of the long-acting β_2-agonist (LABA) indacaterol and long-acting muscarinic antagonist (LAMA) glycopyrronium (NVA237) for the maintenance treatment of COPD. We report the annualized rates of all COPD exacerbations with QVA149 versus the once-daily LAMAs glycopyrronium and tiotropium (SPARK study) and twice-daily LABA/ICS salmeterol/fluticasone (SFC; ILLUMINATE study).
Methods SPARK and ILLUMINATE were multicenter, double-blind, randomized studies with treatment durations of 64 and 26 weeks, respectively. Patients (aged ≥ 40 yrs) with severe-to-very-severe COPD and a history of exacerbations were randomized to once-daily QVA149 (110/50 μg), glycopyrronium (50 μg), or open-label tiotropium 18 μg (1 : 1 : 1) in the SPARK study. Patients (aged ≥ 40 yrs) with moderate-to-severe COPD and no history of exacerbations were randomized to QVA149 110/50 μg or salmeterol/fluticasone 50/500 μg (1 : 1) in the ILLUMINATE study.
Results SPARK and ILLUMINATE randomized 2224 (75% completed) and 523 (83% completed) patients, respectively. In the SPARK study, QVA149 significantly reduced the rate of all exacerbations (mild, moderate and severe) by 15% versus glycopyrronium (Rate Ratio [RR] 0.85; 95% CI 0.77–0.94; p = 0.001) and 14% versus tiotropium (RR 0.86; 95% CI 0.78–0.94; p = 0.002). In the ILLUMINATE study, the rate ratio of QVA149 versus SFC for all COPD exacerbations was 0.69 (95% CI 0.44–1.07; P = 0.098). For time to first exacerbation, QVA149 reduced the risk by 35% versus SFC (Hazard Ratio 0.65; 95% CI 0.44–0.96; p = 0.03).
Conclusions QVA149 significantly reduced the rate of exacerbations compared with glycopyrronium and tiotropium, and delayed the time to first exacerbation compared with salmeterol/fluticasone. This suggests the potential of QVA149 for reducing exacerbations compared to current standard of care (LAMA or LABA/ICS), irrespective of patients having a history of exacerbations or not in the previous year.

OS218

MUSCARINIC RECEPTOR ANTAGONIST INHIBITS CIGARETTE SMOKE-INDUCED AIRWAY INFLAMMATION AND REMODELING

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Background and Aim of Study Currently the interactions between cigarette smoke, muscarinic receptors, airway inflammation and fibrosis in the development of COPD remain unclear. We hypothesized that muscarinic receptor antagonist (MRA) may inhibit cigarette smoke extract (CSE)-induced IL-8 release in human bronchial epithelial cells and collagen production in lung fibroblasts. Moreover, MRA could attenuate airway inflammation and remodeling in a mouse model of cigarette smoke-induced COPD.
Methods Human primary bronchial epithelial cells (PBEC) were stimulated by acetylcholine (Ach) and CSE. IL-8 release and phosphorylation of mitogen-activated protein kinase were determined. Collagen production from fibroblasts and cell proliferation were measured. In the mouse model of cigarette smoke-induced COPD, inflammatory cells, mediators and fibrosis score in the airways and parenchyma were assessed. Long-acting MRA, glycopyrronium bromide (NVA237) and dexamethasone were applied to investigate the treatment effect before and after CSE stimulation and chronic cigarette smoke exposure.
Results Ach and CSE significantly induced IL-8 production at both mRNA and protein levels in PBEC. The IL-8 production was significantly inhibited by NVA237 and p44/42 inhibitor UO126, but not by dexamethasone. Ach and CSE stimulated fibroblast proliferation and collagen production, which again were significantly attenuated by NVA237 and UO126. After chronic cigarette smoke exposure, a significant increase of inflammatory cells, chemoattractant protein-1, macrophage inflammatory protein-2 and total protein was observed in the BAL fluid of mice as well as the increase of inflammatory and fibrosis score. All these actions were significantly blocked by treatment with NVA237 but not dexamethasone.
Conclusion NVA237, as a long-acting muscarinic receptor antagonist, inhibits cigarette smoke-induced airway inflammation and remodeling in vitro and in vivo.

OS37: TUBERCULOSIS 4

OS219

THE ABILITY OF AFB SPUTUM SMEAR AND BACTEC MGIT 960 IN DIAGNOSIS OF PULMONARY TUBERCULOSIS HIV PATIENTS

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Background and Aim of the Study In HIV patients, AFB smear examination generally gave negative results and this condition led to the late diagnosis of pulmonary tuberculosis in HIV patients. Late diagnosis causes delayed provision of antiretrovirals. The aim ofthis study is to know the diagnostic value of sputum AFB smear and BACTEC MGIT 960.
Methods This was a cross-sectional study of HIV patients with suspected tuberculosis who came to Integrated HIV/AIDS Service Unit (POKDISUS) or inpatient care at hospital ward at Cipto Mangunkusumo National Hospital from October 2011 to April 2012. We examine sputum smear and culture using BACTEC MGIT 960 media, as well as the gold standard LJ culture. Logistic Regression model was applied inthe study.
Results Most of the subjects were men (63%) and CD4 counts < 50 ml showed in 48% of subjects. From 100 study subjects, positive AFB smear were found in 11 subjects, positive BACTEC MGIT 960 cultures in 33 subjects and LJ cultures were positive in 29 subjects. Sensitivity and specificity of AFB smear were 33.3% and 98.6%, lower than sensitivity and specificity of BACTEC MGIT 960 which were 90% and 92.8%. From bivariate analysis, AFB smear examination of sputum ($p < 0.0001$) and BACTEC MGIT 960 cultures ($p < 0.001$) were statistically significant. AFB smear of sputum's multivariate analysis ($p < 0.501$) was not statistically significant, but culture using BACTEC MGIT 960 ($p < 0.0001$) was statistically significant in diagnosis making of pulmonary tuberculosis in HIV patients.
Conclusion Addition of culture using the BACTEC MGIT 960 media to AFB sputum smear examination in HIV patients would increase the ability of diagnosing pulmonary tuberculosis in HIV patients.

OS220

ABSTRACT WITHDRAWN

OS221

COMPARISON OF WHOLE BLOOD GAMMA INTERFERON ASSAY AND TUBERCULIN SKIN TESTING IN TUBERCULOSIS CONTACTS

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QuantiFERON-TB GOLD (QTG) assay is a whole blood interferon gamma assay fort he recognition of cee-mediated immun response to Mycobacterium tuberculosis infection. The assay includes M. Tuberculosis specifi ESAT-6 and CFP-10 antigens. To compare the QTG assay with the tuberculin skin test (TST) in household contacts of active tuberculosis patients and to evaluate if there was a correlation between the TST induration diameters and the magnitude of QTG assay. 69 household contacts of 24 active pulmonary tuberculosis patients underwent both assays and the result were compared. TST and QTG assay results were compared with each other with Kappa statistic and good agreement was found. The correlation between the magnitude of QTG response (the levels of interferon gamma) and TST induration diameter was significant. According to the results of both tests; if the contacts were evaluated only with the TST; 16 of them would have taken profilactic chemotherapy unnecessarily and one of them would not have taken altough one had to. Having the advantages of single patient visit, low reader variability, not being affected by prior BCG vaccinations and not having the boosting of subsequent test results; QTG assay seems to be considered as an adequate replacement for the TST in the screening of latent TB infection in the future.

OS222

PROGNOSTIC FACTORS IN PATIENTS WITH TUBERCULOSIS-DESTROYED LUNG ADMITTED TO AN INTENSIVE CARE UNIT

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Aim of Study We evaluated the clinical characteristics of patients with tuberculosis-destroyed lung (TDL) who were admitted to intensive care units (ICU) and the prognostic factors in those requiring ventilator care.
Methods A total of 106 patients were enrolled in 2005–2011. All patients were graded on 4-point scale (field score 1–4) based on the extent of destroyed lung parenchyma on chest radiography.
Results The mean age was 62.7 ± 13.0 years and 88 (83%) were men. Their hospital mortality rate was 27.4%. The mean field score was 2.3 ± 0.9. In patients requiring ventilator care (n = 79), the field score correlated negatively with body mass index (BMI), serum albumin concentration, and PaO2/FiO2 ratio at ICU admission ($p < 0.05$ for each). Also, the Cox proportional-hazard model for them showed that age > 65 years (HR 2.651, 95% CI 1.063–6.613, P = 0.037) and being underweight (BMI < 18.5 kg/m^2) (HR 2.707, 95% CI 1.063–6.897, P = 0.037) were significant prognostic indicators on day 60 after ICU admission.
Conclusion The field score correlated with various clinical parameters in patients with TDL. The elderly patients with a low BMI requiring ventilator care might be associated with poor hospital outcomes.

OS223

LATENT TUBERCULOSIS INFECTION ASSESSED BY INTERFERON-GAMMA RELEASE ASSAY AND CIRCULATING GRANULYSIN LEVELS

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Background and Aim of Study Protective immunity against tuberculosis (TB) infection has not been understood well. Granulysin (GNLY) is a molecule mainly released from natural killer cells and activated cytotoxic T cells, and exhibits anti-microbial activity against *Mycobacterium tuberculosis* and other pathogens. We investigated the relationship between human GNLY expression and latent TB infection detected by interferon-gamma release assay (IGRA).
Methods The study was approved by the relevant ethical committees. Vietnamese healthcare workers were tested for IGRA. Plasma GNLY concentrations were measured by the ELISA method. GNLY gene expression levels in the blood cells were measured by quantitative real-time PCR. Analysis of covariance (ANCOVA) was used to compare means of GNLY levels between IGRA-positive and -negative groups. Correlation coefficients were calculated to assess pairwise correlations between parameters of interest. A logistic regression model was used to analyze risk factors for latent TB infection.
Results Among 109 study participants, 41 (37.6%) showed IGRA-positive results, indicating latent TB infection. Plasma GNLY levels in the IGRA-positive group were significantly lower than those in the IGRA-negative group, even after adjustment for age and sex (adjusted mean = 2.24 ng/ml, 95% CI 1.99–2.50 vs. 2.72, 95% CI 2.48–2.96, $P = 0.0127$). There was a weak inverse correlation between plasma GNLY concentrations and TB antigens-stimulated interferon-gamma values ($r = -0.20$, $P = 0.0333$). Plasma GNLY concentrations were significantly correlated with GNLY gene expression in the blood cells ($r = 0.40$, $P < 0.0001$). By multivariate analysis using a logistic regression model, body mass index >= 25.0 and low plasma GNLY concentrations were significantly associated with IGRA-positive results (adjusted odds ratio = 8.92, 95% CI 1.46–54.57 and 0.52, 95% CI 0.31–0.87, respectively), while other factors including age, sex, job category, and working place did not show associations.
Conclusion GNLY may be involved in protective immunity against TB infection.

OS224

VITAMIN D RECEPTOR GENE FOKI AND BsmI POLYMORPHISMS IN SUSCEPTIBILITY TO PULMONARY TUBERCULOSIS AMONG INDONESIAN BATAK-ETHNIC POPULATION

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Background The active metabolite of vitamin D leads to activation of macrophage and restricts the growth of M. tuberculosis. The effect of vitamin D is achieved by binding to Vitamin D Receptor (VDR) and may be influenced by polymorphisms in VDR gene.
Objective To explore the role of Vitamin D Receptor (VDR) gene polymorphisms in susceptibility to pulmonary tuberculosis (PTB) in Indonesian Batak ethnic population.
Method In a age, sex and ethnic matched case- control study, 76 pulmonary tuberculosis patients and 76 healthy normal control were enrolled. Genetic polymorphisms of VDR gene (FokI and BsmI) were analysed using PCR and RFLP.
Results The frequencies of FokI genotypes were FF 35.5%, Ff 55.3%, ff 9.2% for PTB patients and FF 39.5%, Ff 44.7.% and ff 15.8% for normal control. The BsmI genotypes frequencies were BB 0%, Bb 98.7%, bb 1.3% for PTB patients and were BB 2.6%, Bb 97.4% and bb 0% for control. There was no significant association between PTB and FokI genotype OR 1.373, (95% CI: 0.689–2.734) for Ff genotype and OR 0.648, (95% CI: 0.223–1.885) for ff genotype. There was also no significant association between PTB and BsmI genotype OR 0.449, (95% CI: 0.082–2.451) for BB + bb vs Bb comparison.
Conclusion FokI and BsmI polymorphisms of VDR gene do not appear to be responsible for host susceptibility to pulmonary tuberculosis in Indonesian Batak ethnic population.
Key Word pulmonary tuberculosis, Vitamin D receptor gene, FokI, BsmI polymorphisms, Batak, Indonesia.

OS38: INTERSTITIAL LUNG DISEASE 5

OS225

FLUOROFENIDONE ATTENUATES BLEOMYCIN-INDUCED PULMONARYINFLAMMATION AND FIBROSIS IN MICE VIA RESTORING CAVEOLIN-1 EXPRESSION AND INHIBITING MITOGEN-ACTIVATED PROTEIN KINASE SIGNALING PATHWAY

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Background and Aim of Study Idiopathic pulmonary fibrosis is a progressive, life-threatening, interstitial lung disease with no effective therapy. In this study, we evaluated the effects of fluorofenidone (FD), a novel pyridone agent, on a murine model of bleomycin-induced pulmonary inflammation and fibrosis.
Methods Institute for Cancer Research mice were intravenously injected with BLM or saline for 14 consecutive days. Fluorofenidone, pirfenidone (500 mg. kg^{-1}. d^{-1}, respectively), or vehicle was administered throughout the course of the experiment. Animals were killed on day 28, and various parameters reflecting pulmonary vascular permeability, influx of inflammatory cells, and levels of transforming growth factor β in the bronchoalveolar lavage fluid were assessed. Collagen I, α-smooth muscle actin, and fibronectin were measured by real-time reverse transcriptase-polymerase chain reaction or Western blot. Furthermore, caveolin 1 and activation of P38, extracellular signa-regulated kinase, and c-Jun N-terminal kinase were detected by Western blot.
Results Fluorofenidone treatment significantly attenuated the increased pulmonary damage index score, the levels of proteins, transforming growth factor β and the influx of cells in bronchoalveolar lavage fluid. Fluorofenidone also markedly reduced the expression of fibronectin, α-smooth muscle actin, and collagen I in mouse lung tissues. Inversely, FD restored caveolin 1 protein and mRNA expression, which was significantly downregulated in BLM-induced lung fibrosis. Fluorofenidone also inhibited phosphorylation of extracellular signal-regulated kinase, P38, and c-Jun N-terminal kinase.
Conclusion These findings collectively suggest that FD is an effective agent with antifibrotic and anti-inflammatory properties, and the mechanisms of its antifibrotic effect include regulating caveolin 1 expression and blocking mitogen-activated protein kinase signaling pathways.

OS226

THE EFFECT OF 17(R)-RESOLVIN D1 ON BLEOMYCIN-INDUCED LUNG FIBROSIS IN MICE

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Background Idiopathic pulmonary fibrosis (IPF) is a destructive inflammatory disease leading to pulmonary fibrosis with limited therapeutic options. Neutrophilic inflammation with neutrophil migration, Transforming growth factor-β (TGF-β), and Connective tissue growth factor (CTGF) play a pivotal role in IPF. TGF-β is a multifunctional cytokine that effects on cell proliferation, differentiation, apoptosis, and extracellular matrix production. CTGF is a cysteine-rich mitogenic peptide that is implicated in various fibrotic disorders and induced in fibroblasts after activation with TGF-β. Resolvins are a family of potent lipid mediators and promote the resolution of the imflammatory response back to a non-inflamed state. 17(R)-resolvin D1 (17(R)-RvD1) is an aspirin-triggered epimer of resolvin D1 derived from docosahexaenoic acid and resists rapid inactivation by eicosanoid oxidoreductases. Bleomycin (BLM) is a well-established agent for inducing pulmonary inflammation and fibrosis.
Methods We examined anti-inflammatory and anti-fibrotic effects of 17(R)-RvD1 on lung fibrosis in BLM-treated mice. We chose continuous subctaneous administration of BLM for 1 week to 8-to-10-wk-old female C57BL/6 mice. 17(R)-RvD1 was injected intraperitoneally for five days consecutively.
Results Fourteen days after BLM treatment, 17(R)-RvD1 reduced neutophilia in bronchoaveolar fluid (BAL). Twenty-eight days after BLM exposure, 17(R)-RvD1 attenuated BLM induced pulmonary fibrosis histologically and decreased hydroxyproline content. Gene expression of IL-1β, TGF- β1 and CTGF in the lung tissue of 17(R)-RvD1-treated mice were decreased compared with control mice.
Conclusions These results suggest that 17(R)-RvD1 attenuates pulmonary fibrosis through the promotion of resolution in neutrophilic inflammation and the inactivation of TGF-β signaling.

OS227

TRANILAST INHIBITS PULMONARY FIBROSIS BY SUPPRESSING TGFβ-MEDIATED EXTRACELLULAR MATRIX PROTEIN PRODUCTION

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Background Idiopathic pulmonary fibrosis (IPF) is a chronic pulmonary disorder of unknown etiology, and is characterized by accumulation of extracellular matrix (ECM) protein such as fibronectin and collagen in the lungs. TGFβ-mediated epithelial-mesenchymal transition (EMT) of alveolar epithelial cells may contribute to the pathogenesis of IPF. On the other hand, tranilast, anti-allergic drug, is capable of suppressing TGFβ, and is reported to inhibit interstitial renal fibrosis in murine model.
Materials and Methods We investigated an effect of tranilast on TGFβ2-induced EMT in A549 human alveolar epithelial cells *in vitro*. To evaluate the efficacy of tranilast on lung fibrosis *in vivo*, we developed a mouse model for pulmonary fibrosis by intravenous injection of bleomycin (BLM). Tranilast were administered by oral gavage. We evaluated histological findings and collagen content in the lung of mice.
Result Treatment with TGFβ2-induced EMT in A549 cells *in vitro*, and expression of mesenchymal proteins including fibronectin and type IV collagen were significantly suppressed by the administration of tranilast. Tranilast also markedly inhibited TGFβ2-induced cell motility of A549 cells. Furthermore, treatment with tranilast significantly attenuated BLM-induced lung fibrosis in mice *in vivo*. The collagen content of the lungs was significantly lower in mice treated with tranilast as compared with those in control mice.
Conclusion These findings suggest that tranilast inhibits pulmonary fibrosis by suppressing TGFβ2-mediated ECM protein production from mesenchymal cells. Tranilast may be promising and novel anti-fibrotic agent for the prevention of IPF.

OS228

ROLE OF APOPTOSIS INHIBITOR OF MACROPHAGE (AIM) IN BLEOMYCIN-INDUCED LUNG INFLAMMATION AND FIBROSIS IN MICE

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Background and Aim of Study It has been shown that AIM is involved in a variety of inflammatory diseases since its discovery (Miyazaki T, et al. J Exp Med 1999). In the lung, it is reported that the cell-type-specific AIM overexpression causes inflammation, carcinogenesis, and emphysematous change (Qu P, et al. J Immunol 2009, Li Y, et al. Cancer Res 2011). There is accumulating evidence that abnormal regulation of apoptosis is implicated in several lung diseases, including idiopathic interstitial fibrosis. We thus wondered how AIM is involved in inflammation and/or fibrosis in bleomycin-treated mice.
Methods For wild type (WT) mice and AIM-KO mice (female, 8–12 week-old), we intratracheally administered 25 or 50 μg of bleomycin, using MicroSprayer (PennCentury, USA). On day 7 and 14, we sacrificed the mice, performed bronchoalveolar lavage (BAL), and examined lung tissue for assessment of inflammation and fibrosis.
Results The cell count in BAL fluid in the acute phase (on day 7) revealed that the number of macrophages was significantly increased in AIM-KO mice compared with WT mice. However, in the sub-acute phase (on day 14), the number of inflammatory cells, particularly of lymphocytes was rather decreased significantly in AIM-KO mice compared to WT mice. In the histology, fibrotic changes as well as inflammation in the lung were significantly suppressed in AIM-KO mice on day 14.
Conclusion Role of AIM may be different in the acute phase and the subsequent phase in bleomycin-induced lung injury and fibrosis model. Specifically, AIM may play an accelerating role in continuing inflammation and subsequent fibrosis after the injury.

OS229

THE ENHANCEMENT OF STANNNIOCALCIN-1 (STC1) SECRETION OF MESENCHYMAL-STEM-CELLS (MSCS) INCREASES THE ABILITY TO REDUCE BLEOMYCIN-INDUCED LUNG INJURIES

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Background and Aim of Study Previous study reported that systemically administered mesenchymal stem cells (MSCs) ameliorates bleomycin induced lung injury in murine model prominently. Stannniocalcin-1 (STC1) is a well conserved hormone across various species and many researchers report STC1 induce cell survival under harmful conditions. We also demonstrated that MSCs diminish oxidative stress and rescue lung epithelial cell death through secretion of STC1 via regulating mitochondrial functions under several harmful situations such as excess oxidative stress and ischemic condition. Thus, we hypothesized that the secretion of STC1 deeply contributes the capacities of MSCs to ameliorate lung injury via anti-fibrotic, anti-inflammatory effects and protection from oxidative stress. For validating our hypothesis, we evaluated how MSCs, with enhancing or diminishing STC1 expression using genetically manipulation procedures, affect lung damage in bleomycin induced lung injury model in murine.
Methods C57BL/6 mice were intratracheally injected with bleomycin. After 24 hrs, 5×10^5 UE6E7T-2 cells (immortalized human mesenchymal stem cell line established from bone marrow in RIKEN bio-resource, Japan) transfected with STC1 plasmid, sh-STC1 plasmid or control were injected into the tail vein. After 14 days from bleomycin treatment, pathologic findings, anti-fibrotic, anti-inflammatory effects and oxidative stress were evaluated with hematoxylin eosin staining, measuring total lung collagen, inflammatory substances and reactive oxygen species quantities.
Results STC1-overexpressing MSCs enhanced the capacities to ameliorate bleomycin induced lung injuries in murine model through the reducing of collagen accumulation, inflammation and oxidative stress. For example, STC1-overexpressing MSCs decreased collagen synthesis about 30% in comparison with control. Further STC1-overexpressed MSCs decreased Surfactant protein D (Sp-D) and 8-Hydroxydeoxyguanosine (8-OHdG; a oxidative stress marker) in immunological staining in tissue. shSTC1 transfected MSCs diminished these effects in comparison with control cells.
Conclusion These results suggest that STC1 contributed the abilities of MSCs to ameliorate lung injury through anti-fibrotic, anti-inflammatory and anti-oxidative-stress.

OS230

INDUCED PLURIPOTENT STEM (IPS) CELL-DERIVED MACROPHAGES FROM PATIENTS WITH HEREDITARY PULMONARY ALVEOLAR PROTEINOSIS (HPAP) RECAPITULATE THE DISEASE PATHOGENESIS

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Background and Aim of Study In patients with pulmonary alveolar proteinosis (PAP) syndrome, pathogenic surfactant accumulation from impaired clearance in alveolar macrophages is associated with disruption of granulocyte/macrophage-colony stimulating factor (GM-CSF) signaling. Hereditary PAP (hPAP) is caused by mutations in genes encoding the GM-CSF receptor (*CSF2RA* or *CSF2RB*). However, the mechanism is unknown and investigation is hampered by limited patient-access and difficulty maintaining primary macrophages in long-term culture. The aim of this study was to overcome these barriers by using patient-derived induced pluripotent stem (iPS) cells to recapitulate disease-specific and normal macrophages.
Methods iPS cells were created from children with hPAP caused by recessive *CSF2RA*^{R217X} mutations and a normal person, differentiated into macrophages (hPAP-iPS-Mφs and NL-iPS-Mφs, respectively) and evaluated functionally before and after lentiviral-mediated restoration of GM-CSF signaling in hPAP-iPS-Mφs.
Results Both hPAP and normal iPS cells had human ES cell-like morphology, expressed pluripotency markers, formed teratomas in vivo, had a normal karyotype, retained and expressed mutant or normal *CSF2RA* genes, respectively, and could be differentiated into macrophages with the typical morphology and phenotypic markers (e.g., CD14$^+$, CD49d$^+$, CD68$^+$, CD115$^+$, CD163$^+$, and HLA-DR$^+$). CD116 was expressed on NL-iPS-Mφs but not hPAP-iPS-Mφs, consistent with the presence of normal or mutant *CSF2RA* gene sequences, respectively. Compared to normal, hPAP-iPS-Mφs had impaired GM-CSF receptor function (GM-CSF clearance and GM-CSF-stimulated STAT5 phosphorylation) and reduced GM-CSF-dependent gene expression (PU.1, PPARγ, ABCG1), GM-CSF- but not M-CSF-dependent cell proliferation, proinflammatory cytokine secretion and surfactant clearance. Restoration of GM-CSF receptor signaling corrected the surfactant clearance abnormality in hPAP-iPS-Mφs.
Conclusions Patient-specific iPS cells accurately reproduced the molecular and cellular defects of alveolar macrophages that drive the pathogenesis of PAP in more than 90% of patients. These results demonstrate the critical role of GM-CSF signaling in surfactant homeostasis and PAP pathogenesis in humans and have therapeutic implications for hPAP.

OS39: CLINICAL ALLERGY & IMMUNOLOGY

OS231

GENOMEWIDE ASSOCIATION STUDY FOR TOTAL IGE IDENTIFIES HLA-C IN A JAPANESE POPULATION

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Background Most previously reported loci for total immunoglobulin E (IgE) levels are related to Th2 cell-dependent pathways.
Objective We undertook a genomewide association study (GWAS) to identify genetic loci responsible for IgE regulation and to assess the reproducibility of previously reported gene associations with total IgE levels.
Methods A total of 479,940 single-nucleotide polymorphisms (SNPs) were tested for association with total IgE levels in 1180 Japanese adults. Fine-mapping with SNP imputation was performed in the candidate regions ($P < 1.0 \times 10^{-5}$). Replication of the candidate loci was assessed in 2 independent Japanese cohorts and the results were combined in a meta-analysis. Using our GWAS results, we also examined the impacts of genes previously associated with total IgE levels.
Results Our GWAS demonstrated 6 candidate regions: the PYHIN1/IFI16, MHC classes I and II, LEMD2, GRAMD1B, and chr13: 60576338 regions. Rs3130941 in the HLA-C region was consistently associated with total IgE levels in 3 independent populations, and the meta-analysis yielded genomewide significance ($P = 1.07 \times 10^{-10}$). Nine of 32 candidate genes identified by a literature search were nominally associated with total IgE levels.
Conclusion To the best of our knowledge, ours is the first GWAS that demonstrates a positive result for levels of total serum IgE in an Asian population. It yielded strong association evidence for SNPs in the HLA-C region. Some of the effects of the genetic regions previously reported to be associated with total IgE levels were replicated in a Japanese population.

OS232

A SURVEY OF COMMON ALLERGENS IN PATENTS WITH ALLERGIC DISEASES IN GUANGZHOU, CHINA

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Background To investigate the types and distribution of allergens, and the responsiveness to these allergens as related to development of allergic disorders in a cohort of Guangzhou patients with allergies.
Methods Serum samples were obtained from a cohort of patients with allergic disorders (n = 7047) who visited our Hospital. The sera were subjected to analysis of 16 common allergens by using immune-capture approach. Chi-square test and linear regression were employed for data analysis.
Results The subjects showed mild responses to all common aeroallergens except dust mites or dust mite-containing mixed allergens. Similarly, the responsiveness was mild to 8 types of tested food allergens. By age-group analysis, there were a peak of sensitization to five types of aeroallergens (D1, D2, D5, E1 and H2) between 9 and 12 years of age, and to I6 and I71 between 15 and 18 years of age. For tested food allergens, the peak of sensitization appeared before 3 years of age for milk, between 3 and 6 years of age for eggs (the detection rates for both decreased along with age), between 9 and 12 years of age for F13 and F14, and between 12 and 15 years of age for F23 and F24.
Conclusion House dusts, Dermatophagoide pteronyssinus, Dermatophagoide farinae, milk and egg are major sensitizers responsible for common allergic disorders in Guangzhou. While milk and eggs are major sensitizers during early years of life, a subset of children may gain tolerance to both as their immunity becomes fully developed along with age.

OS233

GUANGDONG PROVINCE PRE-SCHOOL CHILDREN ALLERGIC DISEASE SITUATION AND RELATED FACTORS ON ALLERGIC IMPACT ANALYSIS RESEARCH

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Objective To investigate the allergic disease and its risk factors in pre-school children in Guangdong Province, China through a questionnaire. The results of the present investigation are believed to deepen the understanding of allergic diseases and serve as strong evidence for prevention and treatment of allergic diseases in children.
Methods The questionnaire was designed according to International Study of Asthma and Allergy in Childhood (ISAAC). Parents of kindergarten children in different areas in Guangdong Province, China were selected to fill in the questionnaire. Relevant investigators followed the parents by phone call to confirm the effectiveness of the questionnaires collected. The results were analyzed by descriptive statistics, Chi-square test, logistic regression model and spearman correlation analysis.
Results 1) Of 2761 questionnaires that had been handed out, 2540 were valid, giving a valid answer rate of 92%. Of the valid, 1331 cases were male and 1,209 cases female, with an average age of 4.6 ± 1.1 years. 33.9% of children suffered from allergic diseases. 2) Applied logistic regression analysis of children allergic factors in children food allergies, we can found that the first degree relatives suffered from food allergy and allergy rhinitis, the risk of children with food allergies increased ($P < 0.05$). 3) Analysis of the relevance of various types of allergy revealed by spearman correlation analysis, food allergy and drug allergy, atopic dermatitis, asthma, eye allergy, allergic rhinitis, the correlation coefficient were statistically differences ($P < 0.05$). 4) Applied logistic regression analysis of related risk factors in children with allergic rhinitis: ocular allergies; asthma; food allergies; family history of allergy; home or school near the road; someone smoking at home are some risks factors for allergic rhinitis ($P < 0.05$).
Conclusions Environment, individual and family history of allergy, all of them are risky factor for allergic disorders.
Key Word Allergic factors; Family history; Allergic disease; Children.

OS234

BRONCHIAL ASTHMA PRECEDING IGG4-RELATED AUTOIMMUNE PANCREATITIS

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Background Immunoglobulin (Ig) G4-related disease, originally reported in type 1 autoimmune pancreatitis by Hamano et al. (N Engl J Med 2001;344: 732–738), is a novel clinical disease entity characterized by tumefactive lesions, a high serum IgG4, and tissue infiltration of IgG4-positive plasma cells. Although allergic diseases complicating autoimmune pancreatitis have been reported, the clinical features of bronchial asthma complicated by autoimmune pancreatitis remain unclear.
Patients and Results We retrospectively evaluated five cases of bronchial asthma complicated by type 1 autoimmune pancreatitis in Nagoya University Hospital. All five cases were males with high serum IgG, IgG4, and IgE concentrations and preceded the onset of autoimmune pancreatitis by 3 months to 30 years. The radioallergosorbent tests were positive for common allergens such as mites and house dust. One case had a pulmonary manifestation that proved to be an inflammatory pseudotumor of the lung with an accumulation of IgG4-positive plasma cells. Another case had Mikulicz's disease with sialadenitis and dacryoadenitis. The asthma symptom and respiratory functions were ameliorated by oral prednisolone therapy for autoimmune pancreatitis in all cases. When the corticosteroid doses were reduced, asthma became worse in three of five cases.
Summary It is possible that atopy and increased Th2 cell activity are related to a higher coincidence of IgG4-related diseases such as type 1 autoimmune pancreatitis. Monitoring of IgG4 levels may be helpful to determine the incidence of IgG4-related diseases in patients with atopic type asthma for an overall statistical study.

OS235

HLA CLASS I AND II ALLELE FREQUENCIES IN PAKISTANI PSORIASIS PATIENTS AND CONTROLS

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Background Psoriasis is a complex inflammatory disorder characterized by sharply demarcated erythematous papules and plaques with abundant silvery white scales. The etiology of psoriasis is not completely known. However it is clear that both genetic and environmental factors play role in the pathogenesis of psoriasis. The prevalence of psoriasis varies with ethnic groups and geographical locations, with an overall prevalence of approximately 2% of the world's population. In Pakistan very little information is available regarding the prevalence and genetics of Psoriasis. The association of Human Leukocyte Antigen (HLA) alleles with psoriasis is well documented in several population based studies.
Aim The main aim of this study is to screen Pakistani psoriasis patients and healthy controls for HLA class I and II alleles. This is the first comprehensive study on association of HLA alleles with psoriasis in Pakistani Population.
Methodology Our study included 328 patients and 277 healthy ethnically matched control samples. HLA alleles were typed using sequence-specific primers in polymerase chain reaction. The data was analyzed using statistical programme like SPSS ver 10.0 and Arlequin 3.0 and Vassar stats.
Results In case of HLA Class I A*01, A*3201, B*37, B*57 and Cw*0602 allelic frequencies were found to be higher in patients whereas A*03, A*33, B*07, B*18, B*40, B*51, Cw* 0702 and Cw*15 allelic frequencies were higher in control samples. In case of HLA Class II DRB1*0701, DRB1*1001, DRB1*1302, DQB1*03032 allelic frequencies were higher in patients and DRB1*03, DRB1*11 and DQB1*02 showed higher frequencies in controls.
Conclusion This study will give an insight about the role of HLA alleles in the prognosis of psoriasis and will help in the future diagnosis and treatment of the disease.

OS40: COPD 4

OS236

HHIP GENE PLAYS AN IMPORTANT ROLE IN CIGARETTE-INDUCED AIRWAY INFLAMMATION

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Background and Aim of Study Human hedgehog interacting protein, HHIP is a negative feedback regulator of hedgehog signaling which can be stimulated by smoke. Some single nucleotide polymorphismsof HHIP gene have been found associated with susceptibility to COPD, furthermore, HHIP mRNA and protein expression level in lung tissue of COPD patients decrease significantly compared with lung tissue of health smokers according to previous study. These suggest that this gene participated in COPD development, but its role in cigarette induced airway inflammation remains unclear. Our aim is to explore the role of HHIP gene in cigarette induced airway inflammation.
Methods We devided human alveolar epithelial pulmonary cells into two groups: control and HHIP gene silent cells. The later were constructed with siRNA technic. The two groups were stimulated with cigarette smoking extractwith different concentration for different time, then we compared mRNA and protein expression level of IL6, IL8, ICAM before and after using PCR and western blot.
Results After cigatette stimulation for 24 h, the mRNA and protein expression level of IL6, IL8, ICAM, increased significantly in HHIP gene silent A549 group compared with control A549.
Conclusion HHIP gene plays an important role in regulation of cigaretteinduced airway inflammatory mediators levels. Deficient of the gene may lead to development of COPD. Further gene therapy needs to be investigated.

OS237

DIAGNOSIS OF COPD IN THE FACE OF MULTIMORBIDITY, PATIENTS' PERSPECTIVES

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Background A major cause of morbidity and mortality worldwide, COPD often occurs in the presence of multiple other related or unrelated health conditions, which may have implications for experience and management of the disease; a phenomenon known as multimorbidity. Little research has been done exploring patients' perspectives of COPD and even less is known about impact of comorbidities on the disease.
Aim of Study This qualitative study was conducted to understand the physical, psychological and social impact of a new diagnosis of COPD in the context of multimorbidity.
Methods Participants were diagnosed with COPD during a Sydney-based randomised control trial of case finding and early intervention in COPD. From 254 participants in the trial, 20 participants were identified for the qualitative study using maximum variation sampling based on age, gender, socioeconomic status, geographic location and severity of COPD. Data was collected via semi-structured interviews and recorded for transcription purposes.
Results In spite of accepting the diagnosis, most participants had difficulty recognising the significance and incorporating COPD into their lives. Self-management capacity and ability to use healthcare services were challenged by limited understanding of COPD and its implications, complications presented by comorbidities and financial barriers (eg. cost of consulting a specialist). In many cases, the salience of another chronic condition (eg. diabetes) outweighed that of COPD.
Conclusion The findings provide an insight into how patients prioritise health conditions, highlighting the importance of understanding and incorporating their perspectives through patient-centered practice, tailored education and development of personalised care plans for COPD patients with multimorbidity.

OS238

THE ROLE OF TUMOR NECROSIS FACTOR-α AND INTERFERON-γ IN REGULATING ANGIOMOTIN-LIKE PROTEIN 1 EXPRESSION IN LUNG MICROVASCULAR ENDOTHELIAL CELLS

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Background Angiogenesis in the alveolar septa is thought be a critical factor in pulmonary emphysema. Angiomotin-like protein 1 (AmotL1) is involved in angiogenesis *via* regulating endothelial cell function. However, the role of AmotL1 in the pathogenesis of pulmonary emphysema has not been elucidated.
Objective We evaluated the expression of AmotL1 in lung tissues from a murine model with emphysema, as well as from patients with chronic obstructive pulmonary disease (COPD). Furthermore, we analyzed the regulation of AmotL1 expression by TNF-α and IFN-γ in endothelial cells *in vitro*.
Methods *Nrf2* knockout mice were exposed to cigarette smoke (CS) for 4 weeks, and the down-regulated genes affecting vascularity in the whole lung were identified by microarray analysis. This analysis revealed that the mRNA expression of AmotL1 decreased in response to CS when compared with air exposure. To confirm the protein levels that were indicated in the microarray data, we determined the expression of AmotL1 in lung tissues obtained from patients with COPD and also determined the expression of AmotL1, NFκB and IκBα in cultured normal human lung microvascular endothelial cells (HLMVECs) that were stimulated by TNF-α and IFN-γ.
Results We found that the number of AmotL1-positive vessels decreased in the emphysema lungs compared with the normal and bronchial asthmatic lungs. IFN-γ pretreatment diminished the TNF-α-induced AmotL1 in the cultured HLMVECs by blocking the degradation of IκBα.
Conclusions These results suggested that IFN-γ exhibits anti-angiogenesis effects by regulating the expression of TNF-α-induced AmotL1 *via* NFκB in emphysema lungs.

OS239

INFLUENCE OF VARIATIONS OF GROUP COMPONENT ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ITS PROGRESSION

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Background and Aim of Study Vitamin D decreases pulmonary infections and asthma attacks. Genetic variations of group component (GC) affect immunological capacity and serum vitamin D concentration, and we reported that genetic variations of this gene exhibited a higher frequency of exacerbations and severer emphysema (Ishii T, et al. ATS2012, published as an abstract form). Since frequent exacerbations promote the progression of clinical COPD as well as the progression of emphysema, it is speculated that GC genetic variations affect COPD progression. Thus, we aimed to investigate the association between GC genetic variations and COPD progression.
Methods We performed genotype analysis of 361 chronic obstructive pulmonary disease patients and 219 controls to identify 2 coding single nucleotide polymorphisms (SNPs) of group component, rs4588 and rs7041. We examined whether these SNPs affect susceptibility to COPD, emphysema severity (percentage of the low-attenuation area (LAA%) assessed by computed tomography), and COPD progression, namely the annual decline in airflow obstruction (forced expiratory volume in 1 s (FEV1)). Partial results from a smaller population of these subjects were included in a previous study (Ishii T, et al. ATS2012).
Results The median value of the rate of decline of FEV1 was -26 ± 159 mL/year. Subjects with a C allele at rs4588 of GC, who exhibited a higher frequency of exacerbations, also showed a tendency on FEV1 to decline in a rapid manner ($p = 0.0927$). Subjects with a C allele at rs4588 also exhibited greater susceptibility to COPD ($p = 0.0003$) and severer emphysema ($p = 0.0029$).
Conclusion GC genetic variations may affect COPD progression through exacerbation-prone phenotype. The function of the GC protein should be investigated to elucidate the mechanisms of the progression and exacerbations of emphysema, which may be related to the serum concentration of vitamin D.

OS240

CRITICAL ROLE OF RIG-LIKE RECEPTORS IN THE INFLAMMATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim of Study Virus infection are important causes to the development of chronic obstructive pulmonary disease (COPD) and acute exacerbation COPD. RIG-like receptors (RLRs) including retinoic acid-inducible gene-I (RIG-I) and melanoma differentiation associated gene-5 (MDA-5), are important pattern recognition receptors (PRRs) in the elimination of viral. Once triggered by their respective agonist, the signaling cascade of RLRs can produce amounts of I-IFN and pro-inflammatory mediators in the process of anti-viral. It is unkown about whether RLRs involved in the inflammation of COPD. To investigate this question, we took this study.
Methods Endobronchial biopsies and peripheral blood were obtained from COPD patients and control subjects. Realtime-PCR was used to analysis the RNA expression level of MDA-5 and RIG-I in peripheral blood and lung tissues. The cytokines in peripheral blood was also evaluated by Realtime-PCR. The protein level of the two was respectively assessed by western blot and immunohistochemistry. Cytokine from BALF and serum was detected using ELISA.
Results MDA-5 expression was up-regulated in COPD patients. In peripheral blood, COPD patients have a higher mRNA expression levels of IL-1 and IL-8, and they have a positive relationship with MDA-5. Amazingly, we also found a negative correlation between MDA-5mRNA expression level and FEV 1% Pred. In BALF, the IL-8 concentration was increased. But no matter in the lung tissue or peripheral blood, no difference was observed in the expression of RIG-I in COPD patients compared to control subjects.
Conclusion MDA-5 (but not RIG-I) plays a critical role in airway inflammation of COPD. Better understanding the molecular mechanisms underlying these processes will provide novel avenues in the treatment of COPD.

OS241

POSSIBLE INTRACELLULAR MECHANISMS UNDERLYING THE SYNERGISTIC ACTION BETWEEN LAMAS AND LABAS AGAINST MUSCARINIC CONTRACTION IN AIRWAY SMOOTH MUSCLE

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Rationale Since there are no anti-inflammatory agents for chronic obstructive pulmonary disease (COPD), bronchodilators such as long-acting muscarinic antagonists (LAMAs) and long-acting β_2-adrenoceotor agonists (LABAs) are widely used to improve lung function, dyspnea, and QOL in patients with this disease. This study was designed to determine whether synergistic effects were examined between LAMAs and LABAs in airway smooth muscle. Moreover, intracellular signal transduction pathways were examined in this phenomenon based on the linkage between G proteins and large conductance Ca^{2+}-activated K^+ (BK) channels.
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. The tissues were exposed to cholera toxin and pertussis toxin to activate G_s and to inhibit G_i, respectively. Charybdotoxin, a scorpion venom, was applied to suppress BK channels.
Results 1 nM indacaterol, a LABA, and 10 nM Glycopyrronium bromide (GB), a LAMA, caused 9.1% (n = 26) and 25.8% (n = 18) inhibition of 1 μM methacholine-induced contraction, respectively. However, when 10 nM GB was applied in the presence of 1 nM indacaterol, the inhibitory effects of indacaterol/GB combination were markedly augmented to 51.8% inhibition (n = 14, P < 0.01). On the other hand, this greater effect in indacaterol/GB combination was markedly attenuated in the presence of 100 nM charybdotoxin. When the tissues were treated with 2 μg/ml cholera toxin or 1 μg/ml pertussis toxin for 6 h, the effects of GB was significantly enhanced.
Conclusions The combination of indacaterol with GB causes synergistic action against muscarinic contraction in airway smooth muscle via activating BK channels. This phenomenon is involved in the dual regulation of BK channels by G_s and G_i. Therefore, LAMA/LABA combination may be beneficial to therapy for COPD.

OS41: TUBERCULOSIS 5

OS242

PULMONARY TUBERCULOSIS IN FILIPINO CHILDREN WITH CONGENITAL HEART DISEASE IN A TERTIARY SUBSPECIALTY HOSPITAL

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Objective To determine the factors associated with pulmonary tuberculosis in Filipino children with congenital heart diseases (CHD) 2–18 years old in a tertiary subspecialty hospital.
Methods Patients with congenital heart disease ages 2–18 years old patients were included in the study. Tuberculin skin testing, chest xray, sputum Acid Fast Bacilli (AFB) smear and TB Culture were done. They were classified based on the Philippine Pediatric Society (PPS) TB Concensus of 2010, as to: TB negative, TB exposure, TB infection and TB disease.
Results There were 234 patients, 137 of whom were cyanotic and 97 patients were acyanotic. Majority of patients diagnosed as having TB disease were cyanotic about (58.5%) and (41.5%) belongs to the acyanotic group. The following factors were considered significant ($p = <0.05$) in the development of tuberculosis in cyanotic CHD: presence of BCG scar ($p = 0.004$), living in a household with a smoker ($p = 0.000$) and living in a household with an infectious TB ($p = 0.000$). On the other hand those with acyanotic heart disease, the following were associated with the disease: presence of pulmonic stenosis ($p = 0.000$), presence of pulmonary artery hypertension ($p = 0.000$) and those patients who were exposed to an infectious TB ($p = 0.000$). Age was also significant for both groups. Tetralogy of Fallot (TOF) has the most number of cases of TB Disease among those who are cyanotic.
Conclusion The present study helps us realized that patients classified as cyanotic CHD had greater risks of acquiring pulmonary tuberculosis due to its inherent characteristics that complement with the necessity for growth of the tubercle bacilli which is the need for carbon dioxide for its growth and proliferation.

OS243

NEW CANDIDATE FOR TREATMENT BOTH ACTIVELY GROWING AND DORMANT *MYCOBACTERIUM TUBERCULOSIS*

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Background and Aim of Study Curing latent tuberculosis (TB) infection is a big challenge for modern chemotherapy since there are still no effective drugs for latent TB infection. According to in vivo observations *Mycobacterium tuberculosis*. cells in latently infected individuals are in dormant and probably 'non-culturable' state which is accompanied by metabolic cessation. This impacts on phenotypic resistance to currently available antibiotics and dictates the necessity of finding novel drugs effective for latent tuberculosis. The aim of the study was proposing new compounds active against *M. tuberculosis* and its dormant forms.
Methods As a result of extensive structure-activity studies a new original class of heterocyclic compounds named thienopyrimidines was discovered and their antimycobacterial activity was tested. Several thienopyrimidine derivatives were developed and their expected bactericidal effect was measured both for replicating and dormant *M. tuberculosis cells* by the Most Probable Number assay.
Results Thienopyrimidine compounds have been tested for their activity against *M. tuberculosis* H37Rv. Some derivatives were found to possess high antitubercular activity with MIC 0.1–0.5 μg/ml. The most active compound 11126053 with NHMe group in the pyrimidine ring was selected for further studies on dormant ('non-culturable') *M. tuberculosis* cells imitating latent TB infection in living organisms. Incubation of dormant cells with 10 μg/ml of 11126053 for 7 days led to a more than 4-log killing effect, whereas these cells were highly resistant to rifampicin and isoniazid. Original target and MoA will be discussed.
Conclusion Thienopyrimidine derivatives may be regarded as prominent compounds for further development of new drugs for curing *M. tuberculosis* infection including its latent form.

OS244

NEW GENERATION BENZOTHIAZINONES FOR TUBERCULOSIS THERAPY

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Background and Aim of Study The benzothiazinone, BTZ043 (2-[(2*S*)-2-methyl-1,4-dioxa-8-azaspiro[4.5]dec-8-yl]-8-nitro-6-(trifluoromethyl)-4H-1,3-benzothia-zin-4-one), kills *Mycobacterium tuberculosis* by inhibiting the essential enzyme decaprenylphosphoryl-beta-D-ribose 2′-epimerase, and promise for treating tuberculosis. In mice models of acute, subchronic and chronic TB, BTZ043 showed efficacy approaching with the drugs isoniazid and rifampin. Since the efficacy of BTZ043 in these models of TB was lower than expected from its exceptional potency (MIC – 1 ng/ml; 2.3 nM) we liked to improve pharmacokinetic properties.
Methods Now we synthesized a new series of benzothiazinones by introducing a piperazine moiety into the benzothiazinone scaffold to improve solubility, liphophility, PK and PD properties and tested them in murine model of TB infection.
Results Compared to BTZ043, the new lead compound PBTZ169 (2-[4-(cyclohexylmethyl)piperazin-1-yl]-8-nitro-6-(trifluoromethyl)-4H-1,3-benzothiazin-4-one) has improved potency, bioavailability and efficacy in mouse. In the murine model of acute and chronic TB, PBTZ169 showed better efficacy at reducing the bacterial load and can be used at lower effective concentrations than BTZ043. The full compatibility of PBTZ169 with all the other approved and modern experimental TB drugs tested with objective of curing TB in humans. Highly encouraging results were obtained when PBTZ169 was combined with bedaquiline and pyrazinamide as this combination reduced the bacterial load more rapidly than the standart tri-therapy of rifampicin, isoniazid and pyrazinamide.
Conclusion PBTZ169 is an attractive drug candidate to treat human TB. PBTZ169 well-understood drug candidate that offers great potential not only for the control of TB but also for other related mycobacterial diseases, such as leprosyand Buruli ulcer, as well as for related infections like Nocardiosis.

OS245

RECIPROCAL REGULATION OF AUTOPHAGY BY MYCOBACTERIUM TUBERCULOSIS IN ALVEOLAR EPITHELIAL CELLS

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Background and Aim of Study The interaction of host cells with mycobacteria is complex and can lead to multiple outcomes ranging from bacterial clearance to latent infection. Although many factors are involved, the mammalian autophagy pathway is recognized as a determinant that can influence the course of infection. We want to detect the expression of Microtubule-associated protein light chain 3 (LC3) in human alveolar type two epithelial cells A549 and the effect of Mycobacterium tuberculosis (MTB) on it, and to lay the foundation for studying autophagy resistance in the process of Mycobacterium tuberculosis infection.
Methods Human pulmonary type two epithelial cells were cultured in vitro and stimulated with Mycobacterium tuberculosis. Extract the Ribonucleic acid (RNA) of A549 cells at 0 h and 24 h and detect LC3 mRNA expression by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). Test the necrosis cells of control group, 3-Methyladenine (3-MA) group, MTB group and MTB group added with 3-MA with the necrosis and apoptosis staining kit after 24 h. Detect the OD value of LDH of the control group, 3-MA group, MTB group and MTB added with 3-MA group at 4 h, 8 h, 16 h and 24 h by Non-Radioactive Cytotoxicity Assay respectively.
Results The expression of LC3 mRNA detected by RT-PCR was significantly different. The apoptosis and necrosis staining showed the blank group and 3-MA group was not significantly different, MTB group and MTB added with 3-MA group significantly different. The OD value of LDH test showed MTB group and MTB added with 3-MA group was significantly different and time dependent.
Conclusion Our study indicates that autophagy is a defense mechanism inhibiting Mycobacterium tuberculosis survival in infected Human pulmonary type two epithelial cells.
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OS246

DETECTION OF MUTATIONS IN RPOB GENE OF RIFAMPICIN RESISTANT MYCOBACTERIUM TUBERCULOSIS ISOLATES IN ALIGARH, INDIA

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Background and Aim of Study Rapid detection of drug resistance would help not only to optimize treatment of MDR-TB but also in breaking chains of transmission of resistant strains. Resistance in rifampicin has been attributed to mutations within an 81-bp RRDR of the rpoB gene corresponding to codons 509 to 533 in 96% of rifampicin resistant strains. We evaluated the application of DNA sequencing of RRDR of rpoB gene for prediction of rifampicin resistant M. tuberculosis in clinical samples.
Methods We study on 49 M. tuberculosis isolates, and drug resistance was examined by proportional method. Mycobacterial DNA was extracted by Embeden method and rpoB gene was amplified by PCR using forward and reverse primers and then sequenced by automated DNA sequencing.
Results Out of forty nine rifampicin resistant M. tuberculosis isolates, forty one (83.6%) were resistant to both isoniazid and rifampicin or MDR. In DNA sequencing analysis, total forty six (93.8%) isolates showed mutational change in different codons while three (6.1%) did not show any mutational change. The frequency of mutation (total 65 mutation in 46 M. tuberculosis isolates) in different codons were on codon531, 23 (35.5%), codon526 16 (24.6%) followed by codon516 in 11 (16.9%), codon508 in 10 (15.3%), Codon511 & codon512 mutated in 2 strains each (3%), and codon510 mutation was observed in 1 of the mycobacterial strain (1.5%).
Conclusions The most frequently involved mutation in rpoB gene were at codon531 (35.5%), codon526 (24.6%). DNA sequencing can provide an accurate and rapid prediction of rifampicin resistant M. tuberculosis to be clinically useful for detection of MDR-TB.

OS247

MANNOSE-BINDING LECTIN GENE POLYMORPHISMS IN VIETNAMESE PATIENTS WITH PULMONARY TUBERCULOSIS

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Background and Aim of Study Mannose-binding lectin (MBL) is a serum protein belonging to the collectin family and recognizes pathogens by its carbohydrate-recognition domains. MBL binds to the surface of pathogens and leads to complement-mediated opsonization and phagocytosis or lysis of the microorganisms. Although genetic associations of MBL polymorphisms with tuberculosis (TB) have been studied in various populations, the results are controversial. The aim of this study is to explore whether MBL polymorphisms are associated with susceptibility to TB in the Vietnamese.
Methods Nucleotide sequences of the promoter and exon 1 regions of MBL gene (*MBL2*) were initially analyzed in 65 patients with active TB and 109 healthy health care workers (HCWs), together with their plasma concentrations measured by enzyme-linked immunosorbent assay. X/Y polymorphism in the promoter region and A/B polymorphism in exon 1 of *MBL2* were further genotyped in DNA samples collected from 774 bacteriologically-proven TB patients without HIV infection and 556 controls in Hanoi, Viet Nam.
Results The haplotypes of *MBL2* genetic polymorphisms observed in the Vietnamese were HYPA, LYPA, LYQA, LXPA and LYPB. Plasma MBL concentrations and frequencies of *MBL2* genotypes were not significantly different between HCWs with and without latent TB infection. Since X/Y and A/B polymorphisms have been strong determinants of plasma concentrations of MBL, we focused on these polymorphisms and genotyped them in all other cases and controls. YA/YA genotype was associated with protection against TB (P = 0.038, odds ratio 0.79, 95% confidence interval 0.63–0.98), and the resistant genotype tended to be less frequently found in younger age.
Conclusion *MBL2* YA/YA genotype was associated with high plasma concentrations of MBL and had a protective role against development of TB in younger age, whereas *MBL2* genotype was not associated with latent TB infection. High MBL concentrations may protect development of pulmonary TB after infection.

OS42: INTERSTITIAL LUNG DISEASE 6

OS248

HISTORICAL CHANGES OVER FOUR DECADES IN THE AGE-SPECIFIC DISTRIBUTION OF SARCOIDOSIS CASES AT DIAGNOSIS IN JAPAN

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Background and Aim of Study Sarcoidosis is thought to occur more frequently in adults aged less than 40 years, with incidence peaking in patients aged between 20 and 29 years. However, there is some evidence of an upward shift of age at diagnosis over time in Denmark and the United States. We aimed to identify any historical changes in the age-specific distribution of cases at diagnosis in Japan.
Methods We reviewed 588 consecutive patients newly diagnosed with sarcoidosis (431 biopsy-proven, 157 clinically proven) between 1974 and 2012 at our institution. The diagnosis was made based on the diagnostic criteria developed in Japan in 2006.
Results The study population consisted of 204 males and 384 females; 275 patients were aged less than 45 years at diagnosis (younger diagnosis group) and 313 patients were aged 45 years or older (older diagnosis group). Over the past four decades, the proportion of patients in the older diagnosis group continuously increased from 2.94% (1974–1983) to 42.4% (2004–2012) in men, and from 44.2% to 80.2% in women. In 1974–1983, the age distribution for women showed a biphasic pattern, with the first peak at age 20–24 years and the second peak at age 55–59 years; however, this subsequently changed to a monophasic pattern without the first peak. In regard to men, a monophasic pattern was evident in the period 1974–1983, with a peak at age 20–24 years, but this later changed to a biphasic pattern with an additional second peak.
Conclusion The age at diagnosis has continued to increase in Japan. As the country's population is homogenous in terms of ethnicity, the age-specific distribution at diagnosis could vary not only because of genetic factors at play but also environmental factors, and environmental risk factors might have changed over the past four decades in Japan.

OS249

BRONCHOALVEOLAR LAVAGE CELLULAR PATTERN CAN PREDICT THE PROGNOSIS OF PATIENTS WITH CHRONIC HYPERSENSITIVITY PNEUMONITIS

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Background and Aim of the Study Chronic hypersensitivity pneumonitis (CHP) is induced by persistent exposure to a variety of inhaled antigens and is characterized by varying degrees of inflammatory cells infiltration and progressing fibrosis of the lung. Poor lung function, fibrotic pattern on HRCT, and usual interstitial pneumonia (UIP)-like or fibrotic-non-specific interstitial pneumonia (f-NSIP)-like pattern on surgically resected lung tissue have been reported to correlate with poor prognosis of the patients with CHP, whereas little is known about the correlation between bronchoalveolar lavage (BAL) cellular pattern and prognosis. We conducted this study to clarify whether BAL cellular pattern of the patients with CHP can predict their prognosis.
Methods We retrospectively reviewed the clinical records of 50 patients with CHP and analyzed the correlations between clinical characteristics, lung function values, BAL cellular patterns and prognosis.
Results Median overall survival time of 50 patients with CHP was 1794 ± 219.5 days. According to the log-rank analyses, lower total cell count of the BAL and lower lymphocyte differential count significantly correlated with poorer overall survival ($p = 0.007$ and $p < 0.001$, respectively). Furthermore, multivariate Cox proportional-hazards model analysis confirmed that low total cell count and low lymphocyte differential count were independently correlated with poor prognosis of the patients with CHP.
Conclusion We demonstrate that the BAL total cell count and lymphocyte differential count of the patients with CHP can predict their prognosis.

OS250

LEVELS OF AUTOANTIBODIES AGAINST GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (GM-CSF) IN CLINICAL COURSE OF AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS (APAP)

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Background and Aim of Study Pulmonary alveolar proteinosis (PAP) is a rare diffuse lung disease characterized by excessive accumulation of surfactant proteins in the alveoli and terminal bronchioles. Recent progress in the pathogenesis of PAP is the discovery of elevated levels of autoantibodies against GM-CSF in most of idiopathic PAP (autoimmune PAP, APAP) patients. However, the effects of therapy on the levels of GM-CSF autoantibody and the time-dependent changes in APAP patient remain unclear. The aim of this study is to examine the relationship between GM-CSF autoantibody level in sera and clinical course and therapy in APAP patients.
Method We obtained sera at various clinical points from 11 APAP patients whom we observed more than 2 years in Aichi Medical University School Hospital and measured the levels of anti-GM-CSF antibodies by enzyme-linked immunosorbent assay (ELISA).
Results The levels of GM-CSF autoantibodies were decreased as APAP stabilized. They were not necessarily decreased after whole lung lavage and inhalation of GM-CSF, however; they were decreased after rituximab therapy. The levels of GM-CSF autoantibody and KL-6 levels in sera were positively correlated in stable term.
Conclusion Regular measurement of GM-CSF autoantibody level in sera might be useful for prediction of clinical course of APAP.

OS251

INCIDENCE OF SILICOSIS IN STONE PROCESSING AREAS, BANGLADESH

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Background Silicosis is one of the types of DPLD. Especially in stone processing areas workers are more suffered in this disease. Burimari is one of the major stone processing areas in Lalmonirhat, Bangladesh. Study was done in this area from July to September 2012.
Methods The prospective study was done in Burimari, Lalmonirhat, Bangladesh. The data was collected from the workers randomly.
Results Total 187 samples were collected and analyzed. Silicosis 53 (28%) Nonsilicosis 134 (53%). Age of Respondent 18 (15–25) 34%, 20 (25–35) 37%, 7 (35–45) 13.2%, 9.4 (45–55) 9.4%, 1.9 (55–65) 1%, 2 (75–85) 3.8%. The data shows that most of the respondents are from 15 to 35 years old. Among them 37.7% are 25 to 35 years and 34% are from 15 to 25 years age group. Stone crushing and stone loading are so laborious job but it is significant that 3.8% respondent is from 75 to 85 years age group. In this sector 79.2% are engaged in stone loading and 20.8% are engaged in stone crushing. In this study we (research team) collected data from both current 52 (27.8%) and Ex workers 135 (72.2%). Here research team founded that 131 (70.09% are Ex smokers, 40 (21.40%) are Smoker and 16 (8.51%) are non smoker. Among the workers 24.52% are dyspnoe 86.90% workers had cough, 56.60% workers had sputum. Tuberculosis was diagnosed in 7.55% worker. Crackles were detected in 83.01% worker. Among silicosis patients, chest X ray findings were compatible with silicosis in 94.33% cases. According to the collected data many types of stone are used in stone crushing areas. Lime stone is used for crushing by majority of workers (84%) while sand stone used by 11% and quartz is used by 4% worker.
Conclusion The workers who works in stone processing zone is more suffered by silicosis.

OS252

ASSESSMENT OF MINERAL PARTICLES AND FIBERS IN BALF IN PATIENTS WITH INTERSTITIAL LUNG DISEASES USING ELECTRON MICROSCOPY

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Background Inhalation of mineral fibers and particles increases the risk of developing occupational interstitial lung diseases. Analysis of bronchoalveolar lavage fluid (BALF) is useful for the diagnosis of diffuse lung diseases. However, the diagnostic value of an assessment of mineral particles and fibers in BALF with electron microscopy for the diagnosis of occupational interstitial lung diseases is unclear.
Method We examined mineral fibers and particles in BALF with scanning X-ray analytical electron microscopy (SEM) in 26 patients with interstitial lung diseases, and assessed the correlation of the history of occupational exposure of mineral particles and fibers and the results of BALF with SEM analysis.
Result Fourteen out of 26 patients had positive histories of occupational exposure to mineral dusts. Many of the patients without occupational exposure included patients with several interstitial lung diseases such as collagen vascular disease-related, younger patients, female and non-smoking patients compared with those with occupational exposure. Pulmonary functions, serum levels of KL-6 and high-resolution CT scores were not significantly different between patients with or without occupational exposure. Electron microscopic analysis revealed that the concentration of particles and/or fibers was not significantly different, whereas the percentages of Fe, P, Zr in the particles, Fe, Mg and asbestos in the fibers were significantly higher in patients with occupational exposure.
Conclusion Instead of small sample size in this study, these results suggest that an assessment of mineral particles and fibers in BALF using electron microscopy is useful for the diagnosis of occupational interstitial lung diseases. Further examinations with larger number of patients are necessary to clarify the role of mineral fibers and particles in patients with interstitial lung diseases.

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1-A1: LUNG CANCER 1

PS001

TRICHOPTYSIS IN MATURE INTRAPULMONAL TERATOMA

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Background Teratoma most commonly o, ccur in the gonads but around 3% are known to be extra-gonadal, most of these being intrathoracic. Intrathoracic teratoma usually occurs in the mediastinum, but rarely, these may originate from the lung. Since it reported by Mohr for the first time in 1839, there are only 67 cases reported until 2007. Clinically, patients with intrathoracic teratoma got symptoms of chest pain, haemoptysis, cough with expectoration but pathognomonic symptom that spesific to an intrapulmonary teratoma (IPT) was trichoptysis (expectoration of hair). CaseA 35-year-old woman was admitted with cough with expectoration of hair, accompanied by hemoptysis and expectoration of cheese like material. She complained it since she was 30 years old. The symptoms came periodically every six months with unclear precipitation factors. Based on physical examination there were dullness on percussion and decreased of vesicular sound on 1/3 lower right hemithorax. Radiologic findings suggest a mediastinal mass, there were lack of data whether from transthoracal biopsy or brushing bronchoscopy. Bronchoscopy was performed, and there was a hair in the inferior right bronchus. Serum germ cell tumor markers was normal. Patient had the toracotomy and there was a mass on the right lung medial lobe. The histopatology finding revealed a mature intrapulmonal teratoma.
Conclusion Trichoptysis is a pathognomonic symptom for an intrapulmonary teratoma. Diagnosis is depend on careful clinical consideration and imaging. Surgery is the main treatment for intrapulmonary teratoma but it also could be a diagnostic tool when pre operation diagnosis was unclear.
Keywords trichoptysis, intrapulmonal teratoma.

PS002

HIGHER INCIDENCE OF LUNG CANCER IN FEMALE PASSIVE SMOKERS

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Background/Aim of Study To evaluate whether there is a correlation between passive smoking and lung cancer. Studies which indicate a correlation between passive smoking and an increased risk for developing lung cancer can be used as evidence to encourage further public education and anti-smoking campaigns.
Methods In 2011, 226 patients were evaluated based on their occupation, exposure to passive smoking, family history of cancer and other co-morbidities. The studied sample consisted of men and women with late stage lung cancer who were admitted to Bangkok Hospital. These patients had previously undergone chemotherapy and radiation therapy. The diagnosis was proven by lung pathology. The patients were evaluated retrospectively. Researchers measured the collated data for indications of a significant amount of lung cancer occurrences within the group of females who had been exposed to passive smoking. The rate of 5% was chosen to indicate a significant occurrence.
Results Of 152 male patients, 135 were smokers (59.7%). 17 (7.5%) were non-smokers. The age ranged from 32–82 years. The mean age for male patients was 55.97. The mean age for female patients was 52.98. The mean age for all patients was 54.99. All of the participating patients in the study were Thais. Among these 17 non-smoking males, 3 were passive smokers, 1 worked in a chemical factory. There were 74 females, 10 (4.4%) were smokers and 64 (28.3%) were non-smokers. Among 64 non-smoking females, 40 were passive smokers ($p < 0.001$), 3 worked in a chemical factory. The occurrence of lung cancer in female passive smokers has been found to be significantly high at 17.7%].
Conclusion There is a need to improve health education campaigns and increasing public awareness of the health risks associated with passive smoking, as well as a re-evaluation of current lung cancer screening practices currently accepted by the medical establishment in Thailand.

PS003

THE SENSITIVITY OF CYTOLOGIC EXAMINATION OF PLEURAL FLUID IN THE DIAGNOSIS OF MALIGNANT PLEURITIS

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Back Ground There are some cases that cytological examination of pleural fluid does not allow the detection malignant findings.
Methods We retrospectively reviewed the cytologic and histological findings in 75 patients who underwent medical thoracoscopy under local anesthesia in our institution between 2010 and 2012.
Results 26 patients were diagnosed as malignant pleuritis or malignant mesothelioma by histological diagnosis in pleural biopsy. The cytological findings were consistent with the histological diagnosis in 11 patients. The sensitivity of cytologic examination of pleural fluid was 42.3%. The sensitivity including the cases who diagnosed suspected malignancy was 73.1%. 7 cases that were not diagnosed definitively include 2 cases with adenocarcinoma, 2 cases with malignant mesothelioma, 2 cases with metastatic carcinoma and 1 case with small cell carcinoma. There were two cases that the findings were different between cytology and histology. The cytological findings showed adenocarcinoma in the case who diagnosed as small cell carcinoma in histology. The other case diagnosed with adenocarcinoma was obtained finding as malignant cell in cytological examination.
Conclusions The ability of cytologic examination of pleural fluid has limitation. Thoracoscopic pleural biopsy is recommended for diagnosis of malignant pleuritis.

PS004

THE HIGH PLASMA CONCENTRATION OF GEFITINIB IN PATIENTS WITH EGFR MUTATED NSCLC CAN BE LONGER PROGRESSION-FREE SURVIVAL

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Purpose It is reported that there is a large inter-individual variation in gefitinib pharmacokinetics. The purpose of this study was to examine the correlation between the gefitinib exposure and treatment effects in patients with epidermal growth factor receptor (EGFR) mutated non-small cell lung cancer (NSCLC).
Methods We examined 19 Japanese patients with EGFR mutated NSCLC who received 250 mg daily gefinib as first-line treatment between January 2011 and April 2013 at Akita University Hospital. On day 14 after beginning treatment, plasma samples were collected just prior to and 1, 2, 4, 6, 8, 12, and 24 h after gefitinib administration and were analyzed by high-performance liquid chromatograph. We measured the area under the plasma concentration-time curve (AUC) and the plasma concentration of gefitinib from plasma samples. 19 patiens were divided into high and low AUC groups by the median AUC. Evaluation was performed by CT scan on day 28 after beginning administration and every 2 months. The primary end point was progression-free survival; secondary end points included response rate and toxic effects.
Results In the analysis of data for the 19 patients, response rates were 100% in both groups. The high AUC group tended to have longer progression-free survival than the low AUC group, although there was no significant difference between both groups. The incidence of elevated aminotransferase levels (grade > 2) in the high AUC group tended to be higher than the low AUC group.
Conclusions This study suggested that high gefitinib exposure in patients with EGFR mutated NSCLC could be longer progression-free survival. Further examination is required.

PS005

INCREASED RED BLOOD CELL DISTRIBUTION WIDTH CORRELATES WITH CANCER STAGE AND PROGNOSIS IN PATIENTS WITH LUNG CANCER

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Background Red cell distribution width (RDW), one of many routinely examined parameters, shows the heterogeneity in erythrocyte size. We investigated the correlation of RDW levels with clinical parameters and prognosis of lung cancer patients.
Methods Clinical and laboratory data from 332 patients with lung cancer in a single institution were retrospectively studied by univariate and multivariate analysis.
Results The RDW level was divided into two groups (high RDW (>=15%), n = 73 vs. low RDW, n = 259 (<15%)). Multivariate analysis showed that higher RDW values independently correlated with performance status, presence of other diseases, white blood cell and albumin ($p = 0.033$, 0.010, 0.047, and 0.011, respectively). When patients with comorbid diseases were excluded, stage was the only independent factor of RDW ($p = 0.013$). Kruskal-Wallis post-hoc tests revealed a positive correlation between RDW values and cancer stage in patients irrespective of comorbidity ($p < 0.0001$, < 0.0001). Stage I-IV lung cancer patients (n = 303) with higher RDW values (n = 61) had a poorer prognosis than those with lower RDW values (n = 242) (Log-rank test; $p = 0.03$, Wilcoxon test; $p = 0.0004$). In particular, the survival rates of stage I and II patients (n = 136) were lower in the high RDW (n = 18) group than in the low RDW (n = 118) group (Log-rank test; $p < 0.0001$, Wilcoxon test; $p = 0.0002$).
Conclusion RDW correlated with factors that reflect inflammation and malnutrition in lung cancer patients; moreover, high levels of RDW correlated with poor survival. RDW may be used as a new and convenient marker to determine a patient's general condition and to predict the mortality risk of lung cancer patients.

PS006

EFFICACY AND SAFETY OF CISPLATIN/PEMETREXED AS FIRST-LINE TREATMENT FOR JAPANESE PATIENTS WITH ADVANCED NONSQUAMOUS NON-SMALL CELL LUNG CANCER

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Background Cisplatin/pemetrexed is considered to be the standard of care for the first – line treatment of patients with advanced nonsquamous, non – small cell lung cancer (NSCLC). However, little is known about its efficacy and safety in Japanese patients.
Methods We retrospectively analyzed the efficacy and safety in 40 patients who received cisplatin (75 mg/m^2) and pemetrexed (500 mg/m^2) as first – line treatment for advanced NSCLC.
Results Overall response rate was 37.5%, median progression free survival (PFS) was 5.6 months, and median overall survival (OS) was 20.1 months. In the subgroup analysis, the median OS was 18.8 months in patients with EGFR wild-type or unknown (n = 28). Grade 3 or 4 hematological toxicities including neutropenia in 7 cases (17.5%), leukopenia in 5 cases (12.5%), anemia in 1 case (2.5%), thrombocytopenia in 1 case (2.5%) and febrile neutropenia in 1 case (2.5%) were recorded. Grade 3 or 4 non-hematological toxicities including anorexia, infection, rash and transaminase increase were observed in 3 (7.5%), 1 (2.5%), 1 (2.5%) and 1 (2.5%) patients, respectively. Thus, the adverse events were mostly mild. There was no treatment-related death.
Conclusions Cisplatin/pemetrexed as first-line treatment was well tolerated and effective for Japanese patients with advanced nonsquamous NSCLC.

PS007

CHARACTERISTICS AND OUTCOMES OF ADVANCED NON-SMALL CELL LUNG CANCER OF THE YOUNG PATIENTS

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Backgrounds Lung cancer in the young patients is rare in its prevalence, and was thought to be progressive in the prognosis compared with those in older patients. We investigated the characteristics and outcomes of young patients with advanced non-small cell lung cancer (NSCLC) in our hospital.
Methods We retrospectively studied the advanced NSCLC patients aged 45 or younger from April 2007 to September 2012.
Results A total of advanced NSCLC was 17 (7 males and 10 females). Their performance status (PS) was 0 or 1, and 5 patients had smoking history over 30-pack-year. Histopathology of the lung cancer showed that 13 patients (76.4%) were adenocarcinoma, 2 patients (11.8%) were squamous cell carcinoma and 1 patient (5.9%) was pleomorphic carcinoma and another 1 patient (5.9%) was poorly differentiated carcinoma. EGFR gene mutation was examined in 11 patients. One patient had mutation of exon18 G719A, one patient had exon21 L858R, and two patients had deletion of exon19. EML4-ALK fusion gene was examined in 3 patients and one patient had EML4-ALK fusion gene. Fourteen patients received platinum-based combination chemotherapy, and 3 patients received gefitinib for the first line chemotherapy. One patient with EML4-ALK fusion gene received crizotinib for the second line chemotherapy. Eight patients (47.1%) of 17 patients received over the 4th line chemotherapy. Median overall survival was 17.1 months (2.2–35.3 months).
Conclusions Major histological types of lung cancer in young patients were adenocarcinoma (76.4%) and 5 of 11 patients had EGFR gene mutation or EML4-ALK fusion gene. They are tolerable for a few lines of chemotherapy, and overall survival was not different from the older patients of lung cancer.

PS008

THE SHORTEST SURVIVAL TIME OBSERVED IN LUNG CANCER PATIENTS WITH POSITIVE PLEURAL FLUID CYTOLOGY

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Background and Aim of Study Pleural effusion is one of the poor prognostic factors in lung cancer and indicates an advanced stage of lung cancer with a low life expectancy rate. More than 50% of patients had positive pleural fluid cytology. The aim of this study was to retrospectively analyze in survival time of lung cancer patients with pleural effusion.
Methods A cohort retrospective study was conducted using 729 data of lung cancer patients in Persahabatan Hospital from January 2010 to December 2011. Data showed that 315 of 729 (43.2%) lung cancer patients have pleural effusion. We have used consecutive data in two groups. Both groups contains 50 patients with positive results and 50 patients negative results of pleural fluid cytology. Actuarial survival was calculated using Kaplan-Meier methods. Cox proportional hazards regression was used to ascertain the covariates associated with survival.
Results Median survival time for patients with positive pleural fluid cytology was lower than those with negative cytology results (21 vs 42 days), as well as overall survival time (40.42 vs. 42.83 days, p 0.01). Factors associated including sex, age and volume of pleural effusion do not have significant effect on the survival. However, patients receiving therapy showed a significant increase in the survival time (Hazard ratio 0.157, 95% CI 0.092–0.266, $p < 0.001$). A significant decrease of survival time was found in patients with small cell carcinoma compared to adenocarcinoma patients (Hazard ratio 17.685, 95% CI 2.155–145.146, p 0.007).
Conclusion Lung cancer patients with pleural effusion appear to have poor survival time, particularly those with positive pleural fluid cytology results. Thus, it is important to assess pleural cytology in lung cancer patients.
Keywords Lung cancer, malignant pleural effusion, positive cytology.

PS009

FREQUENCY OF THROMBOCYTOPENIA DUE TO GEMCITABINE AND CARBOPLATIN REGIMEN IN NON-SMALL-CELL LUNG CANCER PATIENTS

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Background and Aim of Study Hematological toxicities often occur in patients with non-small-cell lung cancer (NSCLC) who are treated with chemotherapy. In our data had shown that thrombocytopenia due to carboplatin based chemotherapy was low but there was not any local data about carboplatin and gemcitabine regimen. The aim of this study is to investigate the frequency of hematologic events, such as thrombocytopenia, anemia, leucopenia, neutropenia due to combination of gemcitabine and carboplatin in non-small cell lung cancer patients.
Methods We conducted a retrospective cohort study that enrolled all non-small-cell lung cancer patients who received 1.250 mg/m^2 gemcitabine on day 1,8 and AUC-5 carboplatin on day 1. Patients who received 2 cycles or more are included in this study. We investigated the frequency of thrombocytopenia, anemia, leucopenia, neutropenia, and hemorrhage during chemotherapy period.
Results In our preliminary results, we report that 29 patients with non-small cell lung cancer are included in this study. The mean age was 59.1 ± 9.44 years old (range 41 to 75 years old). The majority histological findings were adenocarcinoma (89.7%). A median of chemotherapy was 4 cycles (range 2–6). The hematological toxicities data have shown that 13.7% patient with grade 3 or 4 leucopenia and 6.9% grade 3 or 4 anemia. However, 6 of 29 (20.7%) patients had grade 3 or 4 thrombocytopenia.
Conclusion Thrombocytopenia was found in gemcitabine and carboplatin regimen but lower than other published data.
Keyword thrombocytopenia, gemcitabine, non-small-cell lung cancer.

PS010

MONITORING SERIAL OF SERUM LEVELS CARCYNOEMBRIONIC ANTIGEN IN LUNG CANCER PATIENTS RECEIVING CHEMOTHERAPY IN ADAM MALIK GENERAL HOSPITAL MEDAN INDONESIA

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Background Lung cancer is leading cause of death in the world. Several studies showed that serum levels of carcynoembryonic antigen (CEA) is more useful in evaluating therapies than used as a diagnostic. Serial CEA determinations are also useful in patients with lung cancer. Patients who responded to chemo- or radiotherapy showed decreased CEA levels when CEA was elevated before therapy. An increase in further determinations means a progressive tumor spread. On the other hand, patients who did not respond to therapy showed increased CEA levels because of tumor progression. Aim of this study is to monitor the levels of CEA lung cancer patients receiving chemotherapy at Adam Malik General Hospital, Medan, Indonesia.
Methods This research is a descriptive study on monitoring serum levels of carcinoembryonic antigen in patients with stage III and IV of lung cancer who received chemotherapy which data is retrieved from secondary data from January 2008 until October 2012.
Results Decreased serum levels of CEA lung cancer patients after chemotherapy with a mean value of CEA levels prior to chemotherapy was 16.043 ng/mL (n = 201). 201 patients get first chemotherapy with a mean CEA 16.062 ng/mL. After second chemotherapy the mean CEA to 9.481 ng/mL (n = 117). In the third chemotherapy with a mean CEA 2.826 ng/mL (n = 67) and after the fourth chemotherapy the average of the CEA to 1.707 ng/mL (n = 34).
Conclusion There is decreased of serial serum levels of CEA in lung cancer patients who received chemotherapy. This assay could be one of tools to assess the effectiveness of chemotherapy.
Keywords carcinoembryonic antigen, lung cancer, chemotherapy.

PS011

SURVIVAL OF SUPERIOR VENA CAVA SYNDROME PATIENTS WITHOUT RADIATION THERAPHY IN CIPTO MANGUNKUSUMO HOSPITAL AND DHARMAIS CANCER HOSPITAL

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Background and Aim of the Study Superior vena cava syndrome (SVCS) is a syndrome due to compression or infiltration to superior vena cava and is a medical emergency that needs to be managed immediately. In treatment of SVCS patients without radiation therapy is important to know it's survival rate. The aim of this study is to obtain the survival rate of SVCS patients in Cipto Mangunkusomo and Dharmais Cancer Hospital.
Methods This is a restrospective cohort study conducted through medical record of SVCS patients within January 2000 to December 2011 in Cipto Mangunkusomo and Dharmais Cancer Hospital.
Results The study population was 26 subjects and most of the patients were male (65,4%). The age of the patient mostly range from 18–60 years old (65,4%). Non small cell lung cancer is the most common etiology of SVCS patient. The cumulative survival of SVCS patient in 120 days is 50 %, mean survival was 38 days (SE 9,8) and the survival rate showed plateau appearance from the day of 60th.
Conclusion Superior Vein Cava Syndrome patients without radiation therapy in this study were mostly due to non small cell lung cancer, found mostly in males and the age range was 18–60 years old. The cumulative survival of SVCS patient in 120 days is 50 %, mean survival was 38 days (SE 9,8) and the survival rate showed plateau appearance from the day of 60th.

1-A2: LUNG CANCER 2

PS012

EGFR DERIVED PEPTIDE ANTIBODY PREDICTS PROGRESSION FREE AND OVERALL SURVIVAL IN NON-SMALL CELL LUNG CANCER PATIENTS RECEIVING GEFITINIB

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Somatic mutations in the epidermal growth factor receptor (EGFR) gene are associated with clinical response to EGFR tyrosine kinase inhibitors (TKIs) such as gefitinib in patients with non small cell lung cancer (NSCLC). However, distribution or biological significance of EGFR antibody in NSCLC patients is not yet investigated. In this study, we investigated whether IgG responses to EGFR derived peptides of NSCLC patients, and report that IgG against EGFR derived peptides were detectable in NSCLC patients treated with gefitinib, and they could be possible prognostic factor for progression free (PFS) and overall survival (OS) of NSCLC patients who received gefitinib treatment. Luminex system were used to measure immunoglobulins (Igs) to each of 58 different peptides in 42 NSCLC patients who were treated with gefitinib. Some kinds of anti-peptide IgG was detected in NSCLC patients and associated with PFS and OS. Detection of EGFR-derived peptide antibody from sera may be promising method for predicting the prognosis of NSCLC patients treated with gefitinib. These results could provide new insight for better understanding of humoral responses to EGFR-derived peptides in NSCLC patients.

PS013

RELATIONSHIP OF PROGRESSION-FREE SURVIVAL, POST-PROGRESSION SURVIVAL AND RESPONSE WITH OVERALL SURVIVAL IN ADVANCED NON-SQUAMOUS NON-SMALL CELL LUNG CANCER OF INDIVIDUAL-LEVEL

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Background and Aim of Study The effects of first-line chemotherapy on overall survival (OS) might be confounded by subsequent therapies in patients with non-small cell lung cancer (NSCLC). We examined whether progression-free survival (PFS), post-progression survival (PPS), or tumor response could be valid surrogate endpoints for OS after first-line chemotherapies in advanced NSCLC by using individual-level data, given the lack of research in this area.
Methods Between April 2009 and June 2011, 50 patients with advanced non-squamous NSCLC treated with cisplatin and pemetrexed as first-line chemotherapy were analyzed. The relationships of PFS, PPS, and tumor response with OS were analyzed at the individual level.
Results Spearman rank correlation analysis and linear regression analysis showed that PPS was strongly correlated with OS ($r = 0.89$, $P < 0.05$, $R2 = 0.79$), PFS was moderately correlated with OS ($r = 0.67$, $P < 0.05$, $R2 = 0.39$), and tumor shrinkage was weakly correlated with OS ($r = 0.36$, $P < 0.05$, $R2 = 0.14$). Performance status at the beginning of second-line treatment, the best response to second-line treatment, and number of regimens used after progression following first-line chemotherapy were significantly associated with PPS ($P < 0.05$).
Conclusions Analysis of individual-level data suggested that PPS could be used as a surrogate for OS in patients with advanced non-squamous NSCLC with unknown oncogenic driver mutations and therefore limited options for subsequent chemotherapy. Our findings also suggest that subsequent treatment after disease progression following first-line chemotherapy may greatly influence OS. These results should be validated in other larger populations.

PS014

CORRELATION BETWEEN MAPK (ERK1/2) ACTIVITY DUE TO DRIVER MUTATIONS AND PROGNOSIS IN NON-SMALL-CELL LUNG CANCER

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Background Epidermal growth factor receptor (EGFR) triggers the RAS-RAF-mitogen-activated protein kinase (MAPK) signaling pathway. In non-small-cell lung carcinoma (NSCLC), known mutations, which are called driver mutations, in EGFR, KRAS, BRAF, and other oncogenes cause continuous activation of tyrosine kinase. In this study, the aim is to clarify the correlation between driver mutations and the activity of MAPK (ERK1/2) in advanced NSCLCs.
Material and Methods Paraffin-embedded lung biopsy samples were obtained from 110 NSCLC patients (2009–2010). EGFR mutations were analyzed using the PCR clamp method. KRAS codons 12 and 13 and BRAF V600E mutations were assessed by mutation-based PCR performed using a quenching probe, with the i-densy system. ALK rearrangement was analyzed by immunohistochemistry. Phosphorylation of MAPK (ERK1/2) was assessed by immunohistochemical analysis with the anti-phospho-p44/42 MAPK antibody. Clinical and prognostic assessments were performed using the Kaplan-Meier method.
Results Phospshorylated p44/42 MAPK was detected in 84 (76.4%) of the 110 patients. In the 79 patients with phospho-p44/42 expression, 14 (17.7%) had EGFR mutations, 8 (10.1%) had a KRAS mutation, and 2 (2.5%) had a BRAF mutation. The phospho-p44/42 expression level, which was assessed on the basis of the immunohistochemical score, was found to be lower in the patients with EGFR mutations and higher in the patients with a KRAS/BRAF mutation. The patients' prognosis tended to worsen with increase in the phospho-p44/42 expression level. These results showed that the activity of the MAPK signaling pathway increased to a greater extent because of KRAS/BRAF mutations than because of EGFR mutations and may have caused poor prognosis. No correlation was found between ALK rearrangement and the phospho-p44/42 expression level.
Conclusions The expression level of phosphorylated MAPK was higher in the NSCLC patients with a KRAS/BRAF mutation than with EGFR mutations, and this higher activity level was associated with poor prognosis.

PS015

IMPACT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON MORTALITY OF PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Background and Aim Lung cancer and chronic obstructive pulmonary disease (COPD) are commonly accompanied pulmonary diseases caused by cigarette smoking. However, the impact of COPD on the mortality and clinical features of patients with lung cancer are not well studied. The aim of this study is to compare mortality and clinical characteristics in patients with non-small cell lung cancer (NSCLC) according to the presence of COPD.
Methods The medical records of 221 smokers who were diagnosed with NSCLC between January 2005 and January 2006 were reviewed. Eligible patients were dichotomized into COPD group (n = 111) and non-COPD group (n = 110). The overall survival and clinical characteristics were compared and predictors for worse survival were analyzed using Cox's proportional hazards regression.
Results COPD was present in 50.2% of all patients with NSCLC and most of the patients (92.8%) with COPD were unaware of the disease before diagnosis of lung cancer. COPD group was older, and had a lower body mass index (BMI), higher pack-years smoking history, higher frequency of dyspnea and more previous malignancy. The overall survival was comparable between two groups (Log-rank test, p = 0.2). The survival among propensity-score matched subjects (n = 176) was also comparable (Log-rank test, p = 0.396). Old age, low BMI, advanced disease stage (stages III and IV), non-squamous histology, poor performance status, weight loss at presentation, and coexistence of interstitial lung disease were analyzed as independent risk factors for shorter survival.
Conclusion COPD coexists with NSCLC frequently and subliminally. Although differences of clinical characteristic do exist, there was no impact of COPD on mortality of NSCLC patients with a positive smoking history.

PS016

IMPACT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON MORTALITY OF PATIENTS WITH NON-SMALL CELL LUNG CANCER

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[1]Gyeongsang National University Hospital, Jinju, Korea, [2]Seoul National University College of Medicine, Seoul, Korea

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Conclusion COPD coexists with NSCLC frequently and subliminally. Although differences of clinical characteristic do exist, there was no impact of COPD on mortality of NSCLC patients with a positive smoking history.

PS017

ATYPICAL PRESENTATION OF COMBINED LARGE CELL NEUROENDOCRINE CANCER OF LUNG: A CASE REPORT

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Introduction This is a case of R.B, a 71 year old female presenting with 2 months history of anorexia and weight loss associated with shortness of breath. Ct scan revealed speculated nodular lesion left upper lobe. CT guided biopsy which showed Squamous Cell Carcinoma poorly differentiated. Patient underwent exploratory thoracotomy with left lobectomy. Metastatic work up such as Bone scan and Ct scan of the abdomen were negative for metastatic spread. Histopathology of tumor specimen revealed a combined tumor: Large cell carcinoma with focal neuroendocrine differentiation (CEA negative and NSE positive. Adenocarcinoma moderately differentiated (CEA positive and NSE negative, Mucicarmine positive).
Discussion Large cell neuroendocrine carcinoma (LNEC) is a rare and aggressive neoplasm of lung with a very poor prognosis. It accounts for approximately 1.6 to 3.1% of all lung cancers. Overall incidence of Large cell neuroendocrine carcinoma (LNEC) ranges from 2.1 to 3.1% as reported in case series and even presents with a smaller percentage for the mixed or combined type. Chest pain is the most common presentation. Local data of its true incidence is unknown since there is no existing registry for such tumors. Immunohistochemistry is seldom routinely performed in other institutions. Thus, after an intensive search no prior study was found.
Conclusion Diagnosis of LCNEC is often difficult, and requires histological analysis, cytological evaluation and immunohistochemistry. Prognosis of LCNEC is poor, the 5 year overall survival rate for LCNEC at 27% and 21%, Treatment is similar to small cell carcinoma however no standard adjuvant therapy regimen has been developed.

PS018

CHEMOTHERAPY FOR NON-SMALL CELL LUNG CANCER IN PATIENTS WITH LONG-TERM OXYGEN THERAPY

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Background and Aim of Study Chemotherapy for non-small cell lung cancer with chronic respiratory failure lacks evidence. OS with best supportive care (BSC) is 4.5 months and 3.2 months in patients with advanced NSCLC and with recurrent NSCLC, respectively.
Methods We retrospectively analyzed the efficacy and safety of the chemotherapy in the non-small cell lung cancer patients with chronic respiratory failure at Yokohama City University Medical Center from January 2010 to December 2012.
Results Five non-small cell lung cancer patients with chronic respiratory failure (three of which with unresectable lung cancer and two with postoperative recurrent lung cancer) underwent chemotherapy. All patients received chemotherapy including taxane agents in first line chemotherapy. One partial response and one stable disease were achieved with first line chemotherapy. Median overall survival was 317 days and 239 days in patients with unresecatble lung cancer and recurrent lung cancer, respectively. Grade 3 lung infection occurred in 4 patients during chemotherapy treatments, but there was no chemotherapy related death.
Conclusion Our study suggests that chemotherapy in non-small cell lung cancer patients with chronic respiratory failure might improve survival.

PS019

RETROSPECTIVE ANALYSIS OF THE EFFECT OF CHEMOTHERAPY IN PATIENTS WITH RECURRENT NSCLC AFTER THE FIRST LINE CHEMORADIOTHERAPY OR CURATIVE RADIOTHERAPY

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Background and Aim of Study There are only few reports concerning about the effect of chemotherapy against the recurrence after 1st line chemoradiotherapy or curative radiotherapy in patients with locally-advanced non-small-cell lung cancer (NSCLC).
Method We retrospectively analyzed 17 patients, who were diagnosed as NSCLC from April 2007 to December 2012, received chemoradiotherapy or curative radiotherapy as 1st line, had recurrence and received cytotoxic chemotherapy as 2nd line treatment.
Results Patient's background was as follows. Median age: 66 years (range 53 to 78), male/female: 14/3, Ad/Sq/AdSq: 6/10/1. Received 2nd line regimens were CBDCA+PEM/CDDP+PEM+Bev/platinum+GEM/DOC/DOC+S-1/CBDCA+S-1(1/1/3/8/3/1), respectively. Response rate was 17.6%(3/17), and progression free survival was 3.0 months. On the other hand, the response rate of 8 patients who had recurrence in the radiation field was 0%.
Conslusion These results suggest that recurrence in the irradiated field might be refractory to 2nd line chemotherapy.

PS020

EVALUATION OF SOCIAL NICOTINE DEPENDENCE USING THE KANO TEST FOR SOCIAL NICOTINE DEPENDENCE (KTSND-K) IN PATIENTS WITH LUNG CANCER

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Background and Aim of Study Smoking is recognized as nicotine dependence, which consists of physical and psychosocial dependence. To evaluate social nicotine dependence, the Kano Test for Social Nicotine Dependence (KTSND) working group developed a questionnaire. However, there was no data obtained relating to lung cancer cases from the questionnaire given. We examined the social nicotine dependence among lung cancer patients.
Methods We applied Korean version of KTSND(KTSND-K) to 120 patients with lung cancer, and analyzed a complete data from all of them. Among 120 patients, 100 data were obtained from patients just after their initial diagnosis of lung cancer, and 20 data were from patients before their diagnosis of lung cancer and after their first cancer treatment, respectively.
Results Among the respondents, males were 67.8%. Current smokers, ex-smokers, and never-smokers were 24%, 47%, and 29% respectively. The average KTSND-K score of 100 patients after their initial diagnosis was 12.2 ± 4.7. According to smoking status, the total KTSND-K scores of current smokers were significantly higher than those of ex-smokers, and of never-smokers (13.8 ± 5.4 versus 12.0 ± 5.5, and 10.5 ± 5.5, $p < 0.001$). The total KTSND-K scores of males were higher than those of females (12.7 ± 5.7 and 11.0 ± 5.4, respectively, $p < 0.05$). According to the status of the diagnosis and treatment, the total KTSND-K scores of 20 patients before diagnosis were significantly higher than those after their initial treatment (18.7 ± 4.7 and 7.9 ± 4.4, respectively, $p < 0.001$). The mean changes of KTSND-K scores of current smokers and ex-smokers after their cancer treatment were significantly larger than those of never-smokers (12.5 ± 3.4 and 13.0 ± 4.5, versus 6.5 ± 3.5, $p < 0.001$).
Conclusion Our study suggested that the KTSND-K questionnaire could be a useful method to evaluate psychosocial aspects of smoking to patients with lung cancer and that it would be useful for lung cancer prevention program.

PS021

THE ADMINISTRATION OF BEVACIZUMAB FOR NON-SQUAMOUS NON-SMALL CELL LUNG CANCER PATIENTS WITH BRAIN METASTASES

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Background Bevacizumab (BEV) has been shown to be effective in the chemotherapy of non-squamous non-small cell lung cancer (NSCLC). In Japan, the administration of BEV for non-squamous NSCLC patients with brain metastases was thought to be contraindication. However, the administration of BEV to those with brain metastases has been shown to be safe from the analysis of clinical trials overseas, which terminated the Japanese policy of contraindication.
Objective We retrospectively investigated the efficacy and safety of BEV administration for non-squamous NSCLC patients with brain metastases.
Result Nine cases from January 2010 to May 2012 were analyzed. The patients consist of six men and three women. The median age was 68. Histology showed seven adenocarcinoma and two NSCLCs. Five patients underwent gamma-knife surgery and one patient had whole brain radiation therapy, while three had no specific therapy for the brain metastases. Six cases could be evaluated for the efficacy of BEV; 4 partial response, 1 stable disease, and 1 progressive disease. There was no any central nervous hemorrhage.
Conclusion The administration of BEV for non-squmous NSCLC patients with brain metastase was safe and effective.

PS022

EFFICACY AND SAFETY OF CHEMOTHERAPY CONTAINING BEVACIZUMAB IN PATIENTS WITH NON-SMALL CELL LUNG CANCER WITH MALIGNANT PLEURAL EFFUSION

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Background The malignant pleural effusion indicates not only poor prognosis but also impairment of their quality of life (QOL) for patients with non-small cell lung cancer. It has been considered that acceleration of vascular permeability caused by vascular endothelial growth factor (VEGF) produced by cancer cells may be cause of malignant pleural effusion formation. The aim of this study is to evaluate efficacy and safety of bevacizumab, an anti-VEGF antibody, containing chemotherapy in patients with non-small cell lung cancer with malignant pleural effusion.
Method We retrospectively evaluated 15 patients with non-small cell lung cancer with malignant pleural effusion, who received bevacizumab containing platina doublet from April 2010 to June 2013.
Results The male/female ratio was 12/3, the median age was 67 (57–76), PS0/1/2 were 1/11/3, given chemotherapeutic regimens were Carboplatin (CBDCA) + Paclitaxel/Carboplatin (CBDCA) + Pemetrexed (PEM): 12/3, respectively. Median progression-free survival (PFS) was 10.8 months, while overall survival was 13.7 months. By RECIST criteria, complete response (CR)/partial response (PR)/stable disease (SD)/progressive disease (PD) were1/7/6/1, respectively. The response rate and disease control rate was 53.3% and 93.3%, respectively. Efficacy of chemotherapy to malignant effusion was as follows: 1 CR, 6 effective and 2 no effective among 9 patients who were treated with chemotherapy without drainage. The median time of re-accumulation of malignant pleural effusion after reduction or elimination was 7 months. Among all toxicities greater than 3, neutropenia was the most frequently observed.
Conclusion Chemotherapy containing bevacizumab appears to be effective in the patients with non-small cell lung cancer having malignant pleural effusion.

1-A3: CLINICAL RESPIRATORY MEDICINE 1

PS023

ONCE-DAILY TIOTROPIUM AS ADD-ON TO ICS + LABA FOR PATIENTS WITH SEVERE SYMPTOMATIC ASTHMA: BASELINE CHARACTERISTICS IN JAPANESE PATIENTS

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Background and Aim of Study Two international, replicate, double-blind, parallel-group studies (NCT00772538, NCT00776984) demonstrated that once-daily 5 μg tiotropium (via Respimat® Soft Mist™ Inhaler) for 48 weeks, as add-on to ICS + LABA, improves lung function and reduces exacerbation risk in patients with symptomatic asthma. Pre-planned subgroup analyses were performed in Japanese patients for regulatory purposes.
Methods Inclusion criteria: 18–75 years; asthma diagnosed before age 40 years; asthma for ≥5 years; ACQ-7 score ≥1.5; post-bronchodilator $FEV_1 \leq 80\%$; non-smoker/ex-smoker (<10 pack-years); ≥1 exacerbation in previous year; ICS + LABA for ≥4 weeks pre-screening. Exclusion criterion: COPD/other lung diseases. Co-primary end points: study medication effect on lung function and exacerbations.
Results Of 912 randomised patients, 65 were Japanese. A higher proportion of Japanese patients were female (73.8%) and mean BMI (24.0 kg/m^2) was lower than in the total study population (60.4% and 28.2 kg/m^2, respectively). Mean age (56.5 versus 53.0 years), smoking history (4.5 versus 5.1 pack-years) and lung function (FEV_1/FVC: 55.2% versus 57.8%) at baseline were comparable between Japanese and total populations. A greater percentage of Japanese patients received oral glucocorticosteroids (41.5%), leukotriene modifiers (66.2%) and omalizumab (15.4%) within 3 months before screening versus total population (16.9%, 22.3% and 3.9%, respectively). In the overall population, tiotropium improved peak and trough FEV_1 (trial 1: 86 ± 34 mL and 88 ± 31 mL, respectively; trial 2, 154 ± 32 mL and 111 ± 30 mL, respectively) and time to first severe exacerbation (21% risk reduction; hazard ratio 0.79; $P = 0.03$) versus placebo. Adverse events were similar across treatment groups within total population.
Conclusion Add-on tiotropium (5 μg) to ICS + LABA can improve lung function and exacerbation rates in patients with severe symptomatic asthma. As expected, some differences at baseline were observed between Japanese and overall study population. Observed variations in concurrent medication before screening between Japanese subset and total population may reflect differences in treatment guidelines.

PS024

SEF CLASSIFICATION FOR COPD MANAGEMENT

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Introduction Chronic Obstructive Pulmonary Disease (COPD) is a burden for both developed and developing countries. Prevalence of COPD in Bangladesh is 4.32%. The primary outcome of therapeutic intervention is measurement of FEV1 but this has several limitations. GOLD classification is based on FEV1 and categorized the patient as mild, moderate, severe and very severe COPD. Considering limitations of FEV1, a new staging and management of COPD is formulated which is based on symptoms (S) frequency of exacerbations (E) and Function (Lung Function = FEV1) and depending on these three parameters, SEF (symptom, exacerbation and Function) classification has been made. According to SEF classification, COPD patients are dividing into four stages on the basis of FEV1 and each stage is again sub-classified on the basis of symptoms (a) and exacerbation (b).
Methodology SEF trial of COPD was conducted from July 2011 to December 2012. It was a prospective case control; cross over trial over one year period.
Results We recruited 153 as control patients in SEF Study. 12 patients excluded from case series as investigation demonstrated primary disease was not COPD. 111 (72.6%) patient responded to treatment and 27 (17.6%) patient not responded to treatment and 3 (2.0%) patient died during treatment 1 patient died due to cerebral stroke, 1 patient died due to taking treatment of Osteoporosis after infusion of Zolendronic Acid and died due to high fever and respiratory failure in ICU 2 days after infusion and 1 patient died due to Exacerbation of COPD in ICU of NIDCH.
Conclusion SEF classification may be an effective tool that it can be a good guide for a Generalist and Pulmonologist to optimize selection of Medicine in COPD Patient. But needs further study to validate the outcome.

PS025

TO STUDY ATTITUDES, BELIEFS, AND PERCEPTIONS REGARDING USE OF INHALERS AMONG CHRONIC PULMONARY DISEASES PATIENTS AND GENERAL POPULATION IN PUNJAB

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Introduction Effectiveness of inhaled drugs depends on the patient's ability to use the inhaler device correctly and adherence to treatment is influenced by their opinions and feelings about therapy.
Aims & Objectives This study was undertaken as there are paucity of studies investigating attitudes, beliefs and perceptions about use of inhalers in chronic pulmonary disease patients and general population.
Methods A questionnaire was constructed and answers were sought during interviews with first contact patients and general public. We studied 1276 patients and 1832 people from general population.
Results 15.1% patients and 17.2% of population considered inhalers as preferred mode of therapy. 86.8% patients and 84.2% people considered inhalers use as social stigma. 90.7% patients and 92.4% people prefer oral medication over inhalers. 89.5% patients and 87.8% people felt inhibition using inhalers in public with 91.6% patients and 93.3% people preferred to keep it a secret. Most patients (95.5%) and people (97.5%) preferred a smaller device and 96.7% patents and 94.2% population preferred single dose inhalers. Misconception that inhalers are use for serious disorder was quite common among patients (84.9%) and (82.6%) common people. 79.6% patients and 75.9% people thought that once inhalers are started, have to be taken life long. Males, literate and urban patients and common people faired better on the awareness scale.
Conclusion Results highlighted misplace beliefs, attitudes and perceptions about inhalers among majority of patients and common population which is definitely inhibiting proper utilization of inhaler therapy and necessitates individual and collective national educative effort to dispel the misconception and inadequate knowledge.

PS026

IMPLICATIONS OF USING THE PHILIPPINE COLLEGE OF CHEST PHYSICIANS (PCCP) CONSENSUS STATEMENT ON THE PERFORMANCE AND REPORTING OF SPIROMETRY TESTING

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Background The recently launched PCCP Consensus Statement on the Performance and Reporting of Spirometry Testing advocates the use of statistically derived lower limit of normality (LLN) in interpreting spirometry tests as recommended by the ATS/ESR task force on standardization of lung function testing. Previous to the implementation of this method, the fixed value of .70 for FEV/FVC ratio and .80 for FVC was used as the cut-off for normality in this institution.
Objective The aim of this study is to determine the diagnostic and interpretative consequences of adopting the PCCP recommendation.
Methods Spirometry reports from the time that the PCCP recommendation was implemented in our institution (December 2012) up to May 2013 were reviewed. We interpreted the spirometric data using the LLN and the fixed cut-off value. The tests were classified as follows: normal, obstructive, restrictive, combined, and obstructive with probable restrictive (where TLC is not available).
Results A total of 445 spirometry results were reviewed. 113 were discordant. Out of this, 81 (72%) were interpreted as normal using the LLN. When the fixed cut-off value was used, these were interpreted as follows: 18 – obstructive, 49 – restrictive, 1 – combined, 13 – obstructive with probable restrictive. 18 (16%) were interpreted as restrictive using the LLN. Using the fixed cut-off value, these were interpreted as follows: 1 – normal, 5 – combined, 13 – obstructive with probable restrictive. The age range where spirometry interpretations were discordant was between 38–80.
Conclusion Using the statistically derived LLN resulted in less finding of abnormal spirometry and less diagnosis of COPD. This concurred with previous observations that using the fixed cut-off value had the tendency towards false-positive results and over diagnosis of COPD. Additional studies are recommended to find out whether using the LLN decreases the sensitivity of spirometry in diagnosing pulmonary diseases.

PS027

PREDICTORS OF MORTALITY FOR ADULT MEDICAL EMERGENCY PATIENTS WITH PNEUMONIA IN INDONESIA

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Background and Aim of Study Patients with pneumonia in Indonesia has a different characteristic with others. Most of the patients come with multiple and complicated diagnosis. We investigated the predictors of mortality for adult medical emergency patients with pneumonia who admitted to Emergency Room of Cipto Mangunkusumo Hospital (CMH), a tertiary referral hospital in Indonesia.
Methods A prospective cohort study was performed on adult patients with pneumonia in Emergency Room of CMH between October and December 2012. We identified age above 65 years old, sex male, presence of health care associated pneumonia or hospital acquired pneumonia, vital signs at admission (blood pressure, heart rate, respiratory rate, temperature, peripheral oxygen saturation, Glasgow coma scale), admission laboratory results (hemoglobin, leukocyte count, platelet count, urea, creatinine, blood glucose, sodium, potassium) as predictors for mortality. Outcome was assessed when the patients were discharge from the hospital (alive or dead). Univarate analysis was done with Chi-square test. Variables with p value less than 0.25 were analyzed further with multiple logistic regression.
Results A total of 261 patients with pneumonia attended during the study. In-hospital mortality was observed in 82 patients (31.4%). After univariate and multiple logistic regression analysis was done, we found that Glasgow coma scale below 12, urea above 60 mg/dL, heart rate above 110 bpm, peripheral oxygen saturation below 92%, and sepsis were the predictors for mortality with adjusted OR 5.2 (95% CI 1.85 to 14.46), 3.1 (95% CI 1.33 to 7.30), 2.8 (95% CI 1.49 to 5.40), 2.6 (95% CI 1.14 to 6.06), and 2.6 (95% CI 1.40 to 4.86), respectively.
Conclusions In Indonesia we found that loss of consciousness, uremia, tachycardia, low peripheral oxygen saturation, and sepsis were the independent predictors for mortality in adult patients with pneumonia.
Key Words Pneumonia, predictors of mortality.

PS028

COMPARISON OF CLINICAL EFFICACY BY RESPIMAT AND HANDIHALAR OF TIOTROPIUM BROMIDE HYDRATE IN PATIENTS WITH COPD

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Aim We compared some clinical effects by using Respimat (RMT) and Handi halar (HH) of tiotropium bromide hydrate (TIO) against patients with COPD.
Subjects HH group: 18 patients with COPD (mean age 70 y. Male: 14, Female: 4, stage1:9, stage2:4, stage3:5). RMT group: 17 patients with COPD (mean age 67 y. Male: 16, Female: 1, stage 1:7, stage 2:7, stage 3:3). All subjects had past smoking history, five of group HH and five of RMT group were current smokers.
Methods Subjects were administered HH (18 umg) or RMT (5 umg) of TIO, and then their symptoms (1.number of cough, 2.volume of sputum, 3.degree of dyspnea, 4.awaking times by cough or sputum during sleep) were assessed by questionnaire before and after the administration for one month.
Results In HH group, there were improvement of 14 patients (78%), no change of 3 patients (17%) and worse of one patient (6%) in total evaluation. Numbers of cough significantly decreased average 2.4 to 1.7 points, volume of sputum significantly reduced average 2.4 to 1.8 points, degree of dyspnea significantly improved 3.9 to 3.5 points, awaking times during sleep decreased average 1.6 to 1.5 points but no significant. In RMT group, there were improvement of 11 patients (65%), no change of 5 patients (29%) and worse of one patient (6%) in total evaluation. Numbers of cough significantly decreased average 1.8 to 1.4 points, volume of sputum significantly reduced 1.9 to 1.4 points, degree of dyspnea significantly improved 2.9 to 2.3 points, awaking times during sleep significantly decreased average 1.5 to 1.1 points. No adverse events were observed in both devices.
Consideration TIO has clinical excellent effects, especially for improvement of dyspnea. And it's interested the volume of sputum reduced as same as cough. RMT was significantly less than HH in awaking times during sleep.

PS029

PROSTACYCLIN AND COUGH IN PATIENTS WITH SINOBRONCHIAL SYNDROME

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Background Sinobronchial syndrome is a major cause of chronic productive cough. Inflammatory mediators are involved in the pathophysiology of chronic productive cough. Accumulating evidences indicate that prostanoids are key elements in the pathophysiological process of a number of inflammatory disorders. However, little is known about the role of prostacyclin in chronic productive cough in patients with sinobronchial syndrome known as neutrophilic bronchial inflammation.
Methods The effect of beraprost, a chemically and biologically stable analogue of prostacyclin, on cough response to inhaled capsaicin was examined in 14 patients with sinobronchial syndrome in a randomized, placebo-controlled cross over study. Capsaicin cough threshold, defined as the lowest concentration of capsaicin eliciting five or more coughs, was measured as an index of airway cough reflex sensitivity.
Results The cough threshold was significantly ($p < 0.05$) increased after two-week treatment with prostacyclin (80 μg twice a day orally) compared with placebo [24.4 (GSEM 1.3) vs. 12.2 (GSEM 1.5) μM].
Conclusions These findings clearly indicate that prostacyclin increases cough reflex sensitivity of patients with sinobronchial syndrome, suggesting that inhibition of prostacyclin may be a novel therapeutic option for patients with sinobronchial syndrome.

PS030

CYCLOOXYGENASE -2 AND COUGH IN PATIENTS WITH SINOBRONCHIAL SYNDROME

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Background Sinobronchial syndrome is a cause of chronic productive cough. Inflammatory mediators are involved in the pathophysiology of chronic productive cough. Accumulating evidences indicate that cyclooxygenase2, one of the inducible isoforms of cyclooxygenase is a key element in the pathophysiological process of a number of inflammatory disorders. However, little is known about the role of cyclooxygenase2 in chronic productive cough in patients with sinobronchial syndrome known as neutrophilic bronchial inflammation.
Methods The effect of etodolac, a potent cyclooxygenase2 inhibitor, on cough response to inhaled capsaicin was examined in 15 patients with sinobronchial syndrome in a randomized, placebo-controlled cross-over study. Capsaicin cough threshold, defined as the lowest concentration of capsaicin eliciting five or more coughs, was measured as an index of airway cough reflex sensitivity.
Results The cough threshold was significantly ($p < 0.03$) increased after two-week treatment with etodolac (200 mg twice a day orally) compared with placebo [37.5 (GSEM 1.3) vs. 27.2 (GSEM 1.3) μM].
Conclusions These findings indicate that cyclooxygenase -2 may be a possible modulator augmenting airway cough reflex sensitivity in patients with sinobronchial syndrome.

PS031

CYCLOOXYGENASE -2 AND COUGH IN PATIENTS WITH BRONCHIAL ASTHMA

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Background Cyclooxygenase is the enzyme for the conversion of arachidonic acid to prostanoids. There are two isoforms of cyclooxygenase, namely cyclooxygenase -1 and cyclooxygenase2. Cyclooxygenase2 is highly inducible by several stimuli and is associated with inflammation. Recent studies revealed that cyclooxygenase2 is upregulated in the airway epithelium of asthmatic patients. However, little is known about the role of Cyclooxygenase2 in cough, a common symptom of bronchial asthma. This study was designed to investigate the role of Cyclooxygenase2 on cough reflex sensitivity in patients with bronchial asthma.
Methods The effect of etodolac, a potent cyclooxygenase2 inhibitor, on cough response to inhaled capsaicin was examined in 17 patients with stable asthma in a randomized, placebo-controlled cross-over study. Capsaicin cough threshold, defined as the lowest concentration of capsaicin eliciting five or more coughs, was measured as an index of airway cough reflex sensitivity.
Results The cough threshold was significantly ($p < 0.02$) increased after two-week treatment with etodolac (200 mg twice a day orally) compared with placebo [36.7 (GSEM 1.2) vs. 21.6 (GSEM 1.2) μM].
Conclusions These findings indicate that cyclooxygenase2 may be a possible modulator augmenting airway cough reflex sensitivity in asthmatic airway.

PS032

PROSTAGLANDIN E1 AND COUGH IN PATIENTS WITH BRONCHIAL ASTHMA

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Inflammatory mediators are involved in the pathogenesis of airway inflammation. However, it has not been fully discussed about the role of prostaglandin E1 (PGE1) in cough, a common symptom of bronchial asthma. The effect of limaprost, a PGE1 anlogue, on cough response to inhaled capsaicin was examined in 21 patients with stable bronchial asthma in a randomized, placebo-controlled cross-over study. Capsaicin cough threshold, defined as the lowest concentration of capsaicin eliciting five or more coughs, was measured as an index of airway cough reflex sensitivity. The cough threshold did not change after two-week treatment with limaprost (30 μg 3 times a day orally) compared with placebo. These findings indicate that PGE1 does not affect airway cough reflex sensitivity in asthmatic airway.

1-A4: CLINICAL RESPIRATORY MEDICINE 2

PS033

COMPARING APPLES WITH APPLES. CLINICO-RADIOLOGICAL DIAGNOSIS OF MULTIPLE CYSTIC LUNG DISEASES

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Characteristic HRCT findings of six patients with multiplc cystic lung disease (MCLD) is presented, which in the presence of supportive investigations can help in establishing the diagnosis and may obviate the need for lung biopsy. Case 1: Lymphangioleiomyomatosis: A 48 years old non smoker house wife on HRCT chest had multiple variable sized thin walled cysts distributed uniformly throughout lung fields from apices to bases with intervening normal lung parenchyma and a right sided loculated pneumothorax. Case 2: Idiopathic Pulmonary Fibrosis: A 70 years old male with IPF on HRCT chest had temporally heterogenous linear infiltrates of fibrotic foci and honey comb cysts of variable sizes located predominantly in peripheral lung regions especially in lower lobes. Case 3: Alpha-1 Antitrypsin Deficiency Emphysema: A 35 years old non smoker male's HRCT showing widespread hypoattenuating spaces with very thin/barely visible walls (especially in lower lobes) due to loss of lung parenchyma and decreased vascularity with apparently preserved upper lobes attenuation. Case 4: Emphysema due to Tobacco Smoking: A 59 years old COPD patient on HRCT chest revealed centrilobular lesions of low attenuation of variable sizes with very thin walls having predominant location in upper lobes consistent with centrilobular emphysema. Case 5. Lymphoid Interstitial Pneumonia: A 45 years old male having Sjogren's syndrome on HRCT chest showed cysts with well defined walls having random distribution with predominant involvement of central portions of lungs mostly involving upper lobes especially on the right side with interspersed normal lung parenchyma. Case 6: Advanced Cystic Bronchiectasis: A 36 years old never smoker male with advanced bronchiectasis on HRCT chest had extensive cylindrical, varicose and cystic bronchiectasis involving all lobes.

PS034

MULTIPLE MYELOMA EXTRAMEDULLARY INFILTRATION MISTAKEN FOR TUBERCULOUS PLEURISY: A CASE REPORT AND REVIEW OF LITERATURE

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Objective To discuss the clinical and pathological characters of multiple myeloma extramedullary infiltration and improve the understanding of the diagnose method of this kind of diseases.
Methods A case of multiple myeloma diagnosed in May 2013 was reported and the related literatures were reviewed.
Results A case of a 53 year-old male patient, who had been misdiagnosed as tuberculous pleursy in local hospital, was admitted to our hospital because of fever, night sweat and short of breath for half a year and aggravated for half a month. After admission, the bone marrow aspiration biopsy showed: hyperplasia of original plasma cells (1.5%) and active hyperplasia of naive plasma cells (15.5%). The pleura biopsy of right side confirmed abnormal proliferation of plasmocytes. Accordingly to the pathological and immunohistochemistry test, it was definitely diagnosed as multiple myeloma extramedullary infiltration.
Conclusions Multiple myeloma extramedullary infiltration rarely occur in pleural, and is easy to be misdiagnosed as tuberculous pleurisy because of similar clinical characters. To make a dedinite diagnosis is rely on the histopathology of bone marrow and pleura biopsy. If we met such patients clinically without clear evidence of tuberculous, case history should be carefully asked. While we giving diagnostic therapy of tuberculous, we should try to find other possible causes at the same time, give thoracoscopy as early as possible, to give timely diagnose and avoid conditions delay of patients.

PS035

PULMONARY MASS-LIKE OPACITIES SECONDARY TO ACUTE HYPERSENSITIVITY PNEUMONITIS IN A PATIENT WITH CHRONIC GRANULOMATOUS DISEASE

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Chronic granulomatous disease (CGD) is a hereditary disease, characterized by failure of phagocytic cells due to defects of nicotinamide adenine dinucleotide phosphate reactive oxygen spicies (NADPH-ROS) production and inability of bacterial killing, which leads to recurrent life-threatening infections. The mechanism for granuloma formation remains unclear, however, a significant subset of patients with CGD have noninfectious inflammatory problems, which might be caused by excessive activation of cytokine production pathway due to loss of NADPH-ROS production. A 20-year-old man, who diagnosed as X-linked recessive CGD at 1 year old age and lacks gp^{91phox}, developed CGD-related colitis and started to be treated with prednisone 45 mg/day. After seven months, taking 7.5 mg/day of prednisone, chest CT revealed diffuse bilateral centrilobular nodules and multiple mass lesions in both lungs, followed by nonproductive cough. These lesions were not responsive to either antibiotics or antifungals, and serum KL-6 turned out to be as high as 4600 U/ml. Transbronchial lung biopsy showed small, loose-formed, non-necrotizing granuloma with giant cells, which led the diagnosis of acute hypersensitivity pneumonitis. The levels of IL-6, IL-8, TNF-α of broncho-alveolar lavage fluid were increased, which might suggest activated T cell caused excess immunological response. Even after 1 month treatment with avoiding environmental antigens, centrilobular nodules still existed and mass lesions got enlarged. Finally, video-assisted thoracic surgery was performed to exclude infectious or neoplastic disease. In addition to the pathological findings with TBLB, the specimen showed that mass-like lesions were consisted from massive granuloma both in airway and lymph tract due to excessive reaction to antigen and poor drainage of those reactions. After the treatment with high-dose prednisone, the centrilobular nodules disappeared, mass lesions shrank, and serum KL-6 also decreased to normal range.

PS036

THE MAGIC IN PREGNANCY

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MAGIC syndrome (Mouth and Genital ulcers with Inflamed Cartilage) was first described by Firestein in 1985. It is thought to be a combination of Relapsing Polychondritis and Behcet Disease. Since then there were few cases published. We describe a young female who presented with severe disease necessitating tracheotomy during pregnancy and discuss the management, followed by review of the literature. A 33 years old Jordanian female attended our ENT clinic for assessment of hoarseness of voice and cough. She had repeated attacks of hoarseness of voice and difficulty of breathing in the past for which she responded to oral steroids. No definite diagnosis was given to the patient although asthma was suggested. In the ENT clinic examination then showed airway inflammation and crusting and so impression of Rhinoscleroma was made and she was found to be pregnant her steroids were stopped. She presented after 1 week with upper airway obstruction which necessitated emergency tracheotomy. Review of her history revealed recurrent mouth & genital ulcers & difficult intubation in the past during her LSCS. Blood investigations revealed ESR 60, CRP 0.1, negative ANA, RF & ANCA. Analysis for HLA B51 and HLA B52 was negative. Radiology and bronchoscopy showed significant subglottic stenosis. Bronchoscopy & tissue biopsy confirmed the presence of an inflamed cartilage. Patient was managed with steroids and Azathioprine. After delivery of her child she was reassessed, tracheostomy capped and she had undergone dilation of the stenosed segment. MAGIC syndrome is a rare disease and even challenging when it presents in pregnancy. Despite reports of abortion and premature birth but the patient was critical and given Azathioprine without complications. The long term outcomes are not clear due to paucity of data. Our patient has improved steadily. This is the first case of MAGIC syndrome diagnosed and managed during pregnancy.

PS037

THE LUNG IN CONNECTIVE TISSUE DISORDERS: A HOSPITAL BASED PREVALENCE STUDY WITH CLINICAL AND RADIOLOGICAL ANALYSIS OF CASES

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Background and Aim of Study Pulmonary manifestations occur commonly in patients with Connective tissue disorders (CTDs) but few Indian studies have documented it. The aim was to analyse the clinical and radiological profiles of diagnosed Connective tissue diseases (CTD) cases presenting with respiratory symptoms to a tertiary care hospital and calculate prevalence of respiratory disorders present in them.
Methods Patients with Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc), Ankylosing Spondylitis (AS), Mixed Connective Tissue Diseases (MCTD) and Sjogren's syndrome (SS) were recruited for the study over a span of four months. Forty patients presenting with respiratory symptoms were evaluated.
Results The median duration of CTD was 15 years and that of respiratory symptoms was 2 years. 12.5% of the Chest radiographs (CXRs) were normal whereas no Computed Tomogram (CT) was. The common findings of CT Chest were ground glass haze and reticular shadows. Consolidation was seen in 20%. Restriction on Pulmonary function test (PFT) was seen in 55% of the cases and small airway disease in 35%. The prevalence of Interstitial lung disease (ILD) was 85% making it the most common respiratory involvement. All cases of SLE and MCTD cases had features of ILD and the prevalence in RA was 89.5% and in SSc 91.7%. 60% of all cases had evidence of pulmonary arterial hypertension (PAH). All patients of MCTD and SLE, 83% of SSc and 42% of RA had PAH.20% of all cases had evidence of infective pneumonia.
Conclusions ILD is the most prevalent disorder of the respiratory system in CTD patients followed by PAH and pneumonia. Respiratory involvement in CTDs is frequent and severe. Since HRCT and PFT are sensitive for diagnosis of ILD, they may be recommended to screen patients of CTDs for possible respiratory involvement.

PS038

THE PROFILE AND SURVIVAL OF SUPERIOR VENA CAVA SYNDROME PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL AND DHARMAIS CANCER HOSPITAL

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Background and Aim of Study Superior vena cava syndrome (SVCS) is a collection of symptoms of superior vena cava due to suppression by the masses in the superior mediastinum and is a medical emergency that needs to be managed immediately. Assessment profiles and survival rate is important in determining the treatment of SVCS patients. The aim of this study is to obtain the profile and survival rate of SVCS patients in Mangunkusomo Cipto Hospital and Dharmais Cancer Hospital.
Methods A cohort restrospective design was conducted in SVCS patients during January 2000 to December 2011 in Mangunkusomo Cipto Hospital and Dharmais Cancer Hospital.
Results The study population was composed 151 study subjects and most of them were male sex (76.2%), 18 to 60 years old (76.8%), the economic status was private financing (51.7%). Type of primary tumor were lung tumor (52.3%). The most frequent signs and symptoms were dyspnea (84,1%), cough (68,2%) and face or neck swelling (12%). Many study subjects presented with a moderate SVCS grade (60.3%). Based on survival rate-analysis, there were several factors that showed significant differences in survival rate, the economic status ($p = 0.021$), SVCS grade ($p = 0.006$), pneumonia ($p = 0.013$), and type of primary tumor ($p = 0.03$).
Conclusion The most SVCS patients are males, age range 18–60 years old, lung tumor, having dyspnea and a moderate SVCS grade. Economic status, SVCS grade, pneumonia, and the type of primary tumor, play a role in survival rate of SVCS patients. Such factors should be considered in decision making for treatment of SVCS patients.
Key Words Superior Vena Cava Syndrome, survival.

PS039

CHARACTERISTICS AND 90 DAYS SURVIVAL OF SUPERIOR VENA CAVA SYNDROME PATIENTS IN CIPTO MANGUNKUSUMO AND DHARMAIS CANCER HOSPITAL

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Background and Aim of Study Superior vena cava syndrome (SVCS) is a syndrome due to compression or infiltration to superior vena cava and is a medical emergency that needs to be managed immediately. The study of characteristic and survival rate of SVCS patients. is important to determine the diagnosis and treatment. This study aims to obtain the characteristic and 90 days survival rate of SVCS patients in Cipto Mangunkusomo and Dharmais Cancer Hospital.
Methods This is a restrospective cohort study conducted through medical record of SVCS patients during January 2000 to December 2011 in Cipto Mangunkusomo and Dharmais Cancer Hospital.
Results The study population was 151 subjects and most of the patients were male (76.2%). The age of the patient mostly range from 46 to 60 years old (46,3%). Dyspnoe, neck vein distention and facial swelling were the frequent chief complains. The location of the mass based on radiological examination was found mostly in superior mediastinum. Non small cell lung cancer is the most common etiology of SVCS patient. The cumulative survival of SVCS patient in 90 days is 54 %, mean survival was 42.5 (SE 5.2) and the survival rate showed plateau appearance from the day of 60th.
Conclusion Superior Vein Cava Syndrome patients in this study mostly due to non small cell lung cancer, found mostly in males and the age range was 46–60 years old. Dyspnoe, neck vein distention and facial swelling were the frequent chief complains. The cumulative survival of SVCS patient in 90 days is 54 %, mean survival was 42.5 (SE 5.2) and the survival rate showed plateau appearance from the day of 60th.
Key Words Characteristic, superior vena cava syndrome, survival.

PS040

BLACK PLEURAL EFFUSION: CAUSES AND PATHOPHYSIOLOGICAL CLASSIFICATION

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Background Black pleural effusions are extremely rare and have been reported in patients withinfection, malignancy, and hemorrhage. However, no review articles appear to have focused on this rareclinical presentation.
Purpose To classify and characterize diseases causing black pleural effusion based on the pathophysiological mechanisms involved.
Methods We searched the medical literature to find reports of black pleural effusion using the PubMeddatabase.
Results We identified 8 cases and classified the underlying diseases into the following 4 entities basedon pathophysiological conditions: 1) infection (Aspergillus niger and Rhizopus oryzae); 2) malignantmelanoma, in which cells contain melanin pigment; 3) hemorrhage and hemolysis associated withnon-small cell lung cancer or rupture of a pancreatic pseudocyst; and 4) other causes (charcoal-containingempyema). Discrimination between biliopleural fistula and pancreatico-pleural fistula, which also mimicking in color, was easily achieved by focusing on pleural amylase levels, elevation of pleural indirectbilirubin, presence of pleural glycoholic acid, and the predominant site of pleural effusion.
Conclusion Black pleural effusions can be divided into 4 major categories based on the underlyingpathophysiological conditions.

PS041

THE RETROSPECTIVE STUDY OF RE-CHALLENGE MALIGNANT PLEURAL MESOTHELIOMA PATIENTS PREVIOUSLY TREATED WITH PEMETREXED

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Background and Aim of Study Cisplatin (CDDP) and pemetrexed (PEM) chemotherapy is used as 1st-line chemotherapy for malignant pleural mesothelioma (MPM). However 2nd-line chemotherapy has not been established yet. So the establishment of 2nd-line chemotherapy is urgently needed.
Methods In our hospital from 2007 to 2012, we examined 20 re-challenge MPM patients previously treated with PEM and platinum.
Results In these patients, we showed response rate (RR) of 15%, and disease control rate(DCR) of 80%. Furthermore, in 10 patients with partial response at 1st-line chemotherapy among them, we found a RR of 20%, and DCR of 90%.
Conclusion Re-challenge treatment with PEM might be effective in 2nd-line chemotherapy for MPM.

PS042

METASTATIC PULMONARY CALCIFICATION IN CHRONIC KIDNEY DISEASE MIMICKING DIFFUSE ALVEOLAR HEMORRHAGE

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Metastatic pulmonary calcification is a rare disease and characterized by diffuse calcium deposition in the lung is known to occur in patient with chronic renal failure. However, this disease is uncommon and has only been detected in a few patients with severe disorders. A 50-year-old man with chronic kidney disease had progressive dyspnea. A chest radiograph showed poorly defined bilateral multiple nodular opacities in the superior to middle lung fields. An axial computed tomography of the chest showed ground-glass nodular opacity of alveolar pattern with focal consolidation relatively preserved peripheral and lower area. The radiologic images were suggestive of infection and diffuse alveolar hemorrhage. Bronchoscopic bronchoalveolar lavage (BAL) fluid had bloody color fluid and hemosiderin laden macrophages were shown. Before confirm lung biopsy, we treated IV steroid therapy for diffuse alveolar hemorrhage. But, the patient did not improve his symptom. Lung biopsy showed that calcium deposited in the alveolar septa. In addition, 99 mTc bone scintigraphy and SPECT/CT findings showed an intense uptake in both lungs. Finally we diagnosed metastatic pulmonary calcification. There was no calcium disorder in this patient. In contrast to the benign course of pulmonary calcification in most patients, some fulminant pulmonary calcifications complicating chronic kidney disease or hypercalcemia have been described. In chronic kidney disease patient, metastatic pulmonary calcification should be considered in the differential diagnosis of patients presenting with respiratory symptoms or pulmonary lesions in chronic kidney disease, especially combined calcium disorder.

PS044

BETA DEFENSIN-1 EXPRESSION AND GENETIC POLYMORPHISMS IN HUMAN AIRWAY EPITHELIAL CELLS

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Background and Aim of Study Human beta defensin-1 is an antimicrobial peptide expressed in the airway epithelium without help of any inducers. Although many studies have shown that major polymorphisms of *DEFB1* encoding the peptide are conserved and significantly associated with infectious and immune-related disorders, roles of DEFB1 in the pathogenesis are mostly unclear.
Methods Expression levels of mRNA of *DEFB1* were measured by real-time RT-PCR and their protein concentrations were determined by using ELISA. Transcriptional activities of cloned segments containing representative promoter haplotypes were determined in airway epithelial cell lines by using the Dual-Luciferase Reporter Assay System. Airway epithelial cells were stimulated with or without an analog of viral double-stranded RNA, polyinosinic-polycytidylic acid(poly IC).
Results & Conclusion Out of four extended *DEFB1* haplotypes carrying three common polymorphisms in the 5'-untranslated regions, the -44G (rs1800972)-carrying haplotype showed overexpression of the baseline mRNA levels of *DEFB1* in A549 cells and primary cultured cells. PolyIC stimulation significantly enhanced DEFB1 mRNA expression and increased DEFB1 protein concentrations and overrode transcription-promoting effect of the -44G haplotype. *DEFB1* is generally thought to be constitutively expressed in human epithelial cells and some immune cells. In this study, we demonstrated that *DEFB1* promoter genotype was associated with cellular gene expression and that *DEFB1* expression was sensitive to exogenous stimuli such as polyIC irrespective of the genotype. Our data might provide insights into inconsistent results in previous disease association studies and the role for their genetic polymorphisms in the airway mucosa.

1-A5: CELL AND MOLECULAR BIOLOGY 1

PS043

ANTITUMOR ACTIVITY OF COMBINED VEGF AND EGFR INHIBITORS IN XENOGRAFT MODELS OF EGFR INHIBITOR RESISTANCE

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Background and Aim of Study The epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) erlotinib benefits some non-small cell lung cancer (NSCLC) patients, but most do not respond (primary resistance). Vascular endothelial growth factor (VEGF) targeted recombinant humanized monoclonal antibody bevacizumab has been used for many types of cancers such as NSCLC. As EGFR TKI resistance is not completely understood, this study was aimed to investigate whether dual inhibition of VEGF and EFGR pathways overcomes EGFR inhibitor resistance.
Methods Three EGFR wild type NSCLC cell lines H157, H460 and A549 were used to establish the xenograft nude mouse models of primary resistance to erlotinib and agent alone or combination of erlotinib and bevacizumab were used to treat mice in vivo. VEGF levels of these cell lines and human bronchial epithelial cell BEAS-2B (as a control cell line) were assayed in cell supernatant using ELISA. Erlotinib concentration in sera and tumor lysates of xenograft models were determined by High Performance Liquid Chromatography (HPLC).
Results 1) VEGF level of H157 was higher than H460's and A549's was the lowest. 2) In vivo, bevacizumab inhibited tumor growth in H157, H460 and A549 models, and TGI (tumor growth inhibition, %) of A549 was relatively lower than the other two. 3) In H157 and H460 models but not A549 model, combination treatment was more effective than either agent alone. 4) Erlotinib concentrations of serum and tumor samples in combination group were higher in various degrees than erlotinib alone group depending on models.
Conclusion Combined of EGFR and VEGFR blockades might enhance antitumor activity and angiogenesis inhibitor may modulate the tumor vasculature resulting in enhanced delivery of targeted agent to cancer cells depending on VEGF levels of cell lines in NSCLC.

PS045

HYPOXIA INCREASES GEFITINIB-RESISTANT LUNG CANCER STEM CELLS THROUGH THE ACTIVATION OF INSULIN-LIKE GROWTH FACTOR 1 RECEPTOR

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Background and Aim of Study Accumulating evidence indicates that cancer stem cells (CSCs) are involved in intrinsic resistance to cancer treatment. On the other hand, hypoxic microenvironment is an important stem cell niche, and promotes the persistence of CSCs in tumors. The aim of this study is to elucidate the role of hypoxia and CSCs in the resistance to gefitinib in non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) mutation.
Methods NSCLC cell lines, PC9 and HCC827, which express EGFR exon 19 deletion mutations, were exposed with high concentration of gefitinib under the normoxic or hypoxic condition. Seven days after gefitinb exposure, small fraction of viable cells could survive, and these cells were referred to as "gefitinib-resistant persisters" (GRPs). We performed quantitative real time polymerase chain reaction and immunofluoresence to evaluate the expressions of stemness genes and insulin-like growth factor 1 receptor (IGF1R)-related factors.
Results GRPs highly expressed stem cell genes including CD133 and Oct4, and showed the sphere-forming capacity in vitro and high tumorigenic potential in vivo. Expressions of IGF1R-related factors were upregulated and IGF1R was also phosphorylated on GRPs. Importantly, hypoxia promoted the activation of IGF1R on GRPs, and increased sphere-formation and the population of CD133- and Oct4- positive GRPs. Furthermore, knockdown of hypoxia inducible factor-1α(HIF-1α) reduced the number of GRPs with activated IGF1R. Finally, inhibition of IGF1R decreased the CD133- and Oct4- positive GRPs under the hypoxic condition.
Conclusion Hypoxia increased the population of lung CSCs which were resistant to gefitinib in EGFR mutation-positive NSCLC through the activation of IGF1R.

PS046

CHARACTERISTICS OF ALVEOLAR MACROPHAGES FROM MURINE MODEL OF OVA-INDUCED AND LPS-INDUCED AIRWAY INFLAMMATION

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Background and Aim of Study Macrophages are divided into the classically activated pro-inflammatory M1 macrophages (M1), and alternatively activated anti-inflammatory M2 macrophages (M2). M1 phenotype is promoted by Th1 cytokines and Toll-like receptor ligands including lipopolysaccharide (LPS), and has potent pro-inflammatory activity. In contrast, Th2 cytokines promote M2 phenotype that is involved in the immune response to parasites, promotion of tissue remodeling and tumor progression, but they also have immune regulatory functions. Although alveolar macrophage (AM) act as the first line of defense to encounter inhaled particulates and pathogens and play an essential role in the initiation and orchestration of inflammatory responses in the pulmonary immune system, little is known about the subsets of AMs.
Methods We used two well-characterized mouse model of airway inflammation. For allergic airway inflammation model, Balb/c mice were immunized by injection of ovalbumin (OVA) with alum on days 0 and 14, and then challenged by inhalation of aerosolized OVA on days 21, 23, and 25. For acute respiratory distress syndrome (ARDS) model, Balb/c mice were administered intranasally LPS on day 0 and 4. On the day following the last inhalation in both models, bronchoalveolar lavage fluid was collected and differential cell count was performed. The lavage cells were incubated in a culture dish for 2 h to allow attachment. The adherent cells were collected for RT-PCR or flow cytometry that were used to define the phenotype of AMs. The concentrations of the cytokines and chemokines in the culture supernatants of AMs were measured using multiplex bead array assays.
Results and Conclusion Our data show that LPS-induced or OVA-induced airway inflammation promotes the differentiation of airway macrophages towards the M1- or M2- skewed phenotype, respectively. These different characterizations of AM may facilitate their contributions to host defense to the innate and adaptive immune responses.

PS047

ANTIFIBROTIC EFFECTS OF FOCAL ADHESION KINASE INHIBITOR IN BLEOMYCIN-INDUCED PULMONARY FIBROSIS IN MICE

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Background and Aim of Study Focal adhesion kinase (FAK) is a non-receptor tyrosine kinase which mediates cell survival, proliferation, and adhesion. FAK is also known to play an important role in TGF-β dependent myofibroblast differentiation. In this study, we investigated whether the targeted inhibition of FAK by using a specific inhibitor, TAE226, has the potential to regulate pulmonary fibrosis.
Methods The effect of TAE226 on fibroblast proliferation *in vitro* was evaluated by ^{3}H-thymidine deoxyribose incorporation assay. Immunobloting was implemented to assess the expresssion of α-smooth muscle actin (SMA) and collagen I. For *in vivo* experiment, mouse bleomycin-induced pulmonary fibrosis model was employed, and mice were treated with TAE226 by oral administration. The lung sections were analyzed immunohistochemically to assess the antifibrotic effect of TAE226.
Results TAE226 inhibited the proliferation of fibroblasts in response to the stimulation of various growth factors. Expression of α-SMA and collagen I in fibroblasts stimulated with TGF-β was suppressed by TAE226 treatment. The administration of TAE226 *in vivo* ameliorated the histlogical findings of bleomycin-induced pulmonary fibrosis. Immunohistochemical analysis showed that the number of Ki67-positive proliferating mesenchymal cells was decreased in the lungs of TAE226-treated mice. Moreover, the phosphorylation of Tyr397 was observed in fibroblasts and epithelial cells including type II like cells, and TAE226 reduced p-FAK-Tyr397 expression in these cells.
Conclusion These results suggest that FAK signal plays a critical role in the progression of pulmonary fibrosis, and it can become a promising target for the therapeutic approaches to pulmonary fibrosis.

PS048

THE ROLE OF PHOSPHORYLATION SITES OF THE PTEN C-TERMINUS FOR TGFβ-INDUCED TRANSLOCATION OF β-CATENIN IN LUNG CANCER CELLS

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Background Transforming growth factor β(TGFβ)-induced β-catenin translocation into cytoplasm is involved in epithelial-mesenchymal transition(EMT). In this congress, we also show that modulation of phosphorylation sites in the PTEN C-terminus (PTEN4A) inhibits TGFβ-induced EMT via blockade of β-catenin translocation. Nevertheless, how PTEN4A could exert the inhibitory effect on β-catenin translocation remains elusive.
Aim of Study We aimed to illuminate the underlying mechanisms, by using several PTEN constructs with deletion mutants.
Methods We prepared four deletion mutants, including 1) the PTEN C-terminus deletion, 2) the C 2 domain deletion, 3) the phosphatase domain deletion, or 4) both the C 2 domain and phosphatase domain deletion. Thus, we established lung cancer cells with a Dox-dependent gene expression system, in which these mutants were induced only when Dox is added. To evaluate the localization of β-catenin, immunofluorescence and confocal laser scanning microscopy were performed.
Results Immunofluorescence images suggested that the PTEN C-terminus did not appear to directly inhibit TGFβ-induced β-catenin translocation into cytoplasm. We showed that both of the C 2 domain and the phosphatase domain might be essential to block the β-catenin translocation.
Conclusions Inhibition of phosphorylation of the PTEN C-terminus, by which both of the C 2 domain and the phosphatase domain could retain the PTEN phosphatase activity, might blunt TGFβ-induced β-catenin translocation as well as EMT.

PS049

EFFECTS OF OXIDATIVE STRESS AND VITAMIN C ON THE ELECTROLYTE SECRETION IN MOUSE TRACHEAL EPITHELIUM

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Background/Aims We investigated the changes in electrolyte secretion of tracheal epithelium in the mice chronically exposed to normobaric hyperoxia (95% FiO_2, 24 h). Also, the effects of vitamin C and H_2O_2 on the epithelium were tested.
Methods The short-circuit current (Isc) of the epithelium was measured using a flow-type Ussing chamber technique. Na+ absorption via epithelial Na+ channel was evaluated by amiloride-sensitive Isc. Cystic fibrosis transmembrane conductance regulator-mediated, cAMP-dependent Cl- secretion was evoked by forskolin and isobutylmethylxanthine applied to the basolateral side. Ca2+-dependent Cl- secretion was evaluated from transient increase in Isc by luminally applied ATP.
Results In the mice exposed to 95 % FiO_2 for 24 hours, the Isc values measured from the above protocol were not affected. Also, neither H_2O_2 (100 μM) nor vitamin C (300 μM) directly affected the Isc of mouse airway epithelium. Interestingly, in the presence of vitamin C, the forskolin induced Cl- secretion was inhibited.
Conclusions Our results suggest that mouse airway epithelium is relatively resistant to hyperoxic stresses under ambient hyperoxia or directapplication of H_2O_2. An excessive dose of vitamin C suppresses the cAMP dependent Cl- secretion.

PS050

STEROID-INDUCIBLE GENES REGULATE AIRWAY EPITHELIAL BARRIER FUNCTION

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Inhaled corticosteroids are the most potent anti-inflammatory medications for the treatment of asthma. We have reported that corticosteroids have not only anti-inflammatory effects but also enhancement effect of airway epithelial barrier. However, the mechanism by which how corticosteroids enhance airway epithelial barrier function is not well understood. We therefore investigated the global gene expression analysis to identify candidate genes and signaling pathways involved in the enhancement of airway epithelial barrier. 16HBE, human airway epithelial cells were cultured on transwell inserts and exposed to dexamethasone (Dex) for 3 days to enhance barrier function. After measuring barrier function using Trans Electric Resistance (TER), we extracted total RNA from epithelial cells and performed microarray analysis. Gene networks were generated using Ingenuity Pathways Analysis to identify signaling pathways involved in airway epithelial barrier function. To determine steroid-inducible genes we identified involve in airway epithelial barrier function, we transfected 16HBE cells with small interfering RNA (siRNA) targeted to these genes, followed by TER measurements. We identified several steroid-inducible genes involved in processes associated with anti-apoptosis and wound healing on airway epithelial cells. Airway epithelial barrier function was reduced by knock-down of these genes. Our results indicate that steroid-inducible genes we identified can regulate the airway epithelial barrier function. These genes and signaling pathways might be new therapeutic targets for the vulnerability of airway epithelium of asthmatics.

1-A6: CELL AND MOLECULAR BIOLOGY 2

PS051

ABLATION OF CD206+ M2 ALVEOLAR MACROPHAGES EXACERBATES ACUTE LUNG INJURY

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In acute lung injury (ALI), alveolar macrophages are one of the main sources of inflammatory cytokines. Macrophages are highly versatile cells and the local environment factors could shape their phenotypic and functional properties. It is necessary to understand the mechanisms involved in the progression of systemic inflammation and to design treatments to reduce the impact of ALI. The activated macrophages were classified into two groups, the classical activated macrophages (M1) and the alternative activated macrophages (M2). M2 macrophages express the mannose receptor, CD206. In this study we generated a line of transgenic mice expressing human diphtheria toxin (DT) receptor under the control of the CD206 gene promoter. In this transgenic mouse, DT induced systemic ablation of M2. In ALI model with LPS, inflammatory cytokines levels were higher in TG than WT. Histologically, ALI was exacerbated by ablation of M2. Alternative activated macrophages may play a protective role in the development of ALI.

PS052

CURCUMIN FACILITATES INDUCTION OF PHASE II ANTIOXIDANT ENZYMES AIDING PULMONARY SURFACTANT HOMEOSTASIS UNDER HYPOXIA

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Background and Aim of Study Pulmonary surfactant is a surface active lipoprotein formed by Alveolar type II cells, involved in preventing high altitude pulmonary edema. Induction of nuclear factor erythroid 2 p45-related factor (Nrf2) has been shown to decrease oxidative stress through the regulation of specific gene pathways. The association of Nrf2 and surfactant proteins (SP) under hypoxia is not well elucidated. Hence, the present study is aimed to determine the role of phase II antioxidant enzymes in enabling pulmonary surfactant homeostasis under hypoxia.
Methods A549 cells were cultured under hypoxic environments (3%) for different time durations (1 h, 3 h, 6 h, 12 h, 24 h and 48 h). Male SD rats were exposed to hypobaric hypoxia (7620 m, 6 h).
Results A549 cells exposed to different hours of hypoxia showed decrease in SP-A transcript expression from 3 h and remained constant though out the hypoxic exposures. Whereas, SP-B expression was decreased by 3 h and nearly abolished upon further exposures; while SP-C and SP-D expression was increased within 1 h of hypoxic exposure and remained constant till 48 h of hypoxic stress over control. The hypoxia exposure of A549 cells (6 h), showed a significant increase in protein and lipid oxidation along with reduced levels of GSH over control. The curcumin supplementation (10 μM) increased the expressions of Nrf-2 and HO-1 which might have enabled the cells in balanced expression of SPs along with reduced levels of oxidants. Our in vivo data also showed increased lipid peroxidation ($p < 0.001$) and protein oxidation ($p < 0.05$) in bronchoalveolar lavage fluid (BALF) which was significantly attenuated by curcumin administration (50 mg/Kg BW) 1 h prior to hypoxia exposure. The curcumin administration also resulted into decreased lung NFkB with increased expression of Nrf-2 and HO-1, followed by stabilised expression of HIF 1α.
Conclusion Our results indicate that, curcumin facilitates the induction of phase II antioxidant enzymes promoting pulmonary surfactant homeostasis under hypoxia.

PS053

THE EFFECT OF EXOGENOUS PTEN4A INDUCTION ON TGFβ-INDUCED EPITHELIAL-MESENCHYMAL TRANSITION (EMT) IN EPITHELIAL CELLS BY USING ADENOVIRUS DELIVERY SYSTEM

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Background and Aim of Study Although persistent TGF β stimulation induces epithelial-mesenchymal transition (EMT), significant increase in the phosphorylation level of the PTEN C-terminus is involved by TGFβ as well, resulting in the loss of PTEN activity. Although recently, we demonstrated that gene modulation of PTEN phosphorylation sites (PTEN4A) could inhibit phenotype changes through EMT in lung epithelial cells, by using the doxycycline (Dox)-inducible gene expression system in vitro, whether or not exogenous PTEN4A induction could exert the inhibitory effect against TGFβ-induced EMT remains elusive.
Methods We evaluated whether or not exogenous PTEN4A induction could be effective on TGFβ-induced EMT in vitro, by establishing the adenovirus delivery system carrying PTEN4A.
Results Both the naive cells and the cells transfected with adenovirus expressing GFP (control) treated with TGFβ showed the decreasing expression of E-cadherin and the de novo expression of fibronectin through EMT. In contrast, only the cells infected with adenovirus expressing PTEN4A kept the expression E-cadherin and inhibited the de novo expression of fibronectin against TGFβ treatment.
Conclusions These data might propose therapeutic strategy to locally deliver the PTEN4A gene in disease models with TGFβ-induced EMT such as tumor or fibrosis.

PS054

EFFECT OF MTOR SIRNA LOADED CYCLODEXTRIN HYBRID NANOSYSTEM ON HYPOXIA-INDUCED PROLIFERATION AND APOPTOSIS OF VASCULAR SMOOTH MUSCLE CELLS

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Background and Aim Study It is well known that abnormal growth of pulmonary vascular smooth muscle cells (PASMCs) cause the pulmonary hypertension. To investigate the effect of mTOR siRNA loaded these nanomaterials on PASMCs proliferation and apoptosis induced by hypoxia.
Methods Intracellular uptake study was performed by confocal laser scanning microscope. Cell transfection efficiency was evaluated by flow cytometry. PASMCs viability was analysed by MTT method. Cell apoptosis analysis was conducted using the Annexin V-FITC and propidiumiodide detection kit according to the manufacture's protocol. The mRNA expression of Bcl-xl was tested by two-step RT-PCR. The levels of Bcl-xl protein was determined by western blot.
Results mTOR siRNA loaded Ac-aCD/PEI nanoaystem could be efficiently transfected into rat PASMCs in dose-dependent manner, and take the inhibition effect on serum-induced cell proliferation. It could significantly suppress the expression of mTOR mRNA/protein, and enhance PASMCs apoptosis under hypoxia condition. Importantly, this data showed that Ac-aCD load mTOR siRNA could inhibit the hypoxia-induced the proliferation of PASMCs. Hypoxia and serum have no obviously effect on the cellular uptake of Ac-aCD/PEI1800 nanomaterials.
Conclusion This pH-responsive hybrid nanosystem Ac-aCD can effectively load mTOR siRNA, which induce hypoxic PASMCs apoptosis and suppress the cell proliferation.

PS055

RAB5 GTPASE MODULATES THE INTRACELLULAR TRAFFICKING OF BETA-ARs IN RPMVECS

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Background Disruption of alveolar-vascular barrier can be an early pathological change in ALI. Beta-adrenergic receptors (beta-ARs) play a critical role in the regulation of vascular endothelial barrier function in both normal and pathological conditions. It is known thatbeta-adrenergic receptor internalization are regulated by Rab5 GTPase in many cell types. However, the effects of Rab5 on the trafficking of beta-AR in pulmonary microvascular endothelial cells are poorly understood.
Aim of the Study To investigate the effects of Rab5 on the endocytosis and cell-surface expression of beta-AR in pulmonary microvascular endothelial cells.
Materials and Methods Rat pulmonary microvascular endothelial cells a(RPMVECs) were achieved by primary culture technology. Knockdown of Rab5 by siRNA and over-expression of Rab5 by transfecting with wild-type Rab5(Rab5WT) were performed in RPMVECs. Cell-surface expression of beta-ARs in RPMVECs was measured by intact cell ligand binding. Internalization of beta-ARs was measured by ligand internalization Assay. Down-regulation of beta-ARs was measured by receptor down-regulation Assay. Sub-cellular distribution of beta2-AR was imaged by Fluorescent microscopy.
Results We found that Rab5 siRNA strongly inhibited the agonist-induced internalization ofbeta2-AR and up-regulate the amount of beta-ARs on the cell surface in RPMVECs, whereas the wild-type Rab5(Rab5WT) promoted the agonist-induced internalization and down-regulation ofbeta2-AR but had a similar effects on the expression of beta-ARs on the cell surface.
Conclusions We propose that Rab5 is essential for endocytosis and cell-surface expression ofbeta-ARs in PMVECs.

PS056

CORTICOSTEROID PLUS LONG-ACTING BETA2-AGONIST PREVENT VIRUS-ASSOCIATED UPREGULATION OF B7-H1/PD-L1 ON AIRWAY EPITHELIUM

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Back Ground and Aim of Study Airway viral infection exacerbates asthma and chronic pulumonary obstructive disease (COPD). B7-H1/PD-L1 is a coinhibitory molecule implicated in an escape mechanism of viruses from the host immune systems. This escape may induce viral persistence and lead to exacerbation of the underlying diseases. We previously showed that an analog of viral double-strand RNA, polyinosinic-polycytidylic acid (poly IC), upregulated the expression of B7-H1/PD-L1 on airway epithelial cells, which was resistant to corticosteroid treatment. We investigated the effects of corticosteroid plus long-acting beta2-agonist (LABA) on the expression of B7-H1/PD-L1. We further investigated the additional effect of long-acting muscarinic agonist (LAMA) that is used as a standard therapy for COPD.
Methods BEAS-2B airway epithelial cell line was stimulated with poly IC. The expression of B7-H1/PD-L1 was assessed by flow cytometry.
Results Poly IC-induced upregulation of B7-H1/PD-L1 was suppressed by high-concentration ciclesonide but not by indacaterol. The upregulation was suppressed by low-concentration ciclesonide when used in combination with indacaterol. No additional effect of glycopyrrolate was observed on the expression of B7-H1/PD-L1.
Conclusion Corticosteroid plus LABA attenuate virus-associated upregulation of B7-H1/PD-L1 on airway epithelial cells. This result may partly explain why the therapy with inhaled corticosteroid plus LABA prevents exacerbation of asthma and COPD.

PS057

TWEAK ENHANCES TGF-β-INDUCED EPITHELIAL-MESENCHYMAL TRANSITION IN BEAS-2B HUMAN BRONCHIAL EPITHELIAL CELLS

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Background Chronic airway inflammatory disorder, such as asthma and chronic obstructive pulmonary disease, are similarly characterized by airway inflammation and remodeling. The chronic inflammation and damage to the airway epithelium caused the airway remodeling which is associated with an improper epithelial repair, and is characterized by elevated expression of transforming growth factor-β (TGF-β). Epithelial-mesenchymal transition (EMT) is an important mechanism during embryonic development and tissue remodeling whereby epithelial cells gain the capacity to increase motility by down-regulation of epithelial markers, and gained expression of mesenchymal markers. TGF-β is well-known as a central inducer in EMT, and pro-inflammatory cytokines enhance the TGF-β-induced EMT. In the present study, we investigated whether a pro-inflammatory cytokine TNF-like weak inducer of apoptosis (TWEAK) enhance TGF-β1-induced EMT in a human bronchial epithelial cell line (BEAS-2B).
Method The quantitative RT-PCR and western blotting were used to define the alterations in epithelial and mesenchymal markers expression in BEAS-2B cells. The BEAS-2B cells were assessed for 48 h after stimulation with TGF-β1 alone or in combination with TNF-α or TWEAK.
Results TGF-β1 induced spidle-like morphology, reduced expression of epithelial marker E-cadherin, and increased expression of mesenchymal markers N-cadherin and Vimentin. Co-treatment with TWEAK enhanced these features of TGF-β1-induced EMT with similarly to co-treatment with TNF-α.
Conclusion These findings suggest that a pro-inflammatory cytokine TWEAK can synergize with TGF-β and contribute to airway remodeling.

PS058

THE EFFECT OF CHITIN ON IL-1β PRODUCTION BY ALVEOLAR MACROPHAGE

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Background and Aim of Study Chitin, a polymer made up of repeating units of β-(1–4)-poly-N-acetyl-d-glucosamine, is a ubiquitous polysaccharide found in the walls of fungi and the exoskeleton of arthropods such as crabs, shrimp and insects. As it does not have a mammalian counterpart, chitin could be important inhalant antigen for bronchial asthma. β1,3-glucan, the cell wall component of fungi and yeast as similar to chitin, promoted the production of Interleukin-1β (IL-1β) by macrophages through the Nod-like receptor family, pyrin domain-containing 3 (NLRP3) inflammasome. IL-1β is an important pro-inflammatory cytokine that is required for the induction of immune responses. Although alveolar macrophages act as the first line of defense to encounter inhaled particulates and pathogens, and play an essential role in the inflammatory responses in the pulmonary immune system, little is known about the alveolar macrophage response induced by chitin. Therefore, we investigated the effect of chitin on IL-1β production by alveolar macrophages.
Methods MH-S cells (Mouse Alveolar Macrophage cell line) were incubated with different sized chitin. The mRNA expressions of IL-1β and NLRP3 in MH-S cells were examined by real-time PCR.
Results The mRNA expression of IL-1β was upregulated by the stimulation of small chitin (<40 μm), but not by large chitin (>40 μm). However, this response was inhibited by cytochalasin D, an inhibitor of actin polymerization and phagocytosis, anti-Toll-like receptor 2 or anti-Dectin-1 neutralizing antibodies. The mRNA expression of NLRP3 was also upregulated by small chitin and this response was inhibited by cytochalasin D.
Conclusion These findings suggest that small chitin could induce the expression of IL-1β and NLRP3 in alveolar macrophages.

PS059

EPIGENETIC REGULATION OF LUNG CANCER STEM-LIKE CELL GENE SOX2

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Background and Aim of Study Cancer stem-like cells (CSCs)/Cancer-initiating cells (CICs) are subpopulation of cancer cells that have the properties of high tumor initiating ability, differentiation ability and self-renewal ability, and are regarded as major causes of cancer recurrence, distant metastasis and treatment resistance. CSCs/CICs have been thought to have similar molecular mechanisms to normal stem cells and keep undifferentiated state. And we thought that lung CSCs/CICs constantly exchange the state of differentiation and dedifferentiation. Previously we showed that SOX2 is overexpressed in stem-like cells of human lung adenocarcinoma cell lines and is related to cancer stem-like phenotype. In this study, we examined the differentiation and dedifferentiation of lung CSCs/CICs in single-cell level and investigated the regulation of SOX2 expression in lung CSCs/CICs.
Methods Lung cancer cell lines were stained with Hoechst33342 dye and CSCs/CICs were isolated as Side population (SP) cells and non-CSCs/CICs were isolated as Main population (MP) cells. Many single cell clones (SP clones, MP clones) were established from SP cells and MP cells respectively. SOX2 expression was addressed by qPCR. They were treated with HDAC inhibitor Trichostatin A (TSA).
Results SP cells and MP cells were generated from each SP clones and MP clones. The SOX2 expression of SP clones were higher than that of MP clones. TSA treatment enhanced the expression of SOX2 and increased the rate of SP cells.
Conclusion These observation indicate that the differentiated lung carcinoma fractions are dedifferentiated into CSCs/CICs and SOX2 expression is important for the mechanisms, and SOX2 expression in cancer cells is regulated by histone acetylation. Therefore, lung cancer stem-like cell phenotype might be regulated by epigenetic mechanisms.

1-A7: ENVIRONMENTAL & OCCUPATIONAL HEALTH AND EPIDEMIOLOGY

PS060

PNEUMOCONIOSIS DUE TO ENVIRONMENTAL CEMENT DUST EXPOSURE AMONG THE RESIDENTS NEAR THE PORTLAND CEMENT FACTORIES IN KOREA

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Background and Aim of Study In 2010, Korean Ministry of Environment implemented a screening program evaluating the respiratory health status among the residents near the Portland cement factories in Korea. The screening program revealed that 133 and 24 participants with suspicious COPD and Pneumoconiosis, respectively. The aims of the present study were to confirm those abnormal findings with radiologic and functional tools, and to evaluate the association between those finding and environmental Portland cement exposure with case series of pneumoconiosis.
Methods A total of 157 residents were source population. Individuals died (n = 4) and refused to participate the examination (n = 15) were excluded (eligible subjects, n = 138). Fourteen individuals did not participate in the examination. A total 124 subjects were included in this study. Pulmonary function test, chest PA and chest CT were carried out by Seoul St. Mary's Hospital.
Results Those participants were diagnosed as chronic bronchitis (n = 59), emphysema (n = 63), interstitial lung fibrosis (n = 22), bronchiectasis (n = 27), and old tuberculosis scarring (n = 25). A total of 19 participants were diagnosed as pneumoconiosis. Fifteen participants were related to occupational exposure to dust (mine workers (n = 5), construction workers (n = 2), and cement factory workers (n = 9)), and the rest of participants (n = 4) with pneumoconiosis were farmers. Those four farmers (2 males and 2 females) lived over 50 years within 3 Km radius of factory, furthermore, two of them within 760 m radius. There was no definite dust exposure except cement dust from factory. One of them had neither tuberculosis nor smoking history.
Conclusion Our findings suggest that environmental exposure to cement dust may contribute to pneumoconiosis among the residents near the Portland cement factories. For prevention and management of respiratory disease, environmental monitoring and longitudinal follow-up should be implemented in the residents near the Portland cement factories.

PS061

INFLUENCE OF ENVIRONMENTAL EXPOSURE ON COPD SUBJECTS IN KOREA

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Background and Aim of Study Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation and results from environmental factors and genetic factors. Although cigarette smoking is a major risk factor, other environmental exposure can influence COPD. The purpose of this study is to investigate clinical characteristics of COPD according to history of environmental exposure.
Methods The study population comprised 347 subjects with COPD who were recruited from the pulmonary clinics of 14 hospitals that belong to the Korean Obstructive Lung Disease Study Group. We classified environmental exposure according to history of living near factory, and direct exposure history to firewood or briquette. According to living environmental exposures, we compared the frequency of respiratory symptoms, pulmonary function, quality of life questionnaire, exercise capacity, and CT phenotypes.
Results Thirty-one subjects (8.9%) had history of living near factory, 271 (78.1%) had exposure history to briquette, and 184 (53.2%) had exposure history to firewood. There were no significant differences in clinical characteristics according to history of living near factory or exposure to briquette. However, subjects with history of firewood exposure had significantly longer duration of cough and sputum. Firewood exposure group showed higher FEV1 (1.27 L vs 1.16 L) and better exercise capacity (6 minute walk distance 707 m vs 492 m).
Conclusion Clinical characteristics were not differed according to history of living near factory nor exposure to briquette. COPD subjects with exposure history of firewood had more frequent respiratory symptoms such as cough or sputum, while their pulmonary function and exercise capacity were preserved. Our data suggest that environmental exposure may influence clinical phenotype of COPD.

PS062

ATMOSPHERIC POLLUTANTS DUE TO FOREST FIRES AND THEIR INFLUENCE ON RESPIRATORY HEALTH IN RUSSIA IN ABNORMALLY HOT SUMMER OF 2010

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Global warming due to human activity lead to abnormal climate changes. Particularly strong impact of climate change has become evident in last decades, as in the industry developed cities of the world were fixed for long periods of smoke air (ex. Moscow -2010, Beijing – 2011–12). Causes of these air pollutions were different factors, but the response of the respiratory system and the impact on public health were similar. Such air contamination in natural and industrial pollutants can cause pathological response from the respiratory tract. The aim of the study was to investigate the influence of air pollution due to forest fires amid to high air temperature on the morbidity respiratory diseases and total mortality in central regions of Russian Federation in abnormally hot summer of 2010 year.
Methods Time series analyses of morbidity and mortality during 2008–2011 years in central regions of Russian Federation. Case-crossover study of influence of pollution levels and air temperature on respiratory health in 2010 year compare with 2008, 2009 and 2011 years. Panel study: examination of 32 patients with asthma and lung function tests with peak expiratory flow measurements during the dusty days in comparison with another non smoky period.
Results Were recorded significant growth in respiratory morbidity and mortality during extreme smoke and abnormal heat. Number of emergency calls due to bronchopulmonary diseases in 2010 was twice higher than in 2008, 2009 and 2011. The most frequent causes of seeking the emergency aid were bronchial asthma, acute bronchitis, exacerbation of chronic obstructive pulmonary disease and SARS. Moreover number of emergency calls with SARS has come to the average annual indicators only 6 weeks later.

PS063

THE FORCED OSCILLATION TECHNIQUE PARAMETERS IN POPULATION SCREENING ON SHIMANE PREFECTURE

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Background Most Graph is a device for measuring respiratory resistance and reactance, using the forced oscillation technique. Because these parameters are measured during tidal breathing of subjects, measuring technique is easy with little burden on elder subjects. In this study, we carried out spirometry and MostGraph at the same time and examined the relation of parameters of spirogram and Most Graph in population screening.
Methods Subjects were 526 residents in Shimane Prefecture (male:210, female:316, 66.7 years old). Spirometry and Most Graph are simultaneously practiced on population screening.
Results There were negative correlation with the MostGraph parameters, the resistance at 5 Hz (R5), resistance at 20 Hz (R20), and frequency of resonance (Fres) and Spirometry parameters VC or FEV1. And there were positive correlations with the reactance at 5 Hz (X5) and Spirometry parameters VC or FEV1.
Conclusion In population screening, there were some correlations with the forced oscillation technique and spirogram parameters.

PS064

EFFECTS OF ACUTE ALTITUDE EXPOSURE ON RESPIRATORY SYSTEM

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Background and Aim of Study Hypoxia training is executed in our Aeromedical Center in which given altitude is simulated by decreasing air pressure of the device. With this training, effects of barometric pressure changes on human physiology (hypoxia, hyperventilation, trapped gases etc.) are simulated in a safe environment. The objective of our study was to analyze effects of acute altitude exposure on respiratory system which were encountered during this training.
Method 30 minutes 100% oxygen is breathed before hypoxia training to prevent decompression sickness. Then, trainers put off their oxygen masks and start to solve their training survey that contains simple arithmetical procedures at 25,000 Ft. simulated altitude ($PO_2 = 59$ mmHg). This survey is used to assess Effective Performance Time (3–5 minutes) on which perception and judgment start to fail. Some predisposing factors (hypoglisemia, fatigue) reduce this time. Hypoxia or anxiety induced hyperventilation may also appear. Medical records and hypoxia laboratory records of trainees were analyzed.
Results 6403 hypoxia trainings were given to trainees between January 2006 and February 2013 in our center. During this period four (0.06%) profound hypoxia, four (0.06%) anxiety induced hyperventilation and one (0.015%) spontaneous pneumothorax cases were encountered.
Discussion Hyperventilated personnel were informed about importance of frequency and volume of respiration and hyperventilation countermeasures. In profound hypoxia cases, first aid (100% oxygen and extremity elevation) was administered in the training device and training was aborted. Hypoxia symptoms have been disappeared rapidly. All trainees have returned to their flight duties safely. Because of pneumothorax disease has a repetitive character and can results in incapacitation of aircrew in an aviation environment, aircrew had been permanently grounded.

PS065

ROLE OF ATMOSPHERIC SAMPLES COLLECTED FROM ASIAN SAND DUST STORM IN ALLERGIC AIRWAY INFLAMMATION AND IMMUNE TOLERANCE

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Epidemiologic studies have demonstrated that atmospheric contamination caused by Asian sand dust (ASD) storm aggravates asthma both in human adults and children. In the present study, two time-course studies (6 weeks and 14 weeks) were performed to investigate the adverse effects caused by ASD in experimental mice. CD-1 Mice were instilled with ASD samples intratracheally four or eight times at 2-week intervals with or without ovalbumin (OVA). In the case of the groups exposed eight times to ASD alone, alveolitis and bronchitis were exacerbated and various inflammatory cytokines and chemokines in the bronchoalveolar lavage fluid (BALF) increased. In the case of the groups co-exposed to ASD and OVA four times, allergic airway inflammation was aggravated. Proliferation of goblet cells in the airway epithelium along with Th2-cytokines such as IL-13 and eosinophil-relevant cytokine/chemokines IL-5, Eotaxin and MCP-3 in BALF was also observed. A moderate fibrous thickening of the subepithelial layer in the airway was also observed pathologically in these groups. However, the eight-time co-exposure attenuated these changes. On the other hand, TGF-β1 and neutrophil number increased in BALF in the eight-time co-exposure groups compared with the four-time co-exposure groups. Adjuvant effects of ASD toward IgG1 and IgE production were recognized in the two time-course studies. However, the eight-time co-exposure did not reduce their productions. These results indicate that short-term sensitization of OVA with ASD aggravates allergic inflammation along with fibrous thickening of the subepithelial layer in the airway, whereas the long-term sensitization attenuates these changes, suggesting that suppressive immune responses are caused by TGF-β1-related immune tolerance.

PS066

THE INFLUEUNCE OF CEMENT DUST EXPOSURE LEVEL TO RESPIRATORY SYMPTOMPS AND PULMONARY FUNCTION IN EMPLOYERS COHORT OF CEMENT FACTORY WORKERS

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Introduction Cement factory can produce dust in almost production processes. Dust exposure level is different among work units in cement factory. Respiratory disorder caused by cement dust exposure has been known for years. This condition could be present in respiratory symptoms and pulmonary impairment. The aim of this study was to find out association between dust cement exposure level with respiratory symptoms and pulmonary function.
Method Cross sectional study; we collected data about dust cement level and respiratory symptoms, we also performed pulmonary function test to the employers of cement factory. Data was analyzed using chi square test with p value < 0,05 considered as significant difference.
Result We randomized study sample and found out 103 study subjects. Chronic cough, breathlessness, purulent sputum, and chest tightness were most common in high level of dust exposure (95,2% vs 4,8%, 100% vs 0%, 88,2% vs 11,80%, and 85,70% vs 14,30%; respectively with p = 0,002, CI 95%). Similarly with pulmonary impairment; obstruction and restriction were more prevalent among employers in high level of dust exposure (100% vs 0% and 68,70% vs 31,3%, respectively; with p = 0,001 CI 95%).
Conclusion Employers who work in high level cement dust exposure had more respiratory symptoms and pulmonary impairment (i.e obstruction and restriction) than the others in low level cement dust exposure.
Keywords cement dust, pulmonary impairment, respiratory symptom.

PS067

EFFECTS OF ASIAN SAND DUST ON RESPIRATORY SYMPTOMS AND HEALTH STATUS IN THE PATIENTS WITH RESPIRATORY DISEASES

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Background Asian Sand Dust (ASD) is a natural phenomenon which originated from northern China and Mongolia in springtime. Particles in ASD are carried to Japan. In this study, we examined effects of ASD on the respiratory symptoms and health status in the patients with respiratory diseases.
Methods Data were collected using self-evaluation forms from 361 subjects aged 50 to 79 who visited clinics or hospitals in Kyushu area, Yamaguchi and Niigata prefectures in 2011. The data were collected in February as pre-ASD season and in April to May as ASD season. Patients with chronic obstructive pulmonary disease (COPD) and/or asthma were classified as "Patient" and those without respiratory diseases were "Healthy volunteer". Distribution of aerosol particles was measured by Aerodynamic Particle Sizer during ASD event.
Results 132 patients and 229 healthy volunteers participated in the study. 39.4% of patients were with asthma, 31.8% were COPD, and 38.8% were with COPD combined with asthma. The odds ratios in patients for worsening of "exacerbation of cough by weather", "production of sputum without any cold-like illness", "production of sputum early in the morning", and "wheezing" were significantly high. In addition, the odds ratios in patients for deteriolating health status measured by COOP/WONCA chart was significantly high in "Physical Fitness", "Change in Health", "Overall Health", and "Quality of Life". Mass concentration and surface area of ambient particles ranging 1–7 μm in diameter and the number of particles smaller than 30 nm were more abundant during ASD event.
Conclusion The respiratory symptoms and health status were worsened during ASD event especially in the patients with respiratory diseases. Aerosol particles less than 7 μm in diameter which thought to be harmful to human health were increased during ASD event, suggesting that such particles increased in ASD season might exacerbates respiratory symptoms and lower the health status.

PS068

SEASONAL CHANGES OF HEALTH STATUS AND RESPIRATORY SYMPTOMS IN ELDERLY PATIENTS WITH CHRONIC PULMONARY DISEASES IN KOREA AND JAPAN

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Background Health effects of substances which are transported over a long distance such as atmospheric dust from Northeast Asia are serious concern. The reason why elderly persons and patients with cardiopulmonary disease are highly sensitive to these substances is not clear. We studied seasonal changes in health status and respiratory symptoms in elderly patients with chronic pulmonary disease compared with control patients in Korea and Japan.
Method Fifty to 79 years old of male and female subjects who lived in the southwest part of Yamaguchi prefecture, Japan (70 patients, 30 control subjects) and in suburbs of Seoul, Korea (60 patients, 37 control subjects) were studied. Subjects who visited the respiratory physicians in hospital or clinics responded twice to the self-evaluation forms including COOP/WONCA chart in February and May. The subjects in the control group were age matched with those in the patient group. Results were analyzed by Chi square test.
Results In both Korean and Japanese study, the patient group showed much worse respiratory problems such as "tenacious sputum not catch a cold" or "tenacious sputum in the morning" in spring than winter. Items under "Change in health", "Overall health" and "QOL" in the COOP/WONCA chart were worse in the patient group compared with the control group in spring than in winter in both Korean and Japanese. However, there were no seasonal changes in both the patient and control groups in other items of COOP/WONCA chart.
Conclusion These evidences suggest that atmospheric particle such as yellow dust during spring season may affect seasonal changes of health status and respiratory symptoms in patients with chronic pulmonary disease.
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1-B1: RESPIRATORY INFECTIONS (NON-TUBERCULOSIS) 1

PS069

CLINICAL CHARACTERISTICS OF NURSING HOME ACQUIRED PNEUMONIA (NHAP) AMONG HOSPITALIZED PATIENTS IN A KOREAN TEACHING HOSPITAL

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Background The new concept of healthcare-associated pneumonia (HCAP) was introduced in 2005, and the guideline recommended broad-spectrum empirical antimicrobial therapy directed at multidrug-resistant pathogens in these patients. However, HCAP is heterogeneous, clinical features and outcomes are different from region to region. Especially, the optimal strategy for treatment of nursing home acquired pneumonia (NHAP) which is a category of HCAP, was controversial among several studies. We aimed to evaluate the clinical features of NHAP patients hospitalized into a Korean teaching hospital.
Methods This study was retrospectively conducted in patients with NHAP or CAP that were hospitalized in Jeju national university hospital between January 2012 and December 2012.
Results A total of 283 patients were enrolled and 66 (23.3%) had NHAP. The median age of the NHAP group was higher than the CAP group (80 vs. 71; $p = 0.001$). The NHAP group showed worse clinical parameters, and the rates of patients with PSI class IV or more (77.2% vs. 57.1%; $p = 0.003$) were higher than in the CAP group. Although potentially drug resistant pathogens were more frequently detected in the NHAP group (18.1% vs. 7.8%; $p = 0.015$), the isolation rates of Pseudomo nas aeruginosa were not significantly different from between both group (10.6% vs. 4.1%; $p = 0.065$). And the pathogen isolated most frequently in both groups was Streptococcus pneumoniae. Multivariable analyses failed to show that the pneumonia type was a prognostic factor for mortality. Only high PSI score was associated with increased mortality ($p = 0.001$).
Conclusions In patients admitted with NHAP or CAP, the risk of excess mortality was not the designation of pneumonia but the severity of pneumonia. We suggested that the empirical treatment of broad-spectrum anti-pseudomonal agents in NHAP should be reserved for patients with severe pneumonia or at high risk of MDR bacterial infection.

PS070

ASSOCIATION OF DECREASED RENAL FUNCTION WITH MORTALITY IN INDONESIAN HOSPITAL ACQUIRED PNEUMONIA PATIENTS

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Background and Aim Mortality due to Hospital Acquired Pneumonia (HAP) is high, its rate reaches up to 50%. Renal function, characterized by the value of eGFR (estimated Glomerular Filtration Rate) is associated with increased mortality and morbidity in many clinical settings. The lower the eGFR is, the higher the mortality. To dates, there is no study conducted to investigate this association in patients with HAP. The aim of this study was to identify the association of decreased renal function marked by eGFR with mortality in HAP.
Methods The design of this study was retrospective cohort. Subject's data were taken retrospectively from Internal Medicine Ward of Cipto Mangunkusumo National General Hospital's medical records January 2006 to December 2012. We categorized the eGFR to 3 groups, group I was those whose eGFR above 60 mL/minutes, group II with eGFR 15–60 mL/minutes and group III with those below 15 mL/minutes, with group I as the reference group. eGFR was calculated using MDRD (Modification of Diet in Renal Disease) formula. We analyzed the association with mortality by using logistic regression test.
Results There were 169 patients included. The mortality proportion of HAP was 42.6%. Patients were mostly men, 89 subjects (52.7%) with age ranging between 18 to 88 years old (mean age 50.43 years). There were 120 patients in group I (38.3% death), 33 patients in group II (45.5% death) and 16 patients in group III (68.8% death). The association with mortality: Group II ($p = 0.46$ OR 1.3 95% CI 0.6 to 2.9) and Group III ($p = 0.027$ OR 3.5 95% CI 1.2 to 10.8).
Conclusion Decreased of renal function marked by decreased eGFR was associated with increased mortality in HAP. Group with eGFR less than 15 mL/minute was significantly associated with increased mortality.
Key Words Hospital Acquired Pneumonia, mortality, eGFR, MDRD.

PS071

CLINICAL FEATURES OF NON-TUBERCULOUS MYCOBACTERIOSIS PRESENTING AS A SOLITARY PULMONARY NODULE

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Background and Aim of Study Non-tuberculous mycobacteriosis (NTM) is an important pulmonary disease. However, NTM presenting as a solitary pulmonary nodule (SPN) is rare and may be difficult to diagnose correctly without an invasive procedure. The aim of this study was to identify the clinical features of NTM presenting as an SPN.
Methods Seven cases of SPN caused by NTM between June 2008 and May 2013 were enrolled. The patients' clinical, laboratory, and radiological findings were investigated. Furthermore, the diagnostic procedures and treatment results were examined.
Results Among the 7 NTM patients (5 men, 2 women; mean age, 69.7 years), the lesions were detected at a regular check-up in 4 patients and during further examinations for other diseases in 3 patients. On chest computed tomography, the diameters of all SPNs were less than 3 cm, and it was necessary to differentiate SPNs from lung cancer in 4 cases. In 5 of 6 patients who underwent positron emission tomography with computed tomography, the maximum standard uptake value was greater than 2.5. The diagnostic procedures were bronchoscopic biopsy in 1 patient and video-assisted thoracoscopic surgery (VATS) in the remaining 6. All cases were caused by infection with Mycobacterium avium complex (MAC). At present, none of the patients who underwent VATS have relapsed; however, the patient who was diagnosed bronchoscopically and received drug therapy for 1 year relapsed.
Conclusion NTM (especially MAC disease) should be considered in the differential diagnosis of an SPN. Given the good prognosis of NTM presenting as an SPN, this study underlines the importance of VATS as a diagnostic procedure, and of the identification of the causative microorganisms in resected lung tissue.

PS072

CLINICAL FEATURES OF PATIENTS WITH POSITIVE SPUTUM CULTURE FOR TRICHOSPORON SPECIES

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Introduction Trichosporon species is an infrequent cause of pneumonia. To date, clinical and/or radiographic features of patients with positive sputum culture of Trichosporon species have not been well characterized.
Methods We first enrolled all patients with positive culture for Trichosporon species from any sources, who had been hospitalized in our hospital since 2003 to now. We then selected only those in whom positive culture was obtained from sputum. We collected demographic information as well as clinical data, and also examined the patients' prognosis.
Results We found only 70 patients who exhibited positive culture for Trichosporon species from any sources. The most common source was urine (50 cases, 71.4%), followed by blood (7 cases, 10%) and sputum (6 cases, 8.5%). Among 6 patients with positive sputum culture, two exhibited positive culture also in blood. All 6 patients demonstrated chest abnormal shadows: diffuse pulmonary infiltrates in 3 cases, bilateral localized infiltrates in 1 case, centrilobular shadows in another, and bronchiectasis with nodular shadows in the last. Of these, four had been receiving immunosuppressive therapy, 3 had been using central catheters, and 2 were in an intensive care unit. Two patients, who exhibited positive culture only once, were recovered without any antifungal therapies. All 3 patients, who demonstrated positive cultures for T. asahii repeatedly, had diffuse pulmonary infiltrates on chest radiograph and two of them died within 30 days after positive sputum culture, despite of intensive antifungal therapy. The remaining one patient, who exhibited uniquely positive for T. mycotoxinivorans, showed bronchiectasis associated with nodular shadows, which was effectively and successfully treated by "voriconazole".
Conclusions Clinical features and/or chest radiographic findings of patients with positive sputum culture for Trichosporon species are highly varied. Positive culture in sputum may be a sign of poor prognosis in some, but not all.

PS073

THE MOLECULAR EPIDEMIOLOGY AND AND ANTIBIOTIC RESISTANCE OF ACINETOBACTER BAUMANNII ISOLATED FROM INTENSIVE CARE UNIT IN HUNAN PROVINCE

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Background and Aim of Study To investigate the Genetic background, Genotype distribution, antibiotic resistance and antibiotic resistance genes distribution of Acinetobacter baumannii which widespreaded in ICU in Hunan province.
Methods We collected 138 non-repeated Acinetobacter baumannii strains isolated from the ICU in-patients'sputum/bronchial secretion samples during December 2010 and December 2011, these patients were from 6 hospitals in different places of Hunan province and their hospitalization time was more than 48 hours. We used REP-PCR and MLST to analyse Genotyping and homology. We detected blaOXA-51, blaOXA-23, blaOXA-24, blaOXA-58 and blaNDM-1 by PCR. All the drug-susceptibility test results and patients' clinical datas were also collected at the same time.
Results All of the 138 Acinetobacter baumannii strains were divided into 6 gene types by REP-PCR, the mayor type was type A. MLST divided the A1 subtype of the type A into 8 distinct sequence types,the main sequence types was ST191,we also discovered the ST381 for the first time in China. The Carbapenemases gene-positive Acinetobacter baumannii widely distributed, all the 138 strains contained OXA-51 but were negative for OXA-24, OXA-58 and NDM-1 gene, 80.43% isolates were positive for OXA-23 gene. Compared Clone A with B, their positive rates of OXA-23 gene were statistal different $P < 0.01$, as the same as Clone A and C. The differences of MDR rate and PDR rate between different Clones were not statistically significant $P > 0.05$.
Conclusion The mayor type Acinetobacter baumannii of ICU in Hunan province was type A; and was the ST191 of MLST. The Carbapenemases gene-positive Acinetobacter baumannii widely distributed, carry the OXA-51 gene and OXA-23 gene was an important reason for antibiotic resistant phenomenon of Acinetobacter baumannii of ICU in Hunan province.

PS074

CLINICAL AND RADIOGRAPHIC FEATURES IN NONTUBERCULOUS MYCOBACTERIAL LUNG DISEASE

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Background Nontuberculous mycobacterial (NTM) lung diseases are generally managed as Mycobacterium avium complex (MAC). However, little is known about the clinical and radiographic differences between M avium and M intracellulare. This study examined the clinical characteristic and radiographic features in NTM lung disease.
Methods Medical records of 113 patients that were given a new diagnosis of NTM lung disease from 1998 to 2013 were retrospectively reviewed.
Results 78 patients (69%) had M avium lung disease, 32 patients (28%) had M intracellulare lung disease and 12 patients (11%) had others. 9 patients had lung disease of multiple species. M avium and M intracellulare are difference in the following clinical characteristics: age (64.6 ± 13.7 and 70.2 ± 12.4, $p = 0.320$), gender ($M : F = 51:49$ and $M : F = 31:69$, $p = 0.084$), receiving quinolone (3% and 15%, $p = 0.026$), having underlying disease (65% and 77%, $p = 0.116$), and radiographic features: having cavity (19% and 42%, $p = 0.020$) and spreading multiple lung lobes (2.6 and 3.0, $p = 0.094$). The patients with lung disease of multiple species do not have clinical and radiographic features compared to patients with lung disease single species of MAC.
Conclusions M avium and M intracellulare have differences clinical and radiographic features. These differences may have implications for diagnosis, treatment and prognostication.

PS075

SURFACTANT PROTEIN A-DERIVED PEPTIDE PROTECTS LUNG EPITHELIAL CELLS FROM CYTOTOXIC ACTIVITY OF HUMAN β-DEFENSIN 3

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Human β-defensin 3 (hBD3) is a cationic antimicrobial peptide with broad spectrum microbicidal activity against both bacteria and fungi. However it also exhibits cytotoxicity against host cells in higher concentrations. In the previous study, we found that the cytotoxicity of hBD3 against lung epithelial cells was attenuated by pulmonary surfactant protein A (SP-A), a collectin implicated in host defense and regulation of inflammatory responses in the lung. Moreover, we identified that the functional region of SP-A lies within Tyr161-Lys201, tentatively called SP-A- derived peptide.
In this study, we further characterized the effects of SP-A-derived peptide on cytotoxicity and antimicrobial activity of hBD3. SP-A-derived peptide significantly decreased membrane permeability of A549 cells treated with hBD3. In mice model, intratracheal instillation of hBD3 resulted in elevated LDH activity and the number of leukocytes in bronchoalveolar lavage fluid (BALF). Moreover, interstitial edema and alveolar septal thickening were seen in histological examination of hBD3 instilled mice. SP-A-derived peptide decreased both LDH activity and the number of leukocytes in BALF to the comparable level in BALF from control mice. The tissue damages were also dramatically improved in the presence of SP-A-derived peptide. To examine the effects of SP-A-derived peptide on the antimicrobial activity of hBD3, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were incubated with hBD3 in the presence of SP-A-derived peptide. Antimicrobial activity of hBD3 against these microbes was not affected in the presence of SP-A-derived peptide at concentration sufficient to decrease cytotoxicity of hBD3. These results suggest that SP-A-derived peptide decreases cytotoxic activity of hBD3 without affecting its antimicrobial activity.

PS076

PREDICTORS FOR SUCCESSFUL ERADICATION OF MULTIDRUG-RESISTANT ACINETOBACTER BAUMANNII IN THE RESPIRATORY TRACT USING AEROSOLIZED COLISTIN

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Background The increased prevalence of multidrug-resistant Acinetobacter baumannii (MDRAB) poses a worldwide treatment challenge. Although aerosolized colistin therapy for MDRAB pneumonia has attracted increasing interest, factors predicting successful eradication remain unclear.
Methods This retrospective study evaluated 135 consecutively admitted adult patients showing positive respiratory secretion cultures for MDRAB who underwent aerosolized colistin therapy between January 2007 and November 2011. Possible factors related to pneumonia and MDRAB eradication were collected for analysis.
Results A shorter interval between the day the positive MDRAB sputum cultures were yielded and the day colistin inhalation treatment began (4.0 ± 2.5 vs 7.3 ± 6.5, $p = 0.002$) can predict successful early MDRAB eradication on Day 14. Patients with a worsening chest X-ray on Day seven of the colistin inhalation had a lower chance of 14-day MDRAB eradication [1/44 (2.3%) vs 8/37 (21.6%), $p = 0.006$]. Patients with diabetes mellitus also had a lower chance of early MDRAB eradication [13/44 (29.5%) vs 20/37 (54.1%), $p = 0.025$].
Conclusions Early intervention using aerosolized colistin in patients with MDRAB pneumonia or colonization can achieve better eradication.

PS077

PATHOLOGICAL EXAMINATION OF TWO CASES OF ACUTE EXACERBATION OF CHRONIC NECROTIZING PULMONARY ASPERGILLOSIS LEADING TO PNEUMONECTOMY

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Background and Aim of Study Chronic necrotizing pulmonary aspergillosis (CNPA), also called semi-invasive pulmonary aspergillosis, is an indolent and cavitary infectious process of the lung secondary to local invasion by Aspergillus species. We sometimes experience CNPA patients demonstrating acute progression of infiltrative shadow although few cases have been reported. In this study, we report two cases of acute exacerbation of CNPA examined pathologically after pneumonectomy.
Methods We retrospectively reviewed medical records of two cases of CNPA demonstrating acute progression of in filtration prior to pneumonectomy.
Result Case1: A 54-year-old man, with medical history of left upper lobectomy due to pulmonary tuberculosis 40 years previously, was diagnosed as pulmonary aspergillosis 4 years before admission based on a pulmonary cavity and positive Aspergillus antigen. Despite of administration of an antifungal drug and predonisolone, filtration in the left lower lung field emerged and deteriorated. An acute exacerbation of CNPA was suspected and residual left pneumonectomy was performed, pathologically revealing organizing pneumonia without evidence of fungus bodies. Case2: A 52-year-old man, with a medical history of pulmonary tuberculosis a long time before, was diagnosed as CNPA based on imaging findings and positive Aspergillus antibody. Although an antifungal agent was administered intravenously and locally, CNPA was uncontrollable with radiological deterioration. Left pneumonectomy was performed. Pathological findings of the resected lung included bronchocentric granulomatosis without evidence of invasion of fungi in the area of infiltrative shadow.
Conclusion In CNPA cases, acute exacerbation with spread of infiltrative shadows was occasionally observed. We suspect that organizing pneumonia and granulomas detected in the area of infiltrative shadows may not be caused by fungal invasion but by allergic reaction to substances produced by Aspergillus.

PS078

A CASE OF PULMONARY ASPERGILLOMA EFFECTIVELY TREATED WITH TRANSBRONCHIAL INTRACAVITARY AMPHOTERICIN B

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Background Surgical resection has always been regarded as standard treatment for pulmonary aspergilloma. However, surgery is not feasible in many cases due to the underlying disease such as low pulmonary function of the host. We report a case effectively treated with transbronchial intracavitary amphotericin B and whose cavity has been observed for 10 years by ultrathin bronchoscope. Case: Approximately 10 years before, a 45-year-old man was diagnosed with pulmonary aspergilloma. At first, he was treated by oral itraconazole for two months, since he refused the surgical resection. However, this had little effect and the hemosputum persisted. Therefore, weekly infusion of AMPH-B into the cavity by transbronchial route was performed 13 times. Moreover, we used fibrin glue mixed AMPH-B 15 times during six years.
Results It was possible to observe chronologically the reduction and disappearance of the fungus ball through an ultrathin bronchoscope. Approximately three years have passed after the disappearance of his fungus ball, he remains alive without evidence of recurrence.
Conclusion The transbronchoscopic infusion of AMPH-B into the cavity is thought to be safe and effective in patients with pulmonary aspergilloma. To the best of our knowledge, this is a rare case of pulmonary aspergilloma followed in the long term by ultrathin bronchoscope.

1-B2: RESPIRATORY INFECTIONS (NON-TUBERCULOSIS) 2

PS079

PREDICTORS OF MORTALITY IN PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA IN INDONESIA

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Background and Aim of Study Ventilator-associated pneumonia (VAP) is a frequent infection in intensive care unit (ICU) with high mortality rate. Studies exploring predictors of mortality in patients with VAP produced conflicting results and there are no reports in Indonesia. This study was designed to determine predictors of mortality in patients with VAP in Indonesia.
Methods We performed a retrospective cohort study on patients admitted to the ICU who developed VAP between January 2003 and December 2012. We compared age, presence of high risk pathogens, comorbidity, septic shock status, blood culture, procalcitonin, appropriateness of antibiotics therapy, presence of acute lung injury (ALI), APACHE II score, and serum albumin between survivors and nonsurvivors. Multivariate logistic regression analysis was performed to identify independent predictors for hospital mortality.
Results A total of 201 patients were included. In-hospital mortality rate was 57.2%. Age, comorbidity, septic shock status, procalcitonin, appropriateness antibiotics therapy, ALI, and APACHE II score were significantly different between survivors and nonsurvivors ($p < 0.05$). Predictors of mortality in multivariate analysis were inappropriate antibiotics therapy (OR: 4.70; 95% CI 2.25 to 9.82; $p < 0.001$), procalcitonin > 1.1 ng/mL (OR: 4.09; 95% CI 1.45 to 11.54; $p = 0.01$), age >= 60 years old (OR: 3.71; 95% CI 1.35 to 10.20; $p = 0.011$), and the presence of septic shock (OR: 3.53; 95% CI 1.68 to 7.38; $p = 0.001$).
Conclusion Age 60 years or older, presence of septic shock, high procalcitonin, and inappropriate antibiotic therapy were independent predictors of mortality in patients with VAP. We suggest physician to perform procalcitonin test routinely and give an appropriate antibiotic to prevent septic shock in patients with VAP.
Key Words Predictors, mortality, ventilator-associated pneumonia.

PS080

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA IN INDONESIA

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Background and Aim of the Study Ventilator-associated pneumonia (VAP) is a frequent infection in intensive care unit (ICU) with high mortality rates. VAP features are not fully known in Indonesia. This study was designed to identify clinical and epidemiological aspects associated with VAP in National Referral Hospital of Indonesia.
Methods We analyzed data from patients admitted to ICU and developed VAP between January 2010 and December 2012. Clinical data, laboratory results, and outcome status were obtained from medical record. Categorical variables were analyzed using chi-square test or Fisher exact test, where appropriate.
Results A total of 147 (22.9%) ICU patients developed VAP. Early onset VAP was occured in 79 (53.7%) patients, and median onset was 4 (range, 2 to 22) days. There were 77 (52.4%) male and 70 (47.6%) female patients. The mean age of VAP population was 45.7 ± 16.8 years old and the median APACHE II score was 14 (range, 3 to 35). Immunocompromised and hypertension were the most common comorbidity (21% and 19%, respectively). Most patients were post major surgery (53.7%). Acinetobacter baumanii was found as the most common etiology (31.3%). Median length of hospital stay was 16 (range, 1 to 155) days. Death occurred in 54.4% of cases and mostly due to septic shock (38.8%). Age 60 years or older ($p = 0.001$), APACHE II score above 16 ($p < 0.001$), the presence of septic shock ($p < 0.001$) and comorbidity ($p = 0.017$) were factors related to mortality.
Conclusion VAP in Indonesia presented with a high frequency and high mortality rate. Attention should be given to patients with age 60 years or older, presence of septic shock, high APACHE II score, and presence of comorbidity.
Key Words clinical profile, Indonesia, ventilator-associated pneumonia.

PS081

THE RELATIONSHIP BETWEEN CRP AND ETIOLOGY PNEUMONIA FOR INPATIENTS PNEUMONIA COMMUNITY IN PULMONARY WARD M. DJAMIL HOSPITAL, PADANG INDONESIA

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Background It is important to distinguish bacterial from non-bacterial pneumonia. Over used of antibiotics lead to high cost burden. C-Reactive Protein (CRP) that produce by liver in acute phase of infection, has proposed as a marker of bacterial pneumonia. The aim of this study is assessing CRP's effectiveness distinguish bacterial from non-bacterial pneumonia in adult community acquired pneumonia.
Methods Cross sectional study. The subject of the study were inpatients with CAP in pulmonary ward M. Djamil Hospital Padang. We performed laboratory test for hematology and CRP in blood and poly chain reaction sputum. Receiver operating curve (ROC) was calculated.
Result We found Out 50 patients CAP, 44 (88%) of them had a final diagnosis of bacterial pneumonia. CRP's level in bacterial pneumonia higher than in non-bacterial pneumonia (mean 60,4632 ± 0,6603 vs 46.9196 ± 16,99). There was strong correlation between CRP's level and bacterial etiology of CAP base on PCR sputum. We performed Rank Spearman test using correlation coefficient $r = 0{,}358$; p value < 0,005 is considering as significant correlation. There was a significant difference in CRP between the 2 groups ($p = 0.011$). ROC analysis demonstrated an area under curve (AUC) of 0.834 (95% CI, 0.00 to 1.00). Cut-off point of bacterial pneumonia was 50 ng/dL.
Conclusion CRP is useful for distinguishing bacterial from non-bacterial pneumonia in adult community acquired pneumonia.

PS082

VALIDATION OF CURB-65 SCORING SYSTEM IN PATIENTS WITH HOSPITAL ACQUIRED PNEUMONIA

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Background and Aim of the Study CURB-65 scoring system has been widely used to predict mortality and stratifies risks in CAP (Community Acquired Pneumonia). Up to date, very few studies ever validate CURB-65 in HAP (Hospital Acquired Pneumonia). This study aims to recognize the sensitivity, specificity and accuracy of CURB-65 to predict mortality in Indonesian HAP patients.
Methods This is a diagnostic-validation study with the design of retrospective cohort. Subject's data were taken retrospectively from medical records within January 2006 to December 2012. We used Hosmer-Lemeshow test for accuracy and area under ROC (Receiver Operating Curve) for discriminating performance of CURB-65 scoring system. We also analyzed the specificity and sensitivity value of CURB-65 to predict mortality in HAP patients.
Results There were 171 patients included, all complete data and no drop-out. The overall mortality proportion of HAP in our cohort was 42.7%. There were 63 patients with score 0, 52 patients with score 1, 37 patients with score 2, 17 patients with score 3 and only 2 patients with score 4. We did not have any patient in our cohort with score 5. Hosmer-Lemeshow test showed a very good accuracy with p value 1.00. The area under the ROC was 0.376, this showed a bad discriminating performance of the scoring system. Mortality proportion increases in accordance to increment of CURB-65 score, from 33% of mortality in score 0 CURB-65 to 76.5% and 100% mortality in score 3 and 4, respectively. Using the cut-off value of score 2, the sensitivity was 71.2% and specificity was 42.9%.
Conclusion The higher the CURB-65 score, the higher the mortality is. CURB-65 has low specificity and sensitivity value to predict mortality in our setting. Therefore, we ought to develop another scoring system that has better mortality predicting performance for our HAP patients.

PS083

PREVALENCE AND RISK FACTORS OF CHRONIC CO-INFECTION IN PULMONARY MYCOBACTERIUM AVIUM COMPLEX DISEASE

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Background and Aim of Study Pulmonary *Mycobacterium avium* complex (MAC) disease has a prolonged course of infection and is often associated with bronchiectasis or cavitary disease. Various pathogenic microorganisms are often infected or colonized in patients with bronchiectasis. This study aimed to identify prevalence of co-infection with other pathogens than MAC and risk factors for the co-infection in patients with pulmonary MAC disease.
Methods We retrospectively analyzed 221 pulmonary MAC patients fulfilling the 2007 ATS diagnostic criteria who visited Kyoto University Hospital from January January 2001 to December 2012. We reviewed patient characteristics, microbiological results and chest computed tomography findings from medical records. We defined chronic pathogenic co-infection that potential pathogens other than MAC had been isolated from consecutive sputum samples taken on more than two visits >3 months apart.
Results Participants were predominantly female (77.8%) and infected with *M. avium* strain (78.7%). Of 221 pulmonary MAC patients, 101 patients (45.7%) had chronic co-infection with any pathogens. Methicillin-sensitive *Staphylococcus aureus* (MSSA) (n = 53), *Pseudomonas aeruginosa* (n = 26) and *Aspergillus species* (n = 14) were the most prevalent pathogens. MSSA co-infection was significantly associated with long duration of MAC disease (>8 years) (odds ratio [OR], 2.5; 95% confidence interval [CI], 1.2–5.5), history of COPD (OR, 6.4; 95%CI, 1.4–38.5), no history of tuberculosis (OR, 9.9; 95%CI, 1.6–203.4) and nodule finding (OR, 3.3; 95%CI, 1.2–11.3). P. aeruginosa co-infection was significantly associated with history of COPD (OR, 5.8; 95%CI, 1.1–36.7) and rheumatoid arthritis (OR, 15.6; 95%CI, 1.6–406.2). *Aspergillus spp* co-infection was significantly associated with pulmonary *M. intracellulare* disease (OR, 7.6; 95%CI, 1.7–38.3).
Conclusion Patients with pulmonary MAC disease had a high prevalence of chronic co-infection with potential pathogens including MSSA, *P. aeruginosa* and *Aspergillus*. Pulmonary *M. intracellulare* disease, long duration of MAC disease and history of COPD and rheumatoid arthritis were risk factors for chronic co-infection.

PS084

EFFICACY OF LONG-TERM LOW-DOSE AZITHROMYCIN ADMINISTRATION IN PATIENTS WITH SINOBRONCHIAL SYNDROME REFRACTORY TO CLARITHROMYCIN

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Background Several case reports have suggested the efficacy of long-term low-dose administration of azithromycin (AZM) in patients with diffuse panbronchiolitis refractory to long-term low-dose administration of clarithromycin (CAM).
Objective To evaluate the efficacy of low-dose AZM therapy in patients with frequent acute exacerbation (AE) of sinobronchial syndrome (SBS) despite long-term low-dose CAM therapy.
Methods Patients requiring hospitalization for frequent AE of SBS despite long-term low-dose CAM therapy were enrolled in this study. AZM, at a single dose of 250 mg, was administered twice a week to these patients. The sputum volume per day, sputum bacteriology and number of AE (additional antibiotics and hospitalizations) were measured during a 12-month period.
Results Three patients with SBS were enrolled. AZM resulted in significant reductions in sputum volume and the use of antibiotics for AE. The number of hospitalizations for AE was not significantly decreased as compared with low-dose CAM therapy. AZM did not influence sputum bacteriology.
Conclusion Long-term low-dose AZM administration might have efficacy in patients with frequent AE of SBS refractory to CAM.

PS085

CHRONIC PULMONARY ASPERGILLOSIS AS A NEGATIVE PROGNOSTIC FACTOR FOR PATIENTS WITH *MYCOBACTERIUM AVIUM* COMPLEX LUNG DISEASE: INCIDENCE AND RISK FACTORS

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Background and Aim of Study The risk factors of chronic pulmonary aspergillosis (CPA) for patients with *Mycobacterium avium* complex lung disease (MAC-LD) are unknown. We assessed the incidence and risk factors of CPA in patients with MAC-LD.
Methods We retrospectively analyzed the medical records of 1079 HIV-negative patients who had MAC-LD with or without CPA.
Results Median patient age was 70 years, and there were 650 female patients. Median follow-up time was 3.3 years. Of the 1079 patients diagnosed as having MAC-LD, 23 were complicated by CPA at the time of MAC-LD diagnosis, and in the remaining 1056 patients, 19 were complicated by CPA after diagnosis of MAC-LD. The overall cumulative 5-year mortality rate of patients with MAC-LD was 25.5% and that with MAC-LD complicated by CPA was 57.5%. A multivariate Cox proportional hazard model showed the presence of CPA to be a negative prognostic factor for patients with MAC-LD. The estimated incidence of CPA in patients with MAC-LD was 4.38 per 1000 patients per year. Risk factors for the incidence of CPA in patients with MAC-LD were presence of interstitial lung disease and radiographic features of fibrocavitary or fibrocavitary + nodular/bronchiectatic disease.
Conclusion The presence of CPA was a negative prognostic factor for patients with MAC-LD. When clinicians examine patients with MAC-LD, it is necessary to identify risk factors for CPA.

PS086

SURVEY OF PULMONARY ASPERGILLOSIS WITH SURGICAL TREATMENT

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Introduction Treatment for pulmonary aspergillosis has been a challenging issue. Despite the introduction and use of recently approved antifungal treatments, treatment for pulmonary aspergillosis remains to be difficult. Sometimes, surgical treatment is required. In this study, the pulmonary aspergillosis cases with surgical treatment were surveyed in our institute.
Method Pulmonary aspergillosis patients who received the surgical treatment were analyzed retrospectively. The data were collected from medical records.
Results The total cases were nine, five female and four male. Median age was 64 years old. As symptoms of pulmonary aspergillosis, four patients had hemoptysis/hemosputa, one cough, one sputum, and four asymptomatic. As an underlying disease, two patients had bullae, one diabetes mellitus, one COPD, one after lung transplantation, and four without an underlying disease. Serum beta-D-glucan was negative in all cases. Aspergillus antigen test showed positive results in four patients. Antifungal agents were not used before surgical treatment. Whereas, antifungal drug was used after surgical resection in five cases, two VRCZ, one L-AMB, one MCFG, and one ITCZ. The severe complications accompanying a surgical treatment have not been experienced. All patients had been doing well one month after surgery.
Conclusion Surgical treatment for pulmonary aspergillosis could be carried out without serious complication and demonstrated good postoperative course in selected cases.

PS087

ROLE OF SYNDECAN-4 IN ACUTE PNEUMONIA

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Background Syndecan-4 is a transmembrane heparan sulfate proteoglycan which is expressed in a variety of cells such as epithelial cells and neutrophils. Heparan sulfate glycosaminoglycan side chains of syndecan-4 have been reported to bind to several proteins such as growth factors and cytokines suggesting to have various biological roles. We have reported that syndecan-4 limits the extent of pulmonary inflammation and lung injury in murine LPS-induced lung inflammation model (Tanino Y, et al. Am J Respir Cell Mol Biol, 2012). The goal of this study was to clarify the role of syndecan-4 on acute pneumonia.
Methods Syndecan-4 in serum was first measured in patients with acute pneumonia and compared with healthy volunteers. Next, the relationship between syndecan-4 in serum and clinical parameters was analyzed. At last, survival rate was compared between wild-type and syndecan-4 deficient mice after intranasal instillation of S. pneumoniae.
Results In patients with acute pneumonia, syndecan-4 in serum was significantly higher compared with healthy volunteers, and had a negative correlation with pneumonia severity score. In addition, serum syndecan-4 on admission was higher in patients who improved in short term antibiotic therapy compared with those who required long term antibiotic therapy. Moreover, serum syndecan-4 gradually increased during therapy in patients who had improved in a short term antibiotic therapy in contrast to the stable levels of serum syndecan-4 in patients who had required long term antibiotic therapy. Furthermore, survival rate of syndecan-4 deficient mice was significant worse compared with wild-type mice.
Conclusions Syndecan-4 regulates pulmonary inflammation, and could be a useful biomarker in patients with acute pneumonia.

1-B3: RESPIRATORY INFECTIONS (NON-TUBERCULOSIS) 3

PS088

CLINICOPATHOLOGICAL FINDINGS OF FOUR CASES OF PURE INFLUENZA VIRUS A INFECTION

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Objective The purpose of this study was to perform clinicopathological evaluation for pure influenza A virus pneumonia.
Methods We performed clinicopathological analysis of four cases of pure influenza A virus infection.
Patients Four patients with pure influenza A virus infection were evaluated. Among them, three cases were caused by influenza A/H1N1pdm virus. Three patients were analyzed by autopsy and one by transbronchial lung biopsy.
Results We suggest that the interval between onset of influenza virus A infection and analysis affected the pathological findings. In acute phase, diffuse alveolar damage was observed. After more than 10 days, organizing pneumonia and marked proliferation of premature type II alveolar epithelium was observed. Clinically, intra-alveolar hemorrhage was observed in two patients. Pathologically, hyaline membrane formation and intra-alveolar hemorrhage were observed in all cases.
Conclusion Severe epithelial damage was determined as the main mechanism of respiratory failure caused by influenza A/H1N1pdm virus infection.

PS089

CLINICAL SIGNIFICANCE OF LYSOPHOSPHATIDYLCHOLINE IN COMMUNITY ACQUIRED PNEUMONIA

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Lysophosphatidylcholine (LPC) is a novel inflammatory lipid mediators, which has been suggested as an important biomarker to predict sepsis related mortality. Previous studies showed that decreased LPC concentration is associated with sepsis related mortality. So, we investigated serum LPC level in community acquired pneumonia to predict outcome and analyzed correlations between serum concentration and clinical parameters. We prospectively collected blood samples from patients who were diagnosed of community acquired pneumonia in Pusan national university yangsan hospital from August 2011 to February 2013. All blood samples were obtained initially (D1) and 7 day (D7) after. Obtained samples were immediately centrifuged and plasma was stored at –80 degree Celcius within 2 hour. We checked plasma LPC levels using ANZWELL LPC Assay Kit (Alfresa Pharma Corporation, Japan) which is an commercial enzymatic assay kit. We retrospectively reviewed medical records of patients and analyzed correlations between plasma LPC levels and clinical parameters such as pneumonia severity index (PSI), CURB65, simplified acute physiology score II (SAPS II). Forty five patients with community acquired pneumonia were included in this study. The mean PSI, CURB65 and SAPS II were 96.27 ± 41.374, 1.78 ± 1.363 and 34.47 ± 21.288, respectively. The mean serum LPC concentrations at day 1 and day 7 were 57.88 ± 43.42 umol/L and 72.60 ± 58.04 umol/L, respectively. The serum LPC concentration at D7 was significantly lower in non-survivor group (16.07 ± 30.83 umol/L vs 92.39 ± 52.15 umol/L, $p < 0.05$) even though the concentration at D1 did not differ between survivors and non-survivors. The serum LPC concentration at D7 were significantly correlated with PSI ($R = –0.444$, $p < 0.05$), CURB 65($R = –0.586$, $p < 0.01$) and SAPS II($R = –0.576$, $p < 0.01$), respectively. The LPC concentration at D7 correlated with clinical parameters of community acquired pneumonia. Persistently decreased concentration of LPC was significantly associated with mortality of community acquired pneumonia.

PS090

DETECTION RATE OF PNEUMOCOCCAL PNEUMONIA USING BINAXNOW STREPTOCOCCUS PNEUMONIAE TEST), A PROSPECTIVE COHORT STUDY IN A TERTIARY HOSPITAL IN MALAYSIA

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Background Pneumococcal pneumonia is the commonest causative agent for pneumonia worldwide. In Malaysia, the reported incidence of pneumococcal pneumonia is low due to poor sensitivity of conventional methods. The use of BinaxNOW, a urinary antigen test for Streptococcus pneumoniae can aid in the diagnosis of pneumococcal pneumonia.
Objective To determine the detection rate of pneumococcal pneumonia using BinaxNOW kit and to compare this with the conventional method, blood and sputum cultures.
Methods This was a prospective cohort study involving patients 18 years and above admitted for community-acquired pneumonia (CAP) or health-care associated pneumonia (HCAP) to UKMMC between December 2011 and June 2012. BinaxNOW test, serology for Mycoplasma, Legionella and Chlamydia and cultures from blood/sputum/respiratory tract including other routine investigations were taken.
Results 102 patients were recruited; 89 patients (87.3%) with CAP, 13 patients (12.7%) with HCAP. 57 patients (55.9%) had unknown aetiology of pneumonia. 11 patients (10.8%) had positive blood cultures. 8 patients (7.8%) had a positive urine BinaxNOW test and 6 patients (5.9%) had positive sputum cultures. Streptococcus pneumoniae was the commonest isolated accounting for 9 cases (8.8%) followed by Klebsiella pneumoniae in 7 cases (6.9%). 8 out of 9 patients with positive urine BinaxNOW test had negative cultures for Streptococcus pneumonia. 1 patient grew Streptococcus pneumoniae from the tracheal aspirate however the urine BinaxNOW test was negative.
Conclusion The use of urine BinaxNOW kit in UKMMC increased the detection rate of pneumococcal pneumonia in hospitalized patients by eightfold.
Keywords Streptococcus pneumoniae, community-acquired pneumonia, health-care associated pneumonia, BinaxNOW.

PS091

CLINICAL CHARACTERISTICS AND OUTCOMES OF NONTUBERCULOUS MYCOBACTERIAL LUNG DISEASE IN KING CHULALONGKORN MEMORIAL HOSPITAL, THAILAND

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Background and Aims The incidence of nontuberculous mycobacterial (NTM) infection has increased over past decades. However, there is variability of species among different regions and populations. We aim to study epidemiological and clinical characteristics of NTM lung disease (NTM-LD) in King Chulalongkorn Memorial hospital (KCMH), the major tertiary hospital in Bangkok, Thailand.
Methods We retrospectively reviewed medical records of patients who had positive NTM culture results from respiratory specimens, in KCMH, during 2006–2010. NTM-LD was defined by updated American Thoracic Society diagnostic criteria 2007. Demographic characteristics, underlying conditions and outcomes were evaluated by using descriptive statistics.
Results Total 178 patients had positive NTM cultures from respiratory specimens, 43 patients (24.1%) had been diagnosed NTM-LD, ten patients had disseminated NTM disease with lung involvement. Their mean (SD) age was 53.1 (19.9) years and 24 patients (56.8 %) were female. Mean (SD) body weight and body mass index (BMI) were 48.4 (9.3) kg and 18.0 (3.5) kg/m^2 respectively. The most common co-morbid illnesses were bronchiectasis or chronic lung diseases (n = 22) and human immunodeficiency virus (HIV) infection (n = 12). The major pathogens were *M.avium* complex (MAC) (n = 21, 48.8%), *M.abscessus* (n = 8, 18.6%) and *M.Kansasii* (n = 4, 9.3%). All patients who had disseminated NTM disease were infected by MAC and had coexisting HIV infection. Overall mortality rate was 23.8% in non-HIV infected patients and 40.0% in HIV infected patients. In addition, there were 17 patients (39.5%) had prior history of *M.tuberculosis* (TB) treatment.
Conclusions Clinical significant NTM-LD was 24.1% of positive NTM cultures isolated from respiratory specimens. Majority of cases had concomitant chronic lung diseases or immunocompromised. MAC and *M.abscessus* were major pathogens. Overall mortality was higher in HIV infected cases.

PS092

COMMUNITY-ACQUIRED PNEUMONIA IN COPD PATIENTS REQUIRING ADMISSION TO THE INTENSIVE CARE UNIT: RISK FACTORS FOR MORTALITY

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Background and Aim of Study The aim of this study is to identify factors predicting mortality in chronic obstructive pulmonary disease (COPD) patients with community-acquired pneumonia (CAP) requiring intensive care unit (ICU) admission, and to examine whether noninvasive ventilation (NIV) treatment reduces mortality.
Methods An analysis was performed on data from patients with CAP hospitalized in the ICUs of 19 different hospitals in Turkey between October 2008 and January 2011. Predictors of mortality were assessed by both univariate and multivariate statistical analyses.
Results Two hundred and eleven COPD patients with CAP were included. The overall ICU mortality was 26.8%. NIV treatment (Odds Ratio (OR) 0.11, 95% Confidence Interval (CI) 0.02–0.48, p = 0.004), hypertension (OR 0.10, 95% CI 0.01–0.87, p = 0.037), bilateral infiltration (OR 9.86, 95% CI 1.68–57.82, p = 0.011), length of ICU stay (OR 0.63, 95% CI 0.44–0.90, p = 0.011) and duration of invasive mechanical ventilation (IMV) (OR 1.13, 95% CI 1.02–1.25, p = 0.025) were independent factors related to mortality.
Conclusion In summary, non-invasive ventilation, hypertension and shorter ICU stay are associated with reduced mortality while bilateral infiltration and longer duration of IMV are associated with increased risk of mortality in COPD patients with CAP requiring ICU admission.

PS093

REAL-TIME LOOP-MEDIATED ISOTHERMAL AMPLIFICATION FOR THE IDENTIFICATION OF STREPTOCOCCUS PNEUMONIAE

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Background and Aim of Study A significant human pathogenic bacterium, Streptococcus pneumoniae was recognized as a major cause of pneumonia, and is the subject of many humoral immunity studies. Diagnosis is generally made based on clinical suspicion along with a positive culture from a sample from virtually any place in the body. But the testing time is too long, this study is to establish a rapid diagnosis method to Identification of Streptococcus pneumonia.
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 Streptococcus pneumonia. Three pairs of amplification primers required for this method were derived from a conserved DNA sequence unique to the Streptococcus pneumonia. The amplification was carried out at 63 degree Celsius using SYBR Green for 40 minutes with the tube scanner set to collect fluorescence signals at 1-minute intervals. Clinical samples of Streptococcus pneumonia and other bacteria were used to determine the sensitivity and specificity of the primers by comparing with an 18S ribosomal RNA-based nested PCR as the gold standard.
Results The new set of primers consistently detected laboratory-maintained isolates of Streptococcus pneumoniae from our hospital. The new primers also proved to be more sensitive than the published species-specific primers specifically developed for the LAMP method in detecting Streptococcus pneumonia.
Conclusion This study demonstrates that the Streptococcus pneumoniae LAMP primers developed here have the ability to accurately detect Streptococcus pneumoniae infections on the RealAmp platform.
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PS094

SAFETY AND TOLERABILITY OF SINGLE-DOSE TEDIZOLID PHOSPHATE IN A JAPANESE PHASE I STUDY

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Background Tedizolid phosphate (TZP) is a novel antibiotic for infections due to Gram-positive pathogens, including MRSA. The current study investigated the safety and tolerability of TZP in Japanese healthy subjects for its clinical development for nosocomial pneumonia (and skin and soft tissue infection).
Methods Japanese healthy male subjects (N = 36) received TZP intravenously (IV) over 60 min as a single infusion of 50 mg in step 1 (n = 9) and 100 mg in step 2 (n = 9), or placebo (n = 3 in each step). In step 3, subjects received TZP orally (PO; 200 mg n = 8, or placebo n = 4), or IV (200 mg n = 8, or placebo n = 4) in a two-way cross-over design. Safety investigations included assessment of adverse events (AEs), vital signs, ECG parameters, and laboratory tests.
Results A total of 3 out of 26 subjects (11.5%) receiving IV TZP experienced AEs: 1 out of 9 subjects (11.1%) in step 2 and 2 out of 8 subjects (25%) in step 3. One out of all 10 subjects (10%) receiving IV placebo solution experienced an AE (i.e. laboratory changes). Only one drug-related AE (3.8%, 1 out of 26 subjects) occurred in a subject receiving IV TZP 200 mg. In this subject, TZP administration was discontinued permanently and the AE (i.e. allergic rash) resolved after appropriate treatment. No AE occurred in subjects receiving IV TZP 50 mg, PO TZP 200 mg, or PO placebo. There were no serious AEs reported in any group. There were no clinically significant changes in vital signs, ECG parameters, and laboratory evaluations after TZP administration.
Conclusion Single-dose administration of TZP (50, 100 or 200 mg, both IV and PO) was well-tolerated in Japanese healthy male subjects.

PS095

SAFETY AND TOLERABILITY OF 7-DAY MULTIPLE-DOSE TEDIZOLID PHOSPHATE IN A JAPANESE PHASE I STUDY WITH A DOUBLE-BLIND, PLACEBO-CONTROLLED DESIGN

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Background Tedizolid phosphate (TZP) is a novel antibiotic currently under clinical development (phase III) for the treatment of nosocomial pneumonia and has successfully completed two global phase III studies for acute bacterial skin and soft tissue infections (ABSSSI). The current phase I study investigated the safety and tolerability of TZP in Japanese healthy male subjects to support its development for nosocomial pneumonia and skin and soft tissue infection in Japan.
Methods Twenty four subjects were randomised to receive TZP 200 mg or placebo once daily for 7 days, either intravenously (IV) over 60 minutes or orally [cohort 1 (IV): TZP n = 8 and placebo n = 4, cohort 2 (oral): TZP n = 8 and placebo n = 4]. Subjects were followed up for further 9 days. Safety investigations included assessment of adverse events (AEs), vital signs, ECG parameters, ophthalmologic examination, and laboratory tests.
Results Nine (37.5%) of 24 subjects experienced AEs (8 subjects receiving TZP in cohort 1 and 1 subject receiving placebo in cohort 2). All 9 subjects reported at least 1 drug-related AE. There were no serious AEs reported in any group. In cohort 1, the most frequently reported drug-related AEs were injection site paraesthesia (75.0%, 6 out of 8) and injection site pain (25.0%, 2 out of 8) in subjects receiving TZP; all were mild in severity. In cohort 2, atrial fibrillation occurred at moderate severity in one subject receiving placebo and was deemed by the investigator as a drug-related AE; placebo administration was discontinued in this subject. No clinically significant changes were found in laboratory evaluations, vital signs, ECG parameters, ophthalmologic examination, and physical examinations in this study.
Conclusions Tedizolid phosphate (both IV and oral) was well-tolerated in Japanese healthy male subjects during the 7-day administration and the follow-up period.

PS096

INCIDENCE OF NONTUBERCULOUS MYCOBACTERIA ISOLATION OUT OF RESIDENTIAL BATHROOMS OF UNTREATED PATIENTS WITH PULMONARY MYCOBACTERIUM AVIUM COMPLEX DISEASE

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Background and Aim of Study Little is known about an incidence of Nontuberculous Mycobacteria isolation out of residential bathrooms of patients with pulmonary Mycobacterium avium complex (MAC) disease (PMD). The aim of this study was to elucidate the incidence for untreated patients with PMD.
Methods Twenty consecutive patients with definitive PMD were included in this study. To examine the recovery of Nontuberculous Mycobacteria isolates, each sample was collected by seed-swab from bathtub inlet (BI), bathtub tap (BT), bathtub drain (BD).
Results Of 20 patients (men: 6, female: 14, mean age: 69 years old), the 15 patients had infection with M.avium (MA), and the 7 patients had infection with M.intracellulare (MI). Of individual 20 samples collected from BI, BT, BD, and SH, Nontuberculous Mycobacteria isolates were recovered from 19 (95%), 12 (60%), 17 (85%), and 4 (20%) samples, respectively, and Non-MAC isolates including M.gordonae, M.fortuitum, M.peregrinum and Mycobacterium sp. were recovered from 12 (60%), 12 (60%), 16 (80%), and 3 (15%) samples, respectively. MA isolates were recovered from 11 (55%) samples from BI, 2 (10%) from BD, and 1 (5%) from SH, and MI isolates were recovered from 1 (5%) from BI. Although MA isolates were recovered from 13 samples out of 10 of 15 bathrooms of the patients who had infection with MA, MI isolates were not recovered from any sample out of 7 bathrooms of the patients who had infection with MI.
Conclusion MA, MI, and the other Nontuberculous Mycobacteria isolates were recovered from the residential bathrooms of the untreated patients with PMD. The incidence of MI isolation from the residential bathrooms was rare, as had been previously reported, we therefore consider at present that residential bathroom of patient with pulmonary MI disease is unlikely as one of environmental sources or routes of MI infection.

1-C1: ASTHMA 1

PS097

MAST CELL-BASED PHENOTYPES OF ASTHMA IN INDUCED SPUTUM SAMPLES

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Background Asthma is now well recognized to be a heterogeneous disease, but no studies have been involved into mast cell (MC)-based phenotypes of asthma in induced sputum.
Methods Induced sputum samples were collected from healthy subjects (n = 16) and adults with stable asthma (n = 55). Inflammatory cell counts and whole-genome gene expression microarrays in induced sputum were analyzed. MC phenotypes in induced sputum were classified according to MC biomarkers (tryptase, chymase and carboxypeptidase [CPA3]). Differential genes over MC phenotypes were validated by qPCR.
Results Non-MC (n = 18), MCTC (n = 29) and MCT (n = 18) phenotypes were successfully identified, which was based on whether the mRNA expression of tryptase, chymase, or CPA3, was present in microarrays analysis of induced sputum at $P < 0.01$ detection value. In MCTC subtype, although it had similar demographic and medical characteristics in comparison with non-MC and MCT subtypes, there was an increase in FENO, eosinophil counts and proportion in induced sputum, bronchial sensitivity and reactivity, and worsening asthma control level (all $P < 0.05$), which would result from differential gene expression profiling such as TPSAB1, CPA3, CD1A, CD1B, CD1C, CEBPE, CLC, CLEC4F, DNASE1L3, GPR56, HDC and LTC4S. Furthermore, it had a higher proportion of MCTC subtype in eosinophilic asthma (EA) than other cellular inflammation phenotypes ($x2 = 22.41$, $P = 0.001$). Although eosinophil proportion and counts in induced sputum were associated with both tryptase ($r = 0.57$, $P < 0.001$; $r = 0.57$, $P < 0.001$, respectively) and CPA3 ($r = 0.68$, $P < 0.001$; $r = 0.65$, $P < 0.001$, respectively), multivariable logistic regression model indicated that only CPA3 (OR = 6.04, 95% confidence interval = [1.10, 32.97], $P = 0.038$) but not trptase (OR = 0.18, 95%CI = [0.02, 1.72], $P = 0.137$) contributed to EA.
Conclusion MC-based phenotypes of asthma in induced sputum have been established, in which MCTC phenotype played an important role in the underlying pathobiology of EA. Targeted MCTC would be a promising approach for treating EA.

PS098

EFFECT OF ZINC SUPPLEMENTATION ON PARTIALLY CONTROLLED AND UNCONTROLLED BRONCHIAL ASTHMA BASED ON ASTHMA CONTROL TEST (ACT)

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Bakground Asthma is a reversible airway narrowing due to airway smooth muscles contraction. There are some intrinsic factors related to the decrease of Zinc (Zn) level in asthma, which leads to severe and uncontrolled asthma. This study was conducted to find out the effect of Zn supplementation on partially controlled and uncontrolled astma. This study used ACT as a predictor of asthma control and FEV1 and ratio of FEV1/FVC.
Method This is an experimental analytic study, performed on Pulmonary Clinic in RSUD Dr. Soetomo Surabaya, Indonesia. 98 asthma patients were divided into two group, 49 patients with Zn supplementation and 49 patient without it. All were given β2 agonist inhalation and corticosteroid inhalation. Zn dispersible tablet were given for one month (30 days). Asthma Control Test (ACT) questionnaire and lung spirometry (FEV1 and FEV1/FVC ratio) test were taken before and after the study. The result was analyzed with Kolmogorov-Smirnov test and examined with Wilcoxon and paired sample t test.
Result There were significant improvement of ACT level on study group (ranging from 4–19 pre study score, increase to 6–25 of ACT score after supplementation). Percent predicted FEV1 was significantly improved, from 60,673% mean value (pre-study) into 66,959% after Zn supplementation. FEV1/FVC ratio was not significantly improved (from 43,24%–94,76% pre-study into 43,51%–100% after Zn supplementation).
Conclusion Zn improves ACT score and percent predicted FEV1 and insignificantly improve FEV1/FVC ratio on patients with bronchial asthma. This study concluded that Zn have the benefit to improve the severity and control of asthma. A question is left regarding the role of Zn in older asthmatic patient which might has an overlapping COPD, as there was no age limitation in this study. This could open some possibilities for another study.
Key Words Bronchial Asthma, Zinc, Asthma Control, ACT,FEV1, FEV1/FVC.

PS099

NUMERICAL DESCRIPTION OF BREATH SOUNDS IN ASTHMATIC PATIENTS

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We studied lung sounds in sixtyeight cases with asthma and tried to describe breath sounds objectively, i.e., numerically. We divided lung sounds into vesicular (V, n = 43), vesicular/broncho-vesicular (V/BV, n = 6), broncho-vesicular (BV, n = 14) and bronchial (B, n = 5) sounds by auscultatory findings. We measured expiratory/inspiratory (E/I) sound power ratio, highest frequency of inspiratory (HFI) and expiratory (HFE) sounds. Both sound power and sound frequency correlated well with auscultatory findings. E/I power ratio for V, V/BV, BV and B were 0.27 +/– 0.16 (mean +/– S.D.), 0.39 +/– 0.23, 0.49 +/– 0.40 and 0.72 +/– 0.55. HFE for V, V/BV, BV and B were 252 +/– 57.2 (Hz), 281 +/– 21.9, 410 +/– 21.9 and 472 +/– 68.6. HFI for V, V/BV, BV and B were 421 +/– 96.6, 443 +/– 60.9, 571 +/– 110.1 and 492 +/– 70.0. In subjects without wheezing (n = 60), E/I, HFE, and HFI were 0.34 +/– 0.032 (mean+/– SE), 293 +/– 12.9, and 460 +/– 15, respectively. In subjects who had wheezes (n = 8), E/I, HFE, and HFI were 0.43 +/– 0.077, 404 +/– 41.8, and 515 +/– 39. Breath sounds of patients with wheezes showed higher HFE, HFI and E/I than those of without wheezes. In subjects who did not have rhonchi (n = 58), E/I, HFE, and HFI were 0.35 +/– 0.047, 305 +/– 14.7, and 462 +/– 15.9. In subjects who had rumbling rhonchi (n = 10), E/I, HFE, and HFI were 0.33 +/– 0.089, 312 +/– 31.8, and 485 +/– 30.5. Basic breath sounds in wheezing patients were bronchial while those of non-wheezing patients were vesicular. Basic breath sounds were not different between patients with or without rumbling rhonchi. We conclude that numerical description of vesicular and bronchial breath sounds was possible. This sound analysis revealed that basic breath sounds of wheezing patients were bronchial breath sounds.

PS100

THE DIFFERENT SUPRESSIVE CAPACITY OF REGULATORY T CELLS ON TH1 AND TH2 CELLS IN PATIENTS WITH ASTHMA ATTACK

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Objective To study the different supressive capacity of regulatory T cells (Tregs) on Th1 and Th2 cells in patients with asthma attack.
Methods Recruited asthmatic patients (n = 30) and healthy control (n = 30), collected peripheral venous blood from healthy control and asthmatic patients in attack stage and stable stage respectively, and then isolated CD4+CD25+ CD127-/low Tregs and CD4+CD25-effect cells with immunomagnetic beads method (purity was above 90%). The effect cells were cultured with PHA stimulation with or without Tregs. Measured the proliferation (3H-Thymidine), expression of T-bet and GATA3 (RT-PCR), production of IFNr and IL-13 (LUMNEX) in effect cells with or without Tregs intervention. Analyzed the supressive capacity of Tregs on Th1 and Th2 cells in asthmatic patients in attack stage and stable stage, comparing with control group.
Results Tregs could suppress the proliferation of effect cells in both asthmatic and healthy groups, and the suppressive capacity of Tregs in patients with asthma attack decreased significantly when compared with healthy group (P = 0.003), but there was no significant decline in stable asthma (P = 0.07). The suppressive capacity of Tregs to the expression of GATA-3 and production of IL-13 in patients with asthma attack was less effective than in healthy group, but the suppressive capacity to the expression of T-bet and production of IFN-r in asthma attack did not decrease. The supressive capacity of Tregs in asthmatic patients in stable stage was modified in some degree, compared with asthma attack.
Conclusion There was deficiency for the suppressive capacity of Tregs on effect cells proliferation and Th2 cells function in asthma attack, but this deficiency was modified in some degree in stable asthma. The deficiency for the suppressive capacity of Tregs to Th2 but not Th1 cells may indicate the Th2-polarization in asthma development.
Key Words Tregs, Th2 cells, asthma attack, suppressive capacity.

PS101

THE SURVEY OF ADULT ASTHMA CONTROL IN JILIN PROVINCE IN CHINA

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Objective To investigate the situation of adult asthma control and management in Jilin province.
Methods Telephone interviewed with adult patients with moderate to severe asthma, who were discharged from the Second hospiatl of Jilin University from 2009–2011. 963 patients out of 1260 visited had finished the questionare by telephone. The questionnaire included possible risk factors such as age, sex, population group, area of residence, occupation, and income, the number of hospital and emergency room admissions in the next year followed dischargement from the Second Hospiatl of Jilin University, the education of physicians to patients, the partnership between physicians and patients, the understanding to GINA and using LABA/ICS in patients. Areas of residence were categorised as urban or rural.
Results 1. Most physicians (95.4%) in emergency, general medicine and respiratory medicine could educate and treatment asthmatic patients based on GINA, when patients were in hospital, but the follow up rate of patients was low (18.6%). 2. The adult asthma control in Jilin province was poor, the rate of hospital and emergency room admissions within one year after dischargement was high to 35.8%. 3. The risk factors to hospital and emergency room admissions within one year after dischargement were female, older than 60, income per month less than 1000 RMB, elementary school or lower education level, rural residence, do not use LABA/ICS regularly, do not keep in touch closely with doctors after dischagement (odds ratio (OR) were respectively 3.1, 7.4, 6.4, 4.7, 8.8, 2.4, 3.2). 4. Compared with urban residence, adult asthma control was worser than that in rural residence.
Conclusion The adult asthma control in Jilin province was poor, specially in rural residence, which may due to partly lower economic and educational level in our province.
Key Words adult asthma control, Jilin province, rural residence.

PS102

THE EFFECT OF ENDURANCE TRAINING-INDUCED PHENOTYPIC CHANGES OF RAT ADRENAL MEDULLA CHROMAFFIN CELLS ON EXERCISE-INDUCED BRONCHOCONSTRICTION

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Background A high prevalence of exercise-induced bronchoconstriction (EIB) can be found in elite athletes, but the underlying mechanisms remain elusive.
Methods Airway responsiveness, NGF and EPI levels, and chromaffin cell structure in high/moderate – intensity training (HiTr/MoTr) rats with or without ovalbumin sensitization were measured in a total of 120 SD male rats. The expression of NGF-associated genes in rat adrenal medulla was tested.
Results Both HiTr and OVA intervention significantly increased airway resistance to aerosolized methacholine measured by whole-body plethysmography. HiTr significantly increased inflammatory reaction in the lung with a major increase in peribronchial lymphocyte infiltration, whereas OVA significantly increased the infiltration of various inflammatory cells with an over 10-fold increase in eosinophil level in bronchoalveolar lavage. Both HiTr- and OVA-intervention up-regulated circulating NGF level and peripherin level in adrenal medulla, but down-regulated phenylethanolamine N-methyl transferase level in adrenal medulla and circulating EPI level. HiTr+OVA and HiTr+ExhEx (exhaustive exercise) interventions significantly enhanced most of the HiTr effects. The elevated NGF level was significantly associated with neuronal conversion of adrenal medulla chromaffin cells (AMCC). The levels of p-Erk1/2, JMJD3, and Mash1 were significantly increased, but the levels of p-p38 and p-JNK were significantly decreased in adrenal medulla in HiTr and OVA rats. Injection of NGF antiserum and moderate-intensity training reversed these changes observed in HiTr and/or OVA rats.
Conclusion Our study suggests that NGF may play a vital role in the pathogenesis of EIB by inducing neuron transdifferentiation of AMCC via MAPK pathways and subsequently decreasing circulating EPI.

PS103

RELATIONSHIP BETWEEN INHALER USAGE TECHNIQUE WITH ASTHMA CONTROLLED TEST (ACT) AND EMERGENCY DEPARTMENT VISITS

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Background and Aim of the Study Many patients have asthma that is inadequately controlled which is a cause of frequent emergency department (ED) visits and hospital admissions. Improper inhaler device technique is most likely one of the major causes associated with uncontrolled asthma. Our objectives were to evaluate the inhaler techniques among asthmatic patients, and its relationship with asthma control and ED visits, also to investigate factors associated with improper use of inhaler devices.
Methods A cross-sectional study was done on all the patients who visited asthma clinic at Persahabatan Hospital in June 2013 with the diagnosis of bronchial asthma and used steroid inhaler as a controller. Data was collect on demography, severity of asthma and asthma management. We assessed the inhaler techniques for each patient using an inhaler technique checklist based on Global Initiative for Asthma.
Results A total of 60 asthma patients were included in the study. Of these, 16 (39.1%) were males with a mean age of 51.00 ± 14.35 years, and 44 (77.3 %) were females with a mean age 51.73 ± 14.09. Improper use of asthma inhaler devices was observed in 36 (60%) of the patients and was associated with level of formal education ($p = 0.016$), irregular clinic follow-ups ($p = 0.01$), uncontrolled asthma ACT (score < 15) ($p = 0.04$), ED visits ($p = 0.00$). Multiple logistic regression analysis revealed that a lack of regular follow-ups ($p = 0.03$) and level of education ($p = 0.043$) were more likely to lead to the improper use of an asthma inhaler device.
Conclusion Improper asthma inhaler device use is associated with level education, irregular clinic follow ups, poor asthma control and ED visits. We suggest a prospective analytic study for determining the risk factors that can lead to improper asthma inhaler technique.

PS104

THE ROLE OF ADIPOKINES IN ASTHMA EXACERBATION

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Background Obesity is a risk factor for developing asthma. Adipokines has also been shown to increase airway inflammation and hyper responsiveness. However, little is known the role of adipokines in asthma exacerbation.
Objectives The purpose of this study is to evaluate the effect of adipokines in asthma exacerbation.
Methods This study enrolled 20 hospitalized patients with acute exacerbation, 43 stable patients with mild to moderate asthma and 10 normal subjects for comparison. Serum leptin and adiponectin levels were evaluated before and after treatment with systemic corticosteroids.
Results The serum adiponectin level differed significantly among the acute exacerbation patients (9.2 ± 6.6 μg/ml), stable asthmatics (10.6 ± 6.0 μg/ml), and normal subjects (7.5 ± 3.5 μg/ml). Moreover, serum adiponectin level in hospitalized patients after treatment (10.1 ± 6.7 μg/ml) was increased significantly. However, there were no difference in serum leptin level among the acute exacerbation patients before (11.8 ± 9.5 ng/ml) and after treatment (10.5 ± 6.2 ng/ml), stable asthmatics (10.8 ± 11.0 ng/ml), and normal subjects (9.6 ± 7.7 ng/ml).
Conclusion Decrease in serum adiponectin level may be associated with acute exacerbation of asthma. It may be considered as one of mechanism of refractory asthma in obese subjects.

PS105

SAFETY AND EFFICACY OF ORAL VERSUS INHALED CORTICOSTEROIDS IN MODERATE PERSISTENT ASTHMA AMONG CHILDREN 6 TO 15 YEARS OLD

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Background One out of 10 Filipino children suffer from bronchial asthma. Its increasing prevalence worldwide over the past decades causes significant morbidity to the patients and their families when uncontrolled. In developing countries, the form of medicine, cost and access to medications are significant factors in achieving good control of symptoms. This study aimed to determine if the use of low dose oral corticosteroid is a safe and effective alternative treatment for children with persistent asthma.
Methods Forty patients, 6 to 15 years old, with newly diagnosed moderate persistent asthma were randomized into two groups. For 3 months, the control group received inhaled corticosteroid (budesonide) at 200 mcg twice daily while treatment group received a single morning dose oral cosrticosteroid (prednisone) at 0.5 mg/kg (maximum dose: 10 mg/day). Efficacy was assessed based on daytime and nighttime coughing, limitation of activity, use of bronchodilators, FEV1, PEFR and level of asthma control. Safety parameters evaluated were blood pressure, pre and posttreatment determination of serum cortisol and fasting blood sugar levels.
Results Study participants from both groups showed comparable improvement in daytime and nighttime cough, need for bronchodilators and limitation of activity. PEFR is the only parameter that showed a significant difference, participants under the inhaled corticosteroid group showed lower PEFR values than the oral corticosteroid group throughout the entire study period. There was no significant difference in their FEV1 but basically had the same trend as that of the PEFR. There was no significant difference in the safety parameters evaluated. Study participants from both groups showed a decrease in cortisol levels after 3 months of treatment but none had signs and symptoms of adrenal insufficiency.
Conclusion There was no significant difference in the safety and efficacy of oral versus inhaled corticosteroid in the treatment of children with moderate persistent asthma after 3 months of treatment.

PS106

EVALUATION OF QUALITY OF LIFE AND EXPERIENCES OF HIGH-RISK ASTHMA PATIENTS TRANSFERRED FROM PAEDIATRIC TO ADULT CARE

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Introduction The transfer of care of paediatric asthma patients to adult hospitals is usually done at approximately 18 years of age. Currently, no structured transition program exists. The aim of this study was to evaluate the quality of life and experiences of high-risk asthma patients transferred from paediatric to adult care.
Methods A cross sectional questionnaire survery of 36 high-risk asthma patients whose care was transferred from KKH to the adult hospitals between 2004 to 2011, was done. The self administered Asthma Quality of Life Questionnaire (Standardised) [AQLQ(S)] was used to assess the quality of life.
Results 20 patients (56% response rate) returned the completed questionnaire and the AQLQ(S). The median (IQR) AQLQ(S) score was 193 (164–210). 75% of the participants felt that they were transferred to the adult service/hospital at the appropriate age. 80% of the subjects stated that they were given sufficient information/guidance about the transfer of care and knew what to expect from the adult service. None of the respondents faced any challenges/difficulties in the transfer of care process. Suggestions for improvement by the respondents included the need for (a) a detailed transfer medical report to the receiving physician, (b) better continuity of care and (c) improved communication at various levels.
Conclusion Asthma patients transferred from KKH to the adult hospitals continue to enjoy good quality of life. The results of this study highlight the need for well coordinated and robust transition of care arrangements for improving the quality of care for adolescents with chronic illnesses.

1-C2: ASTHMA 2

PS107

EFFICACY AND SAFETY OF ONCE-DAILY FLUTICASONE FUROATE/VILANTEROL 200/25 MCG COMPARED WITH TWICE-DAILY FLUTICASONE PROPIONATE 500 MCG IN ASTHMA PATIENTS OF ASIAN ANCESTRY

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Background and Aim of Study Fluticasone furoate (FF), a once-daily inhaled corticosteroid (ICS), and vilanterol (VI), a long-acting beta$_2$ agonist (LABA), are in development as a once-daily (OD) combination therapy for asthma. We assessed efficacy and safety of OD FF/VI, compared with twice-daily (BD) fluticasone propionate (FP), in patients of Asian ancestry.
Methods This was a randomised, double-blind, double-dummy, parallel-group study. Eligible patients using stable high-dose ICS or mid-dose ICS/LABA for >= 4 weeks before screening and ICS alone during run-in were randomised (1:1) to receive FF/VI 200/25 mcg OD or FP 500 mcg BD for 12 weeks. Primary endpoint: change from baseline in daily evening peak expiratory flow (PEF) averaged over the 12-week treatment period. Safety endpoints included adverse events (AEs), vital signs, ECG and laboratory evaluations.
Results The ITT population comprised 309 patients (mean age 47.9 years, 59% female); 255 completed the study. FF/VI produced significantly greater improvement from baseline evening PEF than FP (+28.5 L/min [95% CI: 20.1, 36.9]; $p < 0.001$). Statistically and clinically significant treatment differentiation was apparent at Week 1 and was maintained. The incidence of AEs overall were similar between groups (FF/VI 26%; FP 27%). The incidence of drug-related AEs was 3% in both groups; the most common drug-related AE was oropharyngeal pain (FF/VI 2%; FP < 1%). Three patients (1 FF/VI; 2 FP) reported a total of five serious AEs and all were withdrawn. There were no clinically significant changes in vital signs, 12-lead ECG parameters or laboratory evaluations.
Conclusion Once-daily FF/VI 200/25 mcg demonstrated clinically and statistically significant improvements in lung function compared with FP 500 mcg BD in patients of Asian ancestry, apparent from Week 1 and maintained over 12 weeks. No safety issues of clinical concern were identified with either treatment. Findings were consistent with previous observations in a mixed-ethnicity population (O'Byrne PM, ERS 2012).
Funding GlaxoSmithKline (HZA113714,NCT01498653).

PS108

RELATIONSHIP BETWEEN INFLAMMATORY CELLS ON SPUTUM INDUCTION AND ASTHMA CONTROL LEVEL IN ASTHMA PATIENTS

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Background Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. With appropriate treatment then the clinical manifestations of asthma can be controlled. The association between airway inflammation and asthma control level is not clear at present. The study was conducted to explore the relationship between inflammatory cells on sputum induction and asthma control level as determined by the Asthma Control Test (ACT).
Methods This is a cross sectional analytic study with consecutive sampling that was conducted in the asthma outpatient clinic Dr Soetomo Teaching Hospital, Surabaya, Indonesia. All participants were stable asthma patients who met the inclusion and exclusion criteria.
Results Data from 30 patients were analyzed (well controlled = 10, not well controlled = 8, uncontrolled = 12) with the percentage of eosinophils was 33.58 ± 8.76, basophils 3.92 ± 2.74, neutrophils 19.73 ± 8.44, lymphocytes 26.87 ± 9.66, monocytes 15.90 ± 5.79, and total cells count $39.60 \pm 10.47 \times 102$/ml. There was no significant correlation between inflammatory cells on sputum induction and ACT total scores ($p > 0.05$).
Conclusion Inflammatory cells on induced sputum examination can not be used as a parameter to determine the level of asthma control and vice versa.
Keywords asthma, inflammatory cells on induced sputum, asthma control level.

PS109

LONG-TERM FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE COMBINATION THERAPY IS ASSOCIATED WITH A LOW INCIDENCE OF SEVERE ASTHMA EXACERBATIONS

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Background and Aim of Study Asthma exacerbations are associated with reduced quality of life and increased healthcare cost. Fluticasone (FP) and formoterol (FORM) have been combined in a single inhaler (FP/FORM; *flutiform*(R)) for the maintenance treatment of asthma.
Methods Data for the number of severe exacerbations (requiring oral, IM or IV steroids) were pooled from 2 long-term FP/FORM studies and compared with those for other ICS/LABAs in long-term studies in broadly similar patient populations from 2 Cochrane reviews (Lasserson *et al Cochrane Database Syst Rev* 2011; Ducharme *et al Cochrane Database Syst Rev* 2010). In all, 472 patients with asthma (baseline FEV_1 % predicted 73.0%) received FP/FORM 100/10 μg or 250/10 μg b.i.d. for 6 or 12 months in Study 1; 280 patients with asthma (baseline FEV_1 % predicted 67.1%) received FP/FORM 250/10 μg b.i.d. for up to 14 months in Study 2.
Results The incidence of severe exacerbations with FP/FORM was 3.0% (95% CI 1.4, 4.5) in Study 1 and 2.9% (95% CI 0.9, 4.8) in Study 2; the pooled incidence was 2.9% (95% CI 1.7, 4.1). The reported incidences of exacerbations for FP/salmeterol (SAL) and budesonide (BUD)/FORM were 9.1–13.7% and 8.8–15.3%, respectively, and 2.9–29.5% for free combinations of FP, BUD or beclometasone and a LABA.
Conclusions Long-term FP/FORM therapy was associated with low rates of severe exacerbations in 2 distinct studies and populations; this incidence compares favourably with those from long-term studies of FP/SAL and BUD/FORM, and with free combinations of an ICS and a LABA. These data support the utility of FP/FORM in reducing the incidence of asthma exacerbations.

PS110

FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE IMPROVES ASTHMA CONTROL AND REDUCES EXACERBATIONS COMPARED WITH FLUTICASONE

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Background and Aim of Study The combination of fluticasone (FP) and formoterol (FORM) in a single inhaler (FP/FORM) is approved for the maintenance treatment of asthma. This analysis assessed the efficacy of FP/FORM versus FP in patients who had previously received ICS therapy.
Methods Data were pooled from 5 randomized studies in patients with asthma (aged ≥12 years) treated for 8 or 12 weeks with FP/FORM (100/10, 250/10 or 500/20 μg b.i.d.; N = 528) or FP alone (100, 250 or 500 μg b.i.d.; N = 527).
Results FP/FORM significantly ($p < 0.05$) improved lung function measures and increased the percentage of asthma control days (no symptoms, no rescue medication use and no sleep disturbance due to asthma) compared with FP (Table). The incidence and annualized rate of any exacerbation was significantly lower with FP/FORM.
Conclusions FP/FORM significantly improves lung function and asthma control measures, and is associated with a lower incidence of exacerbations compared with FP.

FP/FORM versus FP
Baseline[a] *pre-dose* FEV_1, *L* 2.034 vs. 2.034
Pre-dose FEV_1, *L* n = 525; n = 524
Change[b] 0.205 (0.163, 0.247) vs. 0.157 (0.115, 0.198)
Treatment difference[c] 0.048 (0.002, 0.095)

2 h post-dose FEV_1, *L* n = 527; n = 521
Change[b] 0.377 (0.338, 0.416) vs. 0.231 (0.192, 0.271)
Treatment difference[c] 0.146 (0.101, 0.190)

Asthma control days, % n = 519; n = 510
Baseline[a] 13.3 vs. 12.1
Change[b] 48.6 (44.9, 52.4) vs. 40.1 (36.3, 43.9)
Treatment difference[c] 8.6 (4.2, 12.9)

Any exacerbation n = 528; n = 527
Patients, % 29.9 vs. 36.6
Odds ratio (95%CI) 0.74 (0.57, 0.95)
Annualized rate 3.6 vs. 5.0
Rate ratio (95%CI) 0.71 (0.54, 0.94)

[a]Mean; [b]Least-squares mean (LSM) from baseline to study end (95%CI); [c]LSM (95%CI).

PS111

EFFICACY OF OMALIZUMAB IN PATIENTS WITH SEVERE ASTHMA USING THE ASTHMA HEALTH QUESTIONNAIRE (AHQ) AND ASTHMA CONTROL TEST (ACT)

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Background and Aim of Study 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 asthmaic 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.
Conclusion Omalizumab significantly reduced the number of emergency visits and methylprednisolone usage. AHQ and ACT were considered useful in the assessment of subjective symptoms in asthmaic patients.

PS112

EFFECTS OF THYMIC STROMAL LYMPHOPOIETIN (*TSLP*) GENOTYPES ON ASTHMA PHENOTYPES DEFINED BY THE ATOPY CLUSTER -INFLUENCE OF SMOKING HABITS-

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Background and Aim of Study Recent progress has been made in understanding the link between innate and adaptive immunity in asthma. We have previously reported that a distinct sensitization pattern was associated with thymic stromal lymphopoietin (*TSLP*) gentype. The aim of this study is to identify the characteristics of asthma phenotypes determined by a cluster analysis of IgE responsiveness and the relationship between asthma phenotypes and *TSLP* genotypes.
Methods We studied 263 adults' patients of asthma from Ibaraki, a prefecture in central Japan and 31 adults from Kamishihoro, a cedar-free, birch-dominant town in northern Japan. Levels of total serum IgE and specific IgE antibodies towards 14 major inhaled allergens were measured. With the use of these measures, cluster analysis was applied to classify the phenotypes of adult asthma. We also examined the genetic effects of 2 TSLP functional single nucleotide polymorphism (SNPs) on the development of each asthma phenotype using multinomial logistic regression analysis.
Results The cluster analysis identified four clusters, including Dust mite dominant ($N = 82$), Multiple pollen ($N = 14$), Cedar dominant ($N = 44$), and Low reactivity ($N = 154$). In current or past smokers, both SNPs (rs2289276 and rs3860933) were associated with the Low reactivity cluster (Odds ratio 2.11 [1.36–3.30] and 2.11 [1.34–3.33], respectively).
Conclusion In subjects of adult asthma who are less likely to be sensitized, the genetic polymorphisms of *TSLP* and smoking may have some important roles in the development of asthma.

PS113

ASTHMA AND ITS MANAGEMENT: IDENTIFYING DISTINCT PATIENT ATTITUDINAL CLUSTERS

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Background and Aim of Study Patient attitudes towards asthma vary and this may impact on disease management. This analysis was designed to group respondents to a large European survey into clusters based on their attitudes towards asthma and its management.
Methods Online surveys were completed by 8000 patients with asthma (aged 18–50 years, ≥2 prescriptions in the last 2 years) from 11 countries. Cluster analysis was used to identify different clusters of patients based on attitudes towards asthma.
Results Four different clusters were identified. Clusters 1 and 2 were defined by a high level of confidence in managing their asthma, and low levels of concern about the disease. Cluster 1 was more adherent to therapy and less likely to ignore HCP instructions than Cluster 2. Clusters 3 and 4 were more concerned about their asthma and considered it serious, and wanted to improve their disease management; these clusters had the lowest levels of GINA-defined control. Cluster 4 was less adherent to therapy and more likely to ignore HCP instructions than Cluster 3. Cluster 4 was most likely to seek additional information about asthma.
Conclusion This survey identifies four distinct clusters of patients with asthma that differ in attitude, adherence and educational need. Understanding these differences may facilitate the development of appropriate asthma management strategies.

Cluster 1($n = 2027$); Cluster 2($n = 1812$); Cluster 3($n = 1496$); Cluster 4($n = 2001$)
Confident in managing asthma %: 64; 64; 32; 36
Concerned about asthma %: 12; 4; 62; 33
Considered asthma serious %: 8; 2; 41; 20
Want to manage asthma better %: 36; 26; 67; 63
Take maintenance inhaler daily %: 52; 40; 60; 36
Ignore HCP instruction on taking maintenance inhaler %: 9; 26; 17; 45
Seek information about asthma %: 5; 1; 14; 38
GINA-defined control %: 25; 29; 2; 16

PS114

SUCCESSFUL OF THE NATIONAL ASTHMA PROGRAM USING THE EASY ASTHMA CLINIC MODEL TO IMPROVE ASTHMA MANAGEMENT IN THAILAND

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Introduction Asthma audit in 2007 found that asthma management in Thailand was suboptimal. Assessment of asthma severity and asthma control was mainly on symptoms. Peak expiratory flow was measured in only 1.08% of asthma visited in out-patient clinic. Inhaled corticosteroid was prescribed in only 10.92% of the visits. The National Asthma Program was undertaken by The National Health Security Office during 2010 to 2012 to improve asthma management using the Easy Asthma Clinic Model.
Method The program supported setting up the Easy Asthma Clinic in the hospitals throughout Thailand. The Easy Asthma clinic is the simplified specialized asthma clinic running by GP. In the clinic we simplified asthma guidelines and organized the system to facilitate the team work, emphasized the role of nurses and pharmacists to help doctors. We also developed on-line web database for registering and monitoring patients. The National Health Security Office also reimbursed for the use of inhaled corticosteroids.
Results There were 823 hospitals participated in this program. There were 44,124, 87,623, 106,693 patients with 133,012, 260,290, 350,834 visits attended the Easy Asthma Clinic in 2010, 2011 and 2012 respectively. Peak flow was measured in 87.76%, 98.62% and 91.34% in 2010, 2011 and 2012 respectively. Inhaled corticosteroids used increased to 79.43%, 86.51% and 86.78 in 2010, 2011 and 2012. Asthma Admissions decreased 17.8% from 67,813 visits in 2010 to 55,745 visits in 2012.
Conclusions The National Asthma Program in Thailand improved asthma management and decreased asthma admissions. The successful of the program was due to setting up the Easy Asthma Clinic and the reimbursed for the use of inhaled corticosteroids policy.

PS115

TIME COURSE OF SYMPTOM AND PULMONARY FUNCTION AFTER TREATMENT WITH FM/BUD

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Background and Aim of Study Particles of FM/BUD (Formoterol/Budesonide) are small enough to reach small airway, and formoterol has a rapid onset of bronchodilating effect. We compared time course of symptom and pulmonary function after treatment of FM/BUD, SM/FP (Salmeterol/Fluticasone), and SB (salbutamol).
Method We administered methacholine chloride inhalation to a healthy adult and started the examination when respiratory resistance rose to 20%. We measured respiratory function, respiratory resistance and Borg scale of four groups; control (no treatment), FM/BUD inhalation, SM/FP, and SB. The measurement points were; before loading methacholine, just after loading methacholine, then 1, 2, 3, 5, 10 and 20 minutes after inhaling the methacholine.
Result Borg scale recovered significantly at five minutes after inhaling the methacholine for the FM/BUD and SB groups, compared with the control group, and no change for the SM/FP group. Twenty minutes after inhaling, improvement of Borg scale was almost the same for the FM/BUD, SB and SM/FP groups. FEV1.0 and R20 did not show a significant difference in each group. R5-R20 declined significantly at three minutes after inhaling for the FM/BUD and SB groups, compared with the control group.
Conclusion An early improvement for Borg scale and R5-R20 was recognized for both FM/BUD and SB. This result was considered that FM/BUD treatment is useful for not only controller but also reliever.

1-C3: ASTHMA 3

PS116

INCREASE OF REGULATORY T CELLS MAY SUPPRESS AN EXACERBATION OF ALLERGIC BRONCHOPULMONARY MYCOSIS

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Introduction Allergic bronchopulmonary mycosis (ABPM) is characterized by type I, III, and IV allergic reactions to fungal antigens. Sero-positive ABPM (s-ABPM) has specific IgE and IgG antibodies to fungal antigens; this condition precedes ABPM characterized by centri-lobular bronchiectasis. We investigated differences in the production of Th17 cells ($CD4^+$ T cells producing IL-17) and regulatory T (T_{reg}) cells ($FOXP3^+CD4^+$ T cells) between patients with ABPM, s-ABPM, and bronchial asthma.
Methods We recruited 20 patients with ABPM, 11 patients with s-ABPM, and 74 patients with bronchial asthma. The diagnosis of ABPM was based on the Rosenberg criteria, and s-ABPM was defined as the presence of specific IgE antibody and an antigen-specific precipitating antibody to fungal antigens by Ouchterlony double immunodiffusion testing in the absence of centri-lobular bronchiectasis. We used flow cytometry to examine the percentages of $FOXP3^+CD4^+$ T cells and $CD4^+$ T cells producing IL-17 in the peripheral blood in our patients with ABPM, s-ABPM, and asthma in the phase without exacerbations.
Results The percentage of $CD4^+$ T cells producing IL-17 was greater in patients with ABPM ($P < 0.01$) or s-ABPM ($P < 0.05$) than in those with asthma. Patients with ABPM had fewer ($P < 0.01$) $FOXP3^+CD4^+$ T cells than did the other 2 groups. However the percentage of $FOXP3^+CD4^+$ T cells did not decrease in patients with s-ABPM compared with those with bronchial asthma.
Conclusion Among patients with ABPM or s-ABPM, peripheral Th17 cells increased relative to the production of specific IgE or IgG antibodies to fungal antigens in serum. The maintenance of $FOXP3^+CD4^+$ T_{reg} cells in patients with s-ABPM may suppress a progression to ABPM.

PS117

THE ONGOING ALLERGIC RHINITIS IMPAIRS ASTHMA CONTROL BY ENHANCING THE LOWER AIRWAY INFLAMMATION

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Background The relationship between allergic rhinitis and asthma is well accepted, however little is known about the mechanism underlying the interactions between the upper and lower airways.
Objective To investigate the symptomatic and inflammatory linkages between allergic rhinitis and asthma in atopic patients.
Methods We enrolled 520 asthmatics taking inhaled steroids, and examined them using the Asthma Control Questionnaire (ACQ), spirometry, exhaled nitric oxide fraction (FENO), visual analog scale (VAS) for nasal symptoms, allergic rhinitis questionnaire, and serum specific IgE (study 1). The symptomatic and inflammatory marker responses to nasal steroids in patients with incompletely controlled asthma (ACQ > 0.75) and moderate/severe persistent allergic rhinitis were also investigated (Study 2).
Results A total of 348 patients (66.9%) had atopy and allergic rhinitis. There was a striking difference in the proportion of patients with incomplete asthma control depending on the presence as well as the activity of rhinitis (no rhinitis, 11.0%; mild intermittent, 20.4%; moderate/severe intermittent, 44.6%; mild persistent, 53.1%; moderate/severe persistent, 65.7%). The FENO levels were increased with the activity of rhinitis, and the nasal VAS was positively correlated with the FENO levels ($r = 0.31$, $p < 0.0001$). The additive treatment with nasal steroids improved the nasal VAS, ACQ, and FENO levels, and the changes in these variables were correlated with each other in all parameters (all $p < 0.001$).
Conclusions This observational study of atopic patients indicates that the ongoing allergic rhinitis is related to worsening of asthma by enhancing the lower airway inflammation. Evaluation of the activity of allergic rhinitis appeared to be useful for assessing the impact of rhinitis on asthma, and effective intervention in that area could improve the management efficacy.

PS118

IP-10 UPREGULATE THE EFFECTOR FUNCTIONS OF EOSINOPHILS

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Background Eosinophils play an important role in the pathogenesis of bronchial asthma and its exacerbation. Recent reports suggest the involvement of IFN-γ-inducible protein of 10 kDa (IP-10) in virus-induced asthma exacerbation. The objective of this study was to examine whether IP-10 modify the effector functions of eosinophils.
Methods Eosinophils isolated from the blood of healthy donors were stimulated with IP-10 and the generation of eosinophil superoxide anion (O2-) was examined based on the superoxide dismutase-inhibitable reduction of cytochrome C. Eosinophil-derived neurotoxin (EDN) release was evaluated to determine whether IP-10 induced eosinophil degranulation. Cytokine and chemokine production by eosinophils was examined using a Bio-plex assay.
Results IP-10 significantly induced eosinophil O2- generation in the presence of ICAM-1. The enhanced O2- generation were inhibited by an anti-β2 integrin mAb or an anti-CXCR3 mAb. IP-10 increased the release of EDN. IP-10 increased the production of a number of cytokines and chemokines by eosinophils.
Conclusions These findings suggest that IP-10 can directly upregulate the effector functions of eosinophils. These effects might be involved in the activation and infiltration of eosinophils in the airway of asthma, especially in virus-induced asthma exacerbation.

PS119

EFFECT OF SWITCHING FROM FORMOTEROL/BUDESONIDE TO SALMETEROL/FLUTICASONE IN PATIENTS WITH ASTHMA

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Background The reduction of mortality rate of bronchial asthma is inversely related to the wide spread of inhaled corticosteroid use. In addition, devices of combined inhaled corticosteroids and long-acting beta-agonists have contributed the ease of controlling asthma symptoms in patients with asthma. Currently, there are two different available devices of combined inhaled corticosteroid and long-acting beta-agonist, salmeterol/fluticasone (SFC) and formoterol/budesonide (FBC) in Japan, but these drug profiles are different and the effect of switching from FBC to SFC is still unclear.
Patients and Methods Asthmatic patients treated with FBC 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). The times of 0, 4, 12 and 24 weeks after switching from FBC to SFC, asthmatic symptoms assessed by ACT and ACQ5, and spirometric analysis (FVC, FEV1, FEV1%, PEF, V50, V25) were evaluated. Airway resistance was assessed by Impulse Oscillation System, and exhaled levels of nitric oxide were measured by NioxMino in available patients. Monthly costs of asthma treatment in these patients were also evaluated.
Results Asthmatic symptoms assessed by ACT an ACQ5 were not statistically significant after switching from FBC to SFC. Spirometric analysis also revealed that the change of FVC, FEV1, FEV1%, PEF, V50, V25 were not statistically significant after switching from FBC to SFC. In addition, monthly costs for bronchial asthma treatment in these patients were significantly reduced after switching from FBC to SFC.
Conclusion Switching from FBC to SFC seems to be an alternative treatment option in terms of not only effectiveness of treating asthma but also treatment costs in patients with asthma.

PS120

THE CHARACTERISTICS OF ATOPY, BRONCHIAL HYPERRESPONSIVENESS AND LUNG FUNCTION IN ELDERLY ASTHMATICS

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Background The prevalence of elderly asthmatics is increasing and the mortality and morbidity are higher than young asthmatics. The characteristics of atopy, bronchial hyperresponsiveness and lung function in elderly asthmatics is worthy of further investigation in order to facilitate asthma management.
Methods In this retrospective, hospital-based study, 992 asthmatic patients, who were newly diagnosed or untreated (>3 months) at outpatient clinic, were recruited and divided into two groups, young (age < 65 years; mean, 32.4 ± 7.7 year old, n = 476) and elderly (mean, 75.2 ± 7.7 year old, n = 516) asthmatics. Lung function, methacholine provocation test (MCT)/bronchodilator test (BDT), smoking history, atopy (defined as positive serum allergen immunoassay), and serum IgE level were obtained.
Results The prevalence of atopy and serum IgE level was significantly lower in elderly group compared with that in young group. The bronchial hyperresponsiveness and reversibility (determined by MCT and BDT) were similar in both groups. In general, patients with bronchial hyperresponsiveness had poor forced expiratory volume in one second predicted value (FEV1 % pred.) and higher proportion of atopy. Elderly asthmatics with atopy had worse FEV1 than elderly non-atopic asthmatics (70.3 % vs. 77.6% pred.). On the contrary, young atopic asthmatics had better FEV1 compared with young non-atopic asthmatics. Young atopic asthmatics were significantly associated with airway hyperresponsiveness than young non-atopic asthmatics (p = 0.002). This was not observed in the elderly group.
Conclusions The characteristics of atopy, bronchial hyperresponsiveness and lung function in elderly asthmatics are different from those in young asthmatics. This may reflect the distinct pathophysiology, at least in part, in the elderly asthmatic airway.

PS121

FRACTIONAL CONCENTRATION OF EXHALED NITRIC OXIDE (NOBREATH®) FOR MONITORING ADULT ASTHMA IN OUTPATIENT CLINIC: RAMATHIBODI HOSPITAL EXPERIENCE

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Background Since fractional concentration of exhaled nitric oxide (FeNO) was set for monitoring of airway eosinophilic inflammation in asthma, the clinical value in real life practice has never been investigated.
Materials and Methods Cross sectional study in adult asthma patients treated at Ramathibodi Hospital between 2012 and 2013. FeNO was measured using portable analyzer NOBREATH® (Bedford UK.). The FeNO was expressed as ppb after 10 second-exhalation through 10 cmH2O positive pressure assuring velum closure. Asthma control was simultaneously assessed by Thai version asthma control test questionnaire (ACT) each visit. Data were analyzed by SPSS version 17.
Results There were 83 consecutive patients completed acceptable FeNO measurement at outpatient clinic. Mean age was 58.5 ± 14.1 years. Female patients were 71.1 %. Asthma treatments were mainly ICS-LABA combination. Asthma control test score (ACT) was performed prior to physician visiting. Therefore, patients were classified as controlled asthma (ACT > 19) and uncontrolled asthma (ACT <= 19). Among patients who were labeled uncontrolled asthma patients (n = 32), mean FENO was 57.0 ± 30.1 ppb. In addition, mean FeNO of controlled asthmatics (n = 51) was 61.8 ± 38.5 ppb. The measured FeNO as not significantly different between two groups of patients (p value 0.52).
Conclusion Despite the presence of controlled asthma assessing by composite score of asthma control (ACT), substantial numbers of patients have considerably high FeNO representing persistent eosinophillic airway inflammation. Discussion: High FeNO level may warrant physicians that those patients who have persistent airway eosinophilia are susceptible to loss of asthma control after discontinuing or reducing asthma treatment.

PS122

PHYSICAL AND COGNITIVE FUNCTION IMPAIRMENT IN ELDERLY WITH ASTHMA TREATED AT RAMATHIBODI HOSPITAL

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Introduction Asthma in the elderly is associated with poor outcome. Physical and cognitive function impairment may be contributing factors.
Material and Methods Cross sectional study in patients aged over 60 years in 2009. Clinical data regarding asthma were collected and physical function and cognitive function was tested.
Results Total 110 elderly with asthma were sampling from asthma clinic having mean age 69.9 years. Female were 78.2 % and overweight were 34.5% of patients. Airflow obstruction was graded as mild, moderate and severe in 38.2%, 22.5% and 14.7%. Common medical co-morbid were hypertension, dyslipidemia, rhinitis and arthritis. Most commonly prescribed inhaled therapy was corticosteroid and long acting β agonist (58.2%) while most common oral agent was theophylline (47.3%). Regarding inhaler devices, MDI was prescribed in 47.3% followed by turbuhaler (24.5%), accuhaler (20.2%) and MDI with spacer (8.2%). Un-scheduled visit due to asthma worsening in past year was noted in 31.8%. Patients ACT score classified as 25 (15.5%), 24–20 (72.7%) and less than 20 (11.8%). Low handgrip strength measured by using dynamometer (<18 kg) was noted in 43.6%. Resting and intention tremor were noted in 2.7% and 13.6%. Complete incisor was noted in 77.3%. All patients have normal mini-mental status examination or MMSE (6–10 points). Inhaler device technique was assessed and graded as good technique in 44.5%. There was no association between hand grip strength and ability to press canister (p < 0.086). Nevertheless, incomplete incisors are associated with ability to completely cover mouthpiece for MDI use.
Conclusion Significant proportion of uncontrolled asthma and experienced unplanned visits were observed in elderly. Half of cases have poor inhaler techniques which may be related to physical impairment. Discussion: Despite of the appropriate asthma pharmacotherapy, majority of elderly are uncontrolled. Inhaler device technique problem related to physical impairment has to be concerned in these patients.

PS123

SUPRAGLOTTIC NEUROFIBROMA MISTAKEN FOR BRONCHIAL ASTHMA: A CASE REPORT AND REVIEW OF LITERATURE

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Objective To improve the understanding of supraglottic neurofibroma, and discuss the atypical clinical signs of larynx neoplasm.
Methods A case of supraglottic neurofibroma diagnosed in April 2013 was reported and the related literatures were reviewed.
Results A case of a 26 year-old female patient, who had been misdiagnosed as bronchial asthma in local hospital, was admitted to our hospital because of short of breath after exercise for half a year and aggravated for 14 days. After admission, the bronchoscopy showed a giant space-occupying lesion which was located above the glottises and has smooth surface with completely encapsulated in supraglottic interarytenoid region. Subsequently, tumor resection under laryngoscope and general anesthesia was proformed. Pathology report after operation showed spindle cell tumor. Immunohistochemistry showed CD34(++), Bcl-2(+) and S-100(++). Accordingly, it was diagnosed as supraglottic neurofibroma. The symptom of short of breath was disappeared after operation. So far, there was no local recurrence and distant metastasis with 2 months follow-up.
Conclusions Supraglottic neurofibroma is rarely occur in the larynx and is easy to be misdiagnosed. To make a definite diagnosis relys on histopathology and immunohistochemistry test especially for the positive result of S100. If met such patients clinically, only if we carefully ask case history and do physical examination, combine of clinical symptom, pay attention to the distinction of wheezing sound between upper and lower respiratory tract, can we effectively lower misdiagnosis possibility, give timely diagnose and right treatment.

PS124

STUDY ON THE ASSOCIATION OF TSLP GENE POLYMORPHISMS WITH ATOPIC STATUS, PULMONARY FUNCTION AND AIRWAY HYPERRESPONSIVENESS IN JAPANESE ASTHMATICS

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Background Single-nucleotide polymorphism (SNP: rs2289276, rs3806933) of thymic stromal lymphopoietin (TSLP) has been reported to have susceptibility to bronchial asthma (Harada et al. AJRCMB, 2011). Association of polymorphisms of TSLP gene with atopic status, pulmonary function (PF) and airway hyperresponsiveness (AHR) has not fully been elucidated.
Objectives We analyzed the relationship between SNP of TSLP (rs3806933) and atopic status, PF and AHR in asthmatics.
Methods We recruited 280 asthmatics to the current study who visited the asthma out-patient clinic in Iwate Medical University Hospital from 2006 to 2012. Subjects were genotyped using rs2289276 and rs3806933 by 7500 Fast Real-Time PCR System, (Applied Biosystems USA). PF was evaluated by spirometer. AHR to methacholine was measured by Astograph; Jupitor 21 (Chest, Japan). AHR was expressed as D min (U). This study was approved by the ethics committee of Iwate Medical University.
Results Genotyping of rs3806933 showed that 165 C/C, 115 C/T and 19 T/T. Atopic status between C/C and C/T+T/T was significantly different (Chi-square analysis). Neither PF or D min of the 3 genotypes was not significantly different. However there was a significant difference of FEV1 %predicted between C/C and C/T+T/T in never smoker with asthma ($p = 0.015$, Mann-Whitney U-test).
Conclusion SNP (rs3806933) in TSLP was associated with atopic status and FEV1 %predicted in the never smoker of the current asthmatic population, suggesting that TSLP was involved in immune response induced by allergens and modification of immune reaction by smoking.

PS125

AGE-RELATED CHANGES IN AIRWAY RESISTANCE AND REACRANCE USING AN IMPULSE OSCILLATION SYSTEM IN PATIENTS WITH ASTHMA

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Background In the daily care of asthma, the degree of airflow obstruction as measured through spirometry is used as an index of asthma control, but because the implementation of spirometry requires the maximal forced expiration of the subject, this examination is a burden for elderly subjects. Impulse oscillation system (IOS) is able to measure airway resistance and reactance under quiet breathing using impulse waves. However, the usefulness of evaluating IOS parameters in elderly asthmatics is not clear. We investigated the usefulness of IOS and the correlation between IOS and spirometry in elderly patients with asthma.
Method IOS, spirometry and flow volume curve were performed for 51 elderly (65 years old or older: elderly group) and 58 non-elderly (below 65 years old: non-elderly group) patients with asthma.
Results There were significant correlation between IOS parameters (R5, R5-R20, Fres, X5) and lung function (%FEV1, %Vdot50, %Vdot25, %MMF) in each group. R5, R5-R20, X5 and Fres were significantly correlated with age, with Fres showing the strongest association. R5 (0.30 vs. 0.40, $P < 0.01$), R5-R20 (0.04 vs. 0.10, $P < 0.01$) and Fres (11.92 vs.15.83, $P < 0.05$) were significantly higher in the elderly group compared with the non-elderly group. X5 showed significantly low value in the elderly group than in the non-elderly group (–0.11 vs. –0.15, $P < 0.05$).
Conclusion These results suggest that IOS can be used to reveal small airway lesions in elderly patients with asthma and is useful as a method of evaluating airway lesions in patients with asthma.

1-D1: TUBERCULOSIS 1

PS126

CORRELATION BETWEEN 1ST LINE ANTI-TB DRUGS SENSITIVITY TEST AND SPUTUM CONVERSION AFTER INTENSIVE PHASE ON NEW CASE TB PATIENTS

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Background WHO acclaimed that between the year of 2002 until 2020 the estimation of one billion population will be infected by tuberculosis. Indonesian Health Ministry had performed sensitivity survey in Papua on 2003, with MDR TB as much as 2 % among new case TB and 14.7% among previously treated cases. The resistance of more than two 1st line anti-TB drugs leads to poor sputum conversion and treatment failure. This study aims to find the correlation between 1st line anti-TB drugs sensitivity test and sputum conversion after intensive phase on new case TB patients.
Methods This is a prospective analytic cohort study performed in the DOTS outpatient clinic at Dr. Soetomo Teaching Hospital during September 2011 until December 2011. Nineteen patients were enrolled in this study. All participants were new case, sputum positive who met the inclusion and exclusion criteria.
Result Of 19 sputum positive new case TB patients, 14 patients (73.7%) were sensitive to first line TB drugs, 3 patients (15.9%) were mono-resistance, 1 patient (5.3%) was poly-resistance, and 1 patient (5.3%) was MDR. Among 14 fully susceptible patients, 13 (92.2%) showed sputum conversion; 2 of 3 mono-resistance patients showed sputum conversion; patient with poliresistance showed sputum conversion. There was no conversion reported on MDR-TB patient at the end of intensive phase.
Conclusion There was no significant correlation between sensitivity test result and sputum conversion at the end of intensive phase in the new case, sputum positive TB patients treated with first category TB drugs.
Key Word(s) TB new case, sensitivity test, sputum conversion.

PS127

AN ENDOBRONCHIAL TUBERCULOSIS AS A PULMONARY MASS WITH METASTASIS-LIKE LESION OF SPINE

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A 26-year-old woman presented initially to Phnom Penh Heart Center with chief complaints of chest pain and dyspnea. As a heart investigation was normal and Chest X ray shows an atelectasis of a lower lobe of the left lung she has been referred to the oncology ward of Calmette Hospital for a further investigation. She presented with three-moth history of dry cough, shortness of breath, anorexia, weight loss, and a progressive back pain. She lived with her mother who has been treated for pulmonary tuberculosis 3 years ago. On physical examination she was thinly built and her vital signs were stable. There was no lymphadenopathy, enlargement of liver or spleen. The examination of respiratory system revealed diminished vesicular breath sound and vocal resonance in the left lower lung. Other examinations were unremarkable. She could not obtain available sputum sample for the examination of acid-fast bacilli. Complete blood count was normal (WBC: 7.04 giga/L, RBC: 5.85 tera/L, Hb: 133 g/L, Platelete: 380 giga/L), CRP: 0,29 mg/L, renal function test and liver function test were normal and HIV serology was negarive. The chest radiography showed an atelectasis of a lower lobe of left lung. The chest computed tomography demonstrated a mass of left lower lobe, with destruction of vertebral body of T11. Flexible bronchoscopy showed a mass of carina where the biopsy was performed. The result of anapathology showed an inflammatory reaction of granuloma tissue suggestive of tuberculous infection. The patient was put on a classic antituberculosis treatment (Category I: 2HRZE/4HR). After one month of treatment, she reported a remarkable improvement of her symptoms with an increased appetite.

PS128

PREVALENCE OF MULTIDRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS IN AND AROUND POPULATION OF VARANASI DISTRICT OF INDIA

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Background Multi-drug resistant (MDR) Mycobacterium tuberculosis is a serious threat to the national TB control programs of developing countries. For proper management and control of MDR-TB, understanding drug susceptibility pattern of M. tuberculosis isolates and their transmission pattern are essential. We carried out this study to assess the current prevalence of MDR-TB in new and previously treated cases of pulmonary TB in Varanasi district, Uttar Pradesh, and our observations on transmission of MDR isolates among populations in and around this area.
Methods A total of 713 M. tuberculosis isolates were obtained from 1691 patients diagnosed as pulmonary tuberculosis (PTB), of which 298 were from untreated subjects and 415 were from patients who were treated for tuberculosis in the past. Sputum samples were cultured on Lowenstein- Jensen media to isolate Mycobacteria. Drug susceptibility patterns of isolated M. tuberculosis isolates were recorded using 1 per cent proportion method. Transmission of MDR isolates in community was accessed by random amplified polymorphic DNA (RAPD). Isolates showing same band pattern on RAPD were retyped using different primers targeted to the inverted repeat sequence of IS6110 copies in M. tuberculosis genome.
Results 1. Prevalence of MDR was 18.6 per cent, initial and acquired being 10.3 and 26.4 per cent respectively. 2. Prevalence of resistance to any drug, MDR and individual drug resistance to isoniazid, streptomycin, ethambutol and rifampicin was significantly higher in patients who were treated in the past. 3. Genotypically similar clusters were seen at all levels of health care. It was not always possible to establish geographic connections within clusters.
Conclusion High prevalence of both initial and acquired MDR was noted in M. tuberculosis isolates collected from pulmonary tuberculosis patients. Presence of small clusters of MDR isolates at all health care levels suggests transmission within the studied community.

PS129

ADDITIONAL ROLE OF SECOND WASHING SPECIMEN OBTAINED BY FLEXIBLE BRONCHOSCOPY IN DIAGNOSIS OF TUBERCULOSIS

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Background Gaining bronchial washing is useful for diagnosis of pulmonary tuberculosis (TB), in patients with negative sputum smear or lack of sputum. However, the benefit of gaining serial bronchial washing specimens for TB diagnosis has not been studied. Therefore, we conducted a retrospective study to determine the diagnostic utility of additional bronchial washing specimens in suspected patients.
Methods A retrospective analysis was performed on 174 patients [sputum smear-negative, n = 95 (55%); lack of sputum specimen, n = 79 (45%)] who received bronchoscopy with two bronchial washing specimens with microbiological confirmation of TB in Samsung Medical Center, between January, 2010 and December, 2011.
Results TB was diagnosed by first bronchial washing specimen in 141 patients (81%), and an additional bronchial washing specimen established diagnosis exclusively in 22 (13%) patients. Smear for acid-fast bacilli was positive in 46 patients (26%) for the first bronchial washing specimen. Thirteen patients (7%) were positive only on smear of an additional bronchial washing specimen. Combined smear positivity of the first and second bronchial washing specimens was significantly higher compared to first bronchial washing specimen alone [Total cases: 59 (34%) vs. 46 (26%), $p < 0.001$; cases for smear negative sputum: 25 (26%) vs. 18 (19%), $p = 0.016$; cases for poor expectoration: 34 (43%) vs. 28 (35%), $p = 0.031$]. The diagnostic yield determined by culture was also significantly higher in combination of the two serial bronchial washing specimens compared to the first bronchial washing. [Total cases: 163 (94%) vs. 141 (81%), $p < 0.001$; cases for smear negative sputum: 86 (91%) vs. 73 (77%), $p < 0.001$; cases for poor expectoration: 77 (98%) vs. 68 (86%), $p = 0.004$].
Conclusions Obtaining an additional bronchial washing specimen could be a beneficial and considerable option for TB diagnosis.

PS130

IMPACT OF SOCIOECONOMIC STATUS ON NET OUTCOME OF DOTS CAT I & CAT II CASES

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Background Tuberculosis in developing countries like india has historically been associated with poverty and low socioeconomic status The purpose of this study was to assess the association of socio economic status (SES) on the outcome of tuberculosis drug therapy in patients of direct observed therapy (DOTS).
Methods Total 300 cases of tuberculosis, diagnosed by sputum microscopy & Chest radiography, were put on DOTS therapy. Cases were divided in two groups. Group A included 213 patients (73 patients of cat I & 140 patients of cat II) who were mostly patient belonging to low SES (below poverty line). Group B included 93 patients (53 cases of CAT I & 30 of CAT II) who could afford satisfactory lifestyle.
Results 11 of 73 cases on CAT 1 in group A resulted in treatment failure & became smear positive after 3 months of treatment (failure rate 15.06%) & 53 of 73 patients were cured (cure rate 78.08%). 7 patients defaulted during treatment. In group A cat II cases 53 of 140 patients came out MDR cases and were sputum positive after the 5 th month of treatment as Gene xpert was showing R resistance (failure rate:37.85%). 63 patients of CAT II completed the treatment of 6 months & were declared cured.24 patients defaulted during treatment. In group B 41 of 53 cat I patients were cured (cure rate 77.35%. 5 cases failed treatment (9.4 %). 7 cases defaulted. 22 of 30 cases in cat II (73.33%) were cured. 3 cases were declared MDR.5 cases defaulted the treatment.
Conclusion The result of present trial supports that most of the failure & drug resistant cases belong to low SES & were mostly smokers or alcoholics. Patients with satisfactory living style were more compliant &failure rate wassignificantly low as compared to Group A patients.

PS131

TRACHEOPATHIAOSTEOCHONDROPLASTICA AND TUBERCULOSIS: A CASE REPORT

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Patient is E.R. a 57 yo female, non-smoker seen at the outpatient for 4 weeks history of non-productive cough and hoarseness. There was no note of fever, weightloss and anorexia. She was treated as a case of pnuemonia, given several courses of antibiotics with no relief. 1 week after, there was difficulty of breathing and difficulty in sleeping described as choking sensation. Patient had stable vital signs, afebrile, 98% O2 saturation at room air, stridor and basal ronchi. Laryngoscopy showed hyperemic vocal cords with a polypoid mass on the right vocal fold. Cxray: infiltrates on the left upper lobe. Ct scan showed ground glass opacities in the superior segment of both lower lobes,fibrosis left apical lobe and narrowing of the right main stem bronchus and no lymphadenopathies. Neck Ct scan : no masses, but with irregular borders on the right bronchus,collapse of the right upper lobe Bronchosocpy : cobble stoning with hard protruding cartilaginous structures covered with cottony exudates seen from the trachea to the right main bronchus. Bronchial washing was positive for Kliebsiella Pnuemonia. Biopsy showed cartilage and fibrin material with inflammatory cells. AFB stain was positive for acid fast bacilli. She was started on INH/RIF/PZA/EMB for 6 months. Rigid bronchosopy was done to remove the remaining cartilaginous material. Histopathology confimed the diagnosis of Tracheopathiaosteochondroplastica revealing cartilage with areas of ossification. There was note of improvement of symptoms. Tracheopathiaosteochondroplastica is a rare disorder of affecting the large airways. It is described as multiple osseous and cartilageinous nodules in the submucosa of the trachea and main bronchi. Ecchondrosis, exositosis from tracheal rings or metaplasia of submucosal and connective tissue cartialage and/or bone tissue are theories to its development. The association of this rare disease entity with active pulmonary tuberculosis has not been presented.

PS132

PREVALENCE AND RISK FACTORS INDUCING HEPATITIS IN TUBERCULOSIS PATIENTS AT UTTARADIT HOSPITAL, UTTARADIT PROVINCE IN THAILAND

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The new tuberculosis patients are treated by standard medication regimen which has influenced to be hepatitis which may be severe until death. Hepatitis patient must stay in hospital and some of them are died because of severe hepatitis. This study is to examine prevalence and risk factors that influence to hepatitis. Descriptive retrospective study 187 samples treated at Uttaradit hospital in Uttaradit province, Thailand, South-east Asia from 1st January 2011–30th June 2012. The characteristic, medicine, liver function test, risk factors were collected and analyze from patient profile and question the patients. The result shows the hepatitis are male (16.4%), female (18.5%). There is a relationship between level of malnutrition and hepatitis ($p = 0.043$), then malnutrition stage is severe (20.7%), moderate (16.2%), mild (24.5%) and normal experienced hepatitis (5.4%) respectively. Risk factors ($p = 0.017$) influence hepatitis consisting of chronic diseases (45.2%). In addition, high dose of medicine induce hepatitis about 25 times of normal dose significantly ($p = 0.033$). Malnutrition induce hepatitis about 8.18 times of normal nutrition ($p = 0.031$). In conclusion, high dose of medicine, malnutrition and chronic diseases influence to induce hepatitis. Hence, the pharmacists must evaluate risk factors for monitoring liver function test and counseling the patient to evaluate sign/symptoms with themselves for preventing severe hepatitis.

Key Word Risk factor, hepatitis, Thailand.

PS133

AN INTERESTING CASE OF TUBERCULOSIS

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Psoas abscess is a rare clinical disorder which be a primary; following haematogenous dissemination or a secondary one; with local extension of an infectious process near the psoas muscle. Our case was a 21 year old male patient. His complaints presented as cough (began 8 months ago, more evident at last 2 months), loss of appetite, fatigue, weight loss (8 kg approximately), night sweat, back pain. The patient was a textile worker, nonsmoker. On physical examination; fever 36,7C, blood pressure 120/80 mmHg, pulse 84/min, breathing was 22/min, lomber and parasacral regions were painful with palpation. Right hip extension was painful, right hip joint range of motion (ROM) was limited. Posteroanterior chest X-ray revealed no abnormality but in lower sections of thorax CT a retroperitoneal abscess was observed. At lumbar MR dated 2/14/2013: the view was evaluated as psoas abscess with spondylodiscitis. He was BCG vaccined and his PPD was 10 mm. CRP: 85, ESR: 95 mm/h Serological tests: Rose Bengal test was negative. 24 hours urine smear was AFB (-) negative respectively. Sputum smear and culture results were reported as AFB (-) negative three times. He was HIV (-) negative. the case evaluated as a seconder psoas abscess with local extension of spondylodiscitis. The abscess was fully drained with an operation. The abscess material was AFB (+) positive with EZN staining. So a short course tuberculosis treatment was started on 02.20.2013 with (INH, RIF, ETB, MPZ). After two months dual treatment (INH, RIF) was continued. In the process patients pain was decreased, night sweat decreased, had an increase in body weight of 8 kilograms, also as an interesting finding his cough was disappeared. After 3 month treatment regimen a control MR was seen; complete response was achieved.

PS134

DIAGNOSTIC PROBLEMS IN UROGENITAL TUBERCULOSIS

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Background Urogenital tuberculosis is a common extrapulmonary manifestation of primary tuberculosis and is caused by the dissemination of Mycobacterium tuberculosis from the primary complex. Although the incidence of urogenital tuberculosis is 15–20% from extrapulmonary tuberculosis, but the diagnosis of urogenital tuberculosis is not easy.
Case A 44-years-old female came to Sanglah Hospital with chief complaint dysuria. She also complained of right back pain, hematuria and fever. She had an unclear history of lung tuberculosis. From the urology USG we found right moderate hydronephrosis with simple cyst and cystitis. Retrograde pyelography-ureterorenoscopy showed ureter stricture et causa suspicion of urethritis tuberculosis. The PCR TB from the pus was positive.
Conclusion A 44-years-old female with chief complaint dysuria, after undergone a series of examination and tests was diagnosed with urogenital tuberculosis. Patient was given antituberculosis drugs.
Keywords tuberculosis, urogenital, pcr.

1-D2: TUBERCULOSIS 2

PS135

DEMOGRAPHIC PROFILE OF PATIENTS REFERRED TO TUBERCULOSIS DIAGNOSTIC COMMITTEE (TBDC) AT UNIVERSITY OF SANTO TOMAS HOSPITAL, MANILA, PHILIPPINES

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Background and Aim of the Study The TBDC is a committee that is responsible for evaluating cases of TB symptomatics that are smear (-), but whose chest radiographs show lesions suggestive of tuberculosis. It was set up originally by the Department of Health, National TB Program (NTP) with the advise by WHO- Western Pacific Regional Office. The meetings being held at least every two weeks at University of Santo Tomas Hospital (UST), Manila, Philippines (high TB burden country). This study aimed to describe the demographic profile of patients referred to the committee.
Methods All outpatient and inpatient cases of the UST Hospital seen by TBDC from March 2012 to March 2013 were included in the study. A review of TBDC forms was done. The summary of report for each meeting was tabulated and descriptive statistics was done using SPSS version 16.
Results 211 patients were included in the study. 50.2% are males, most are 60–70 years old, 67.3% are non smokers, and 77.3% have no other known co-morbidities, but for those with co-morbidities, 10% are hypertensive, 3.8% diabetic and 2.8%known cancer. 57.8% have prior intake of anti-TB medications, of at least one month or more, in which 18% have completed outcome while 14.2% are not known. Majority (65.4%) have active TB requiring treatment under Category I and 26.5% under Category II. Most have multiple signs and symptoms, namely cough, weight loss and dyspnea. The common chest x-ray findings include fibrotic and ill defined infiltrates (74%), fibrocystic, fibronodular and granuloma (24%), suspicious fibrotic infiltrates (18%), cavitary (14%) and disseminated TB (14%).
Conclusion Clinicians must look into the many possibilities why direct sputum smear microscopy of a number of patients with cavitary and disseminated TB are negative. A significant percentage of patients are also Multi Drug Resistant TB(MDR-TB) suspects.

PS136

A NOVEL ASSAY TO DETECT NEUTRALIZING ANTI-INTERFERON-GAMMA AUTOANTIBODY IN CLINICAL SAMPLES WITH DISSEMINATED NON-TUBERCULOUS MYCOBACTERIAL INFECTION

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Rationale All of exposed subjects with non-tubelculouse mycobacterium (NTM) species do not develop active infection, which likely reflects underlying host susceptibility factors. Recent reports have shown that anti Interferon-Gamma (IFN-gamma) neutralizing autoantibodies (IFN-gamma Ab) are associated with disseminated NTM patients without known evidence of immunodeficiency. The purpose of this study is to establish the screening method if subjects have IFN-gamma Ab. Here, we report a novel bioassay to evaluate IFN-gamma signaling in whole blood and human T-cell line with patients plasma based on IFN-gamma stimulated, IFN-gamma receptor-mediated phosphorylation of STAT1, which is named the STAT1 phosphorylation index (STAT1-PI).
Method Blood was obtained from patients with disseminated NTM, pulmonary NTM and healthy controls. To evaluate neutralizing capacity to IFN-gamma, STAT-1 phosphorylation in leukocyte and T-cell line after stimulation with various concentrations of exogenous IFN-gamma (ranging from 1 to 1000 ng/ml) was evaluated by using flow cytometer. The strength of phosphorylation was described as STAT1-PI which was calculated as the mean fluorescence of cells primed with assigned concentration of IFN-gamma minus that of unprimed cells divided by that of unprimed cells multiplied by 100. Antigen capture assay was performed to measure the relative titer of Ig-G fraction of IFN-gamma Ab.
Result The STAT1-PI increased in proportion to IFN-gamma concentration reaching a maximum value near 1000 ng/ml and to time reaching in 30 minutes after stimulation. STAT1-PI with plasma from disseminated NTM patients was inhibited, while it from other disease and healthy subjects were not ($n = 6$: 7.3 plus or minus 27.8, $n = 3$: 424.8 plus or minus 21.9, $n = 6$: 243.4 plus or minus 133.9, $p < 0.01$). All of subjects with inhibited STAT1-PI have high concentration of IFN-gamma Ab(mean: 493 E.U.).
Conclusion The STAT1-PI is simple, useful flow cytometry-based method to measure IFN-gamma signaling in the evaluation of disseminated NTM patients suspected of having IFN-gamma Ab.

PS137

HYPERTONIC SALINE INDUCED AT CLINIC VISIT AND MORNING SELF-EXPECTORATED SPUTUM SHOWED NO DIFFERENCE IN THE BACTERIOLOGIC CONFIRMATION OF PULMONARY TUBERCULOSIS

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Backgrounds The bacteriologic diagnosis in pulmonary tuberculosis is confirmative, even though successful rates in self-expectorated sputum are limited. In the previous studies, sputum specimens induced by hypertonic saline nebulization facilitated bacteriologic diagnosis with higher sensitivity over those from self-expectorated sputum. The benefits of the sputum induction were investigated in the diagnosis of pulmonary tuberculosis.
Methods A prospective randomized case-control study in one hospital. The subjects highly suspicious of pulmonary tuberculosis were asked to provide 3 pairs of sputum specimens in 3 consecutive days. The first pairs of the specimens were obtained either by self-expectoration (SE) from the next day of the visit or sputum induction with 7% saline nebulization at presentation (HS) and the other pairs were collected in the same ways. The samples were used for acid fast bacilli staining, mycobacterial culture and PCR. The outcomes of bacteriologic detections were compared.
Results Seventy one patients were assigned either into SE (35 subjects, age of 52 ± 17, 69% male) and HS (36, 54 ± 17, 47%). Forty one subjects with pulmonary tuberculosis (57.7%) and 3 with non-tuberculous mycobacterial infection (4.2%) were diagnosed. At presentation, 21 (60%) of SE and 20 (55.6%) of HS revealed scanty amounts of sputum. ($p = 0.705$) In the mycobacterial detection, HS (13 subjects, 36.1%) and SE (13, 37.1%) showed no difference. ($p = 0.928$) Consequently, 22 (62.9%) of SE and 19 (52.8%) of HS were clinically diagnosed and treated as pulmonary tuberculosis. ($p = 0.39$).
Conclusions Sputum induction with hypertonic saline, even in patients with scanty sputum does not facilitate the bacteriologic confirmation of pulmonary tuberculosis.

PS138

INCREASED RISK OF PULMONARY TUBERCULOSIS IN PEOPLE WITH HEPATITIS C VIRUS INFECTION: A POPULATION-BASED COHORT STUDY

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Background and Aim of Study Both chronic hepatitis C virus (HCV) infection and pulmonary tuberculosis (TB) are prevalent worldwide, however, the association between HCV infection and pulmonary TB is not completely understood.
Methods We identified 4,094 adults newly diagnosed with hepatitis C infection in 2002–2004 from the Taiwan National Health Insurance Research Database. Comparison group consisted of 16,376 adults without hepatitis C infection randomly selected from the same dataset, frequency matched by age and sex. Events of pulmonary TB from 2002 to 2008 were ascertained from medical claims (International Classification of Diseases, Ninth Revision, Clinical Modification, ICD-9-CM, codes 011). Multivariate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for potential associated factors including HCV infection, age, sex, low-income status, urbanization, cessation of cigarette smoking, alcohol-related illness, obesity, history of chronic diseases and medication use.
Results During the follow-up period, there were 293 newly diagnosed pulmonary TB cases. After adjustment, the results showed that male (HR = 2.26, 95% CI = 1.77–2.88), age with 10-year increment (HR = 1.07, 95% CI = 1.06–1.08), and low-income status (HR = 1.94, 95% CI = 1.11–3.38) were risk factors for the risk of pulmonary TB. The cumulative risk of pulmonary TB for people with hepatitis C and without HCV infections was 2.1% and 1.3%, respectively ($p < 0.0001$). Compared with people without hepatitis C infection, the adjusted HR of pulmonary TB was 1.62 (95% CI = 1.24–2.11) for people with HCV infection.
Conclusion Chronic HCV infection increases the risk of pulmonary TB and should be considered an important and independent risk factor.

PS139

POTENTIAL FUNCTION OF GRANULYSIN, PERFORIN, IFN-γ AND LYMPHOCYTE SUBSETS IN PATIENTS WITH TB AND HIV/TB COINFECTION

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Background and Aim of Study Host effector mechanism against *Mycobacterium tuberculosis* (*Mtb*) infection is dependent on innate immune response by macrophages and neutrophils and the alterations in balanced adaptive immunity. Coordinated release of cytolytic effector molecules from NK cells and effector T cells and the subsequent granule-associated killing of infected cells have been documented; however, their role in clinical tuberculosis (TB) is still controversy. This study aims to investigate whether circulating granulysin and other effector molecules are associated with the number of NK cells, *i*NKT cells, $V\gamma9^+ V\delta2^+$ T cells, $CD4^+$ T cells and $CD8^+$ T cells, and such association influences the clinical outcome of the disease in patients with pulmonary TB and HIV/TB coinfection.
Methods Circulating granulysin, perforin, granzyme-B and IFN-γ levels were determined by ELISA. The isoforms of granulysin were analyzed by Western blot analysis. The effector cells were analyzed by flow cytometry.
Results Circulating granulysin and perforin levels in TB patients were lower than healthy controls, whereas the granulysin levels in HIV/TB coinfection were much higher than in any other groups, TB and HIV with or without receiving HAART, which corresponded to the number of $CD8^+$ T cells which kept high, but not with NK cells and other possible cellular sources of granulysin. In addition, the 17 kDa, 15 kDa and 9 kDa isoforms of granulysin were recognized in plasma of HIV/TB coinfection. Increased granulysin and decreased IFN-γ levels in HIV/TB coinfection and TB after completion of anti-TB therapy were observed.
Conclusion The results suggested that the alteration of circulating granulysin, perforin and IFN-γ have potential function in host immune response against TB and HIV/TB coinfection. This is the first demonstration so far of granulysin in HIV/TB coinfection.

PS140

CLINICAL PROFILE OF HIV-INFECTED PATIENTS WITH PULMONARY TUBERCULOSIS CAUSED BY MDR-TB IN INDONESIA

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Background and Aim of Study Tuberculosis is one of the most common presenting illness and the leading cause of death among HIV-infected patients. HIV infection increases the risk of pulmonary tuberculosis due to MDR-TB, but the clinical features are not fully known. We investigated clinical profile of HIV-infected patients with pulmonary tuberculosis caused by MDR-TB.
Methods We performed a cross-sectional study on HIV-infected patients with pulmonary tuberculosis during April 2012 to April 2013 in Cipto Mangunkusumo Hospital, National Referral Hospital of Indonesia. MDR-TB was confirmed by phenotypic drug-susceptibility testing.
Results Pulmonary tuberculosis was confirmed by sputum culture on 79 patients. MDR-TB was confirmed as etiology in 11 (13.9%) patients, 4 patients with new onset and 7 patients in recurrent pulmonary tuberculosis. Among patients with MDR-TB, there were 9 (81.8%) male and 2 (18.2%) female patients. Median age was 35 years. Four (36.4%) patients were diagnosed as HIV patients at admission, 5 (45.5%) patients had HIV for less than one year, and 2 (18.2) patients had HIV for more than one year. The most presenting symptoms were cough (81.8%), fever in 72.7%, night sweat 72.7%, and weight loss (100%) with mean BMI 18.8 kg/m^2. The median mean LED was 94.9 mm/hour and CD4 at diagnosis was 40 cells/ml. Normal plain chest radiography was seen in 4 patients. The most common abnormality found in plain chest radiography was bilateral extensive lungs infiltrate (5 patients).
Conclusion MDR-TB in Indonesia presented with high frequency. Early detections of MDR-TB should be performed in HIV patients with pulmonary tuberculosis since the clinical features were similar with pulmonary tuberculosis due to non MDR-TB pathogen.
Key Word clinical profile, HIV, MDR-TB.

PS141

PERFORMANCE OF XPERT MTB/RIF COMPARES TO LIQUID MEDIA CULTURE IN DIAGNOSING PULMONARY TUBERCULOSIS IN HIV-INFECTED PATIENTS IN INDONESIA

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Background and Aim of the Study The clinical features of pulmonary tuberculosis in HIV-infected patient are not typical. The accurate diagnosis of pulmonary tuberculosis in HIV-infected patient remains a clinical challenge. Xpert MTB/RIF is a new molecular modality for rapid diagnostic of tuberculosis. However, there is still no data regarding the performance of Xpert MTB/RIF in HIV-infected patients in Indonesia. We evaluated the accuracy of Xpert MTB/RIF in diagnosing pulmonary tuberculosis in HIV-infected patients in Indonesia.
Methods This is diagnostic test study of HIV-infected patients suspected of pulmonary tuberculosis from October 2012 to April 2013 in Cipto Mangunkusumo Hospital. We determined the diagnostic accuracy of Xpert MTB/RIF compared to liquid media culture.
Results A total of 66 patients were suspected having pulmonary tuberculosis, and 43 patients were confirmed by culture examinations. Most of the patients were 25 to 35 years olds (58%), male (73%), have a low BMI (53%) and low CD4+ (56%). Most of HIV-infected patients were intravenous drugs user (62%). Overall, the sensitivity and specificity of Xpert MTB/RIF were 93.0% (95% CI, 87.0% to 99.0%) and 91.3% (95% CI, 84.5% to 98.1%). The positive and negative predictive values were 95.2% (95% CI, 90.1% to 100%) and 87.5% (95% CI, 79.5% to 95.5%). Compares with smear microscopy (n = 20), Xpert MTB/RIF detected an additional 23 cases (n = 43) relative increase in the rapid TB case detection. The sensitivity Xpert MTB/RIF in a greater than or equal to 200 cells/ml better sensitivity than CD4 count less than 200 cells/ml in HIV-infected patients (91.4% vs 100%). Xpert MTB/RIF correctly identified rifampicin resistance in five cases of multidrug-resistant TB but incorrectly identified multidrug-resistant in one other patients (positive predictive value 83.3%).
Conclusion Xpert MTB/RIF has a good performance in diagnosing pulmonary tuberculosis in HIV-infected patients.
Key Words Diagnostic test, HIV, tuberculosis, Xpert MTB/RIF.

PS142

POST TUBERCULOSIS SEQUELAE: LUNG FIBROSIS AND HEMOPTYSIS

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Introduction Massive hemoptysis is frightening event for many patients and one of respiratory emergency that is associated with high mortality. Tuberculosis, along with bronchiectasis and lung abcess, account for 90% of cases. Case report We report 46 years old male patient, refererred with chief complain of hemoptysis 9 days before admission. Patient had a history of tuberculosis 3 years prior and several rehospitalisation because of hemoptysis. Chest radiograph showed old tuberculosis lesion at right upper lobe. Sputum and bronchoalveolar lavage smear examination result was negative for acid fast bacilli. Chest CT scan showed lung cavity which pulls trachea to lateral. Flexible bronchoscopy showed teleangiectasia at one third distal portion of trachea. Broncoalveolar lavage was taken, and citology result was suppurative inflammation. Despite medication, patient still experienced recurrent hemoptysis. Patient was planned to undergo thoracothomy procedure to control bleeding.
Conclusion Pulmonary fibrosis caused by cicatrix in airway and lung parenchym is one of tuberculosis sequelae. Other complication is hemoptysis caused by rupture of Rasmussen aneurysm. Surgery option may be taken to treat recurrent and uncontrolled bleeding.
Key Words hemoptysis, tuberculosis sequelae, lung fibrosis.

PS143

ASSOCIATIONS BETWEEN RECURRENT PULMONARY TUBERCULOSIS AND MDR-TB INFECTION EVENT IN PATIENTS WITH HIV

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Background and Aim of the Study Tuberculosis is one of the most common presenting illness and the leading cause of death among HIV-infected patients. HIV infection increases the risk of pulmonary tuberculosis due to MDR-TB. It's still unknown whether the occurence of recurrent increase the event of MDR-TB infection in patients with HIV. We investigated associations between pulmonary tuberculosis category and MDR-TB infection event in patients with HIV.
Methods We performed a cross-sectional study to HIV-infected patients with pulmonary tuberculosis during January 2012 to April 2013 in Cipto Mangunkusumo Hospital. MDR-TB was confirmed by phenotypic drug-susceptibility testing. We compared the proportion of MDR-TB event between new onset (Group-1) and recurrent (Group-2) pulmonary tuberculosis with Fisher's exact test.
Results A total of 79 patients were involved in this study, 47 patients were included in Group-1 and 32 patients were included in Group-2. MDR-TB was found in 11 patients, 4 patients in Group-1 and 7 patients in Group-2. Fisher's exact test showed no difference of MDR-TB infection event between groups (p = 0.109).
Conclusion Recurrence of pulmonary tuberculosis was not related to the increasing event of MDR-TB infection in patients with HIV.
Key Words HIV, recurrent, MDR-TB.

1-D3: TUBERCULOSIS 3

PS144

PROFILE OF TB-HIV PATIENTS IN CIPTO MANGUNKUSUMO HOSPITAL

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Background and Aim of the Study Tuberculosis (TB) is the most common opportunistic infection and the main cause of death in patients infected with Human Immunodeficiency Virus (HIV). TB-HIV cases showed a marked increase during the last few years. There has not been any study on the profile of TB-HIV patients in Cipto Mangunkusumo Hospital. The aim of this study is to assess the demographic, clinical, laboratory and radiologic characteristics of TB-HIV patients.
Methods We conducted a descriptive cross-sectional study by browsing through the medical records of TB-HIV patients who seeked medical treatment to Integrated HIV Outpatient Clinic (POKDISUS), Cipto Mangunkusumo Hospital within the period of July 2008–July 2012. Patients' medical records and confidentiality was maintained throughout the study.
Results A total of 667 patients were eligible as study subjects, mostly males (79.6%) and majority were in the 18–40 age group (91%). Demographic characteristics showed the following: 55.1% were married, 29.2% belonged to Batavian ethnic group, and 64.2% of the subjects were high school graduate. Transmission through intravenous drug user was the main mode of transmision (62.9 %). Oral candidiasis (37.12%) and hepatitis C (24.6%) were the most common co-infections. Chronic cough was the most common clinical manifestation (62.9%), followed by prolonged fever (53.8%) and weight loss (49.9%). Negative Acid Fast Bacilli smears were found in 39.6%, 51.3% had CD4+ counts of lt; 200 cells/μ 181;L and 47.4% showed radiologic (chest X-ray imaging) characteristics of TB.
Conclusion Profile of TB-HIV patients in our study is more or less similar with studies reported from other developing countries. High rate of intravenous drug user as mode of transmission showed the need for intervention in order to reduce this risk factor.

PS145

COMPARATIVE ANALYSIS OF WHOLE-BLOOD INTERFERON-γ AND FLOW CYTOMETRY ASSAYS FOR DETECTING POST-TREATMENT IMMUNE RESPONSES IN PATIENTS WITH ACTIVE TUBERCULOSIS

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Background Intracellular cytokine flow cytometry (ICCFC) has been explored to detect tuberculosis (TB) infections; however, there are little data regarding its use to examine the dynamic responses of Mycobacterium tuberculosis (MTB)-specific T-cells after anti-tuberculous therapy. The aim of the present study was to analyze both dynamic changes in functional MTB antigen-specific T-cell subsets and interferon-gamma (IFN-γ) levels using ICCFC and the QuantiFERON-TB Gold In-Tube (QFT-IT) test, respectively, following anti-tuberculous treatment in patients with active TB.
Methods Twenty-six patients with active TB were enrolled in the study, and QFT-IT and ICCFC were performed simultaneously both before and after treatment. IFN-γ levels (QFT-IT test) and the numbers of IFN-γ- or tumor necrosis factor-alpha (TNF-α)-expressing T-cells (ICCFC assay) were examined after stimulation with MTB antigen.
Results There was no significant reduction in the mean IFN-γ concentrations measured by the QFT-IT test after anti-tuberculous treatment ($p = 0.314$). ICCFC analysis showed that the numbers of IFN-γ^+/CD4$^-$ T-cells and CD4$^+$T-cells producing TNF-α, either alone or in combination with IFN-γ, were significantly reduced after anti-tuberculous treatment. The IFN-γ^+/TNF-α^+/CD4$^+$T-cell subset showed the greatest difference between untreated and treated patients with active TB (area under the curve = 0.734, $p = 0.004$).
Conclusions Unlike the QFT-IT test, ICCFC provides diverse immunological information about dynamic changes in the number of MTB antigen-specific T-cells following anti-tuberculous therapy. Thus, analysis of MTB antigen-stimulated T-cell responses using ICCFC might have a role to play in monitoring treatment responses in patients with active TB.

PS146

EFFICACY OF LATER-GENERATION FLUOROQUINOLONE FOR THE TREATMENT OF OFLOXACIN-RESISTANT MULTIDRUG-RESISTANT TUBERCULOSIS

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Background and Aim of Study To investigate treatment outcomes for patients with ofloxacin-resistant and moxifloxacin-susceptible multidrug-resistant tuberculosis (MDR-TB).
Methods Of 223 patients diagnosed with MDR-TB between January, 2006 and December, 2012 at Asan Medical Center, the 70 (31.4%) with ofloxacin-resistant MDR-TB were enrolled in this retrospective cohort study and their treatment outcomes analysed.
Results The mean age (SD) of the patients was 40.6 (12.9) years, 43 (61.4%) were male, and 26 (37.1%) had extensively drug-resistant TB. Of the 70 patients, 22 (31.4%) had moxifloxacin-susceptible TB. The remaining 48 (68.6%) had moxifloxacin-resistant TB. The moxifloxacin-susceptible and -resistant groups were comparable in terms of baseline characteristics (including age, sex, and radiologic severity), and 90.9% (20/22) and 70.8% (34/48), respectively, were treated with later-generation fluoroquinolone (FQ)-containing regimens ($p = 0.074$) [mostly moxifloxacin (40/54, 74.1%)]. Treatment success was achieved in 72.7% (16/22) of the moxifloxacin-susceptible patients and in 41.7% (20/48) of the moxifloxacin-resistant patients ($p = 0.021$). Treatment failure was significantly higher in the moxifloxacin-resistant group [41.7% (20/48) vs. 9.1% (2/22); $p = 0.006$].
Conclusion The treatment outcome for ofloxacin-resistant MDR-TB patients was significantly better for those with moxifloxacin-susceptible TB than for those with moxifloxacin-resistant TB.

PS147

COMPARATIVE CHEST COMPUTED TOMOGRAPHY FINDINGS OF NON-TUBERCULOUS MYCOBACTERIAL LUNG DISEASES AND PULMONARY TUBERCULOSIS IN PATIENTS WITH AFB SMEAR-POSITIVE SPUTUM

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Background Early diagnosis and treatment of nontuberculous mycobacterial lung diseases (NTM-LD) and pulmonary tuberculosis (PTB) are important clinical issues. The present study aimed to compare and identify the chest CT characteristics that help to distinguish NTM lung disease from PTB in patients with acid-fast bacilli (AFB) smear-positive sputum.
Methods and Patients From January 2009 to April 2012, we received 467 AFB smear-positive sputum specimens. A total of 95 CT scans obtained from the 159 patients were analyzed, 75 scans were from patients with PTB and 20 scans from NTM-LD. The typical chest CT findings of mycobacterial diseases were analyzed.
Results In patients with PTB, the prevalence of pleural effusion (38.7% vs. 15.0% ; $P = 0.047$), nodules < 10 mm in size (76.0% vs. 25.0%; $P < 0.001$), tree-in-bud pattern (81.3% vs. 55.0%; $P = 0.021$), and cavities (31.1% vs. 5.0%; $P = 0.018$) were significantly higher than patients with NTM. Of the 20 patients with NTM lung diseases, honeycomb appearances were significantly higher than patients with PTB (20.0% vs. 4.0%; $P = 0.034$). In multivariate analysis, CT scan findings of nodules was independently associated with patients with diagnoses of PTB (odds ratio = 0.07; 95% confidence interval [CI], 0.02–0.30). Presence of honeycombing in CT scans was strongly associated with patients with NTM-LD (OR, 33.04; 95% CI, 3.01–362.55).
Conclusions The CT distinction between NTM-LD and PTB may help radiologists and physicians to know the most likely diagnoses in AFB-smear positive patients and avoid unnecessary adverse effects and the related costs of anti-TB drugs in endemic areas.

PS148

COMPARISON OF SPOT AND EARLY MORNING SPUTUM COLLECTION

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Background Sputum examinations are still the gold standard to confirm tuberculosis and to evaluate treatment outcome of anti-tuberculosis medication. However, poor quality of the sputum can lead to a lack of growth from the specimen. This study aims to investigate the sputum detection rate by comparing two collection methods (1) the negative pressure room (spot) and (2) at home (early morning).
Methods Subjects in Changhua hospital presented with cough over 2 weeks, sputum, abnormal X-Ray or with existing tuberculosis were included in the study. All sputa were taken after subjects rinsing with distilled water. The spot collection was performed in the negative pressure room with supervision from a medical staff. Home (early morning) collection was undertaken when the patient first woke up. All the sputa were smeared and cultured, and the results were compared and analyzed to determine the positive tuberculosis (TB) rate, nontuberculous mycobacterium (NTM) rate and contaminate rate.
Results A total of 1294 set sputum samples were collected from 01 January 2010 to 31st December 2012 and analyzed in this report. The early morning sputa generally yield the best number of organisms, however, our study showed a higher positive TB detective rate from the spot collection (5.6%) than the early morning collection (4.9%). The NTM (15.2%) and contaminant rates (3%) were much higher in the early morning collection than in the spot collection (7.6% and 0.9% respectively). These could be due to poor sputum quality collected from home as subjects failed to rinse with distilled water before sputum collection, and a lack of staff supervision and collection of saliva instead of the deep respiratory secretion from the chest.
Conclusion The supervision of the medical staff and rinsing with distill water were found to improve the quality of the sputa.

PS149

CLINICAL FEATURES AND OUTCOMES OF DISSEMINATED INFECTIONS CAUSED BY NON-TUBERCULOUS MYCOBACTERIA IN A UNIVERSITY HOSPITAL IN TAIWAN

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Objective This retrospective study investigated the clinical characteristics and prognostic factors of patients with disseminated infections caused by nontuberculous mycobacteria (NTM) in Taiwan.
Methods All patients who fulfilled the criteria for disseminated NTM infection at a medical center in Taiwan from January 2004 to December 2008 were analyzed.
Results Disseminated NTM infection was diagnosed in 40 patients. More than half of the patients (n = 22, 55%) had HIV infection and fever was the most common initial presentation (n = 21, 52.5%). There were 13 episodes of co-infection with other bacterial pathogens in 11 patients (30%). The most common site of NTM isolation from culture was blood (62.5%) followed by respiratory tract (52.5%). M. avium complex was the most common isolated species (70%). The overall mortality rate due to disseminated NTM infection was 30%. Univariate survival analysis showed significantly higher mortality rates in female patients, patients without anti-NTM treatment, and patients co-infected with other bacterial pathogens. Multivariate analysis showed that lack of anti-NTM treatment was the only prognostic factor for poor outcome ($p = 0.001$).
Conclusions Maintaining a high level of suspicion and starting appropriate anti-NTM treatment promptly after diagnosis are crucial to improve outcome of patients with disseminated NTM infection.

PS150

ASSOCIATION OF TUMOR NECROSIS FACTOR-ALPHA LEVEL WITH PULMONARY TUBERCULOSIS INCIDENCE

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Background Tuberculosis can occur anywhere in the body, but most of the lung parenchym. Factors that play a role in the control of M.tb infection are T cells, macrophages, and cytokines IFN-γand TNF-α. After fagosits M.tb, macrophages stimulated to produce TNF-α. TNF-αcauses proinflammatory cells migrated transendothelial to the lungs to form a granuloma which prevents the spread of M.tb by locking it.
The aims of this study to identify and analyze the mean levels of TNF-αin pulmonary TB patients and those without TB, and investigate the relationship of TNF-αlevels with the incidence of pulmonary TB that can be used in the evaluation of TB treatment.
Method A case-control prevalence analytical design with cross sectional approach. Performed in the pulmonary clinic and inpatient of internal medicine of RSMH Palembang, from March 2012 to January 2013. Samples that meet the inclusion and exclusion criteria drawn up by consecutive sampling until number of 30 cases and 60 controls.
Results A total of 90 subjects, comprising of 57% men and 43% women with a mean age of 37 years. TNF-αcut-off point levels is 2.927 pg/ml, odds ratio 2.983 and 95% confidence interval 1.202–7.408. The mean TNF-α serum level in pulmonary TB is 6.99 ± 10.45 pg/ml, were significant higher than no TB 3.59 ± 3.11 pg/ml.
Conclusion There is significant difference TNF-αserum level in pulmonary TB and no TB. There is a significant association between TNF-α serum level with pulmonary tuberculosis incidence.
Keywords Pulmonary tuberculosis, TNF-α.

PS151

CORRELATION OF INTERFERON GAMMA LEVEL WITH INCIDENCE OF PULMONARY TUBERCULOSIS

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Background T cell helper-1 (Th-1) plays an important role in immune system, especially for intracellular bacterial infections. One of the cytokines produced by Th-1 cells is interferon-gamma (IFN-γ), which plays an important role in eliminating the M.tuberculosis. This study aimed to see if there was a level of IFN-γwith pulmonary TB incidence.
Method Serum levels of IFN-γwere measured by ELISA in 30 TB patients, 32 patients with tuberculin test >10 mm and 28 patients with tuberculin test < 10 mm. We use Receiver Operating Characteristic (ROC) and Odd Ratio (OR) to analyze the relationship between the levels of IFN-γwith tuberculosis.
Result The result of the IFN-γserum levels of 30 pulmonary tuberculosis patients obtained 11.80 ± 9.55 pg/mL with a range from 4.54 to 43.90 pg/mL, 32 subjects with tuberculin test >10 mm 8.36 ± 1.76 pg/mL with a range of 5.56 to 12, 80 pg/mL, and in 28 subjects with tuberculin test < 10 mm 7.99 ± 1.81 pg/mL with a range from 5.82 to 12.90 pg/mL. There were no significant differences in serum IFN-γlevels between the three groups ($p = 0.210$). Cut-off point gained 8.43 pg/mL with a sensitivity of 60% and specificity of 62%. There was no significant association of serum levels of IFN-γwith the incidence of pulmonary tuberculosis ($p = 0.052$).
Conclusion There were no significant differences among the three groups and no correlation with the incidence of pulmonary tuberculosis. Serum levels of IFN-γcan be used as a marker of TB infection but can not determine active or latent TB.
Key Words Pulmonary tuberculosis, tuberculin skin test, IFN-γ.

PS152

PROFILE OF TUBERCULOSIS PATIENTS OVER 6 MONTHS AT SINGAPORE GENERAL HOSPITAL (SGH)

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Background Poor compliance to tuberculosis (TB) treatment has many adverse consequences including longer treatment period, drug resistance, relapse and the possibility of infecting others.
Aim To profile tuberculosis patients who missed their appointments.
Method Between June and December 2012, all patients who were actively followed up for TB but missed their scheduled appointments were contacted via telephone to elucidate reason for default.
Results Over the 6 months, there were a total of 319 patients accounting for 879 visits to Singapore General Hospital (SGH) for follow up of TB treatment. 78 (24.5%) patients were absent for their appointments whereby 53(67.9%) patients missed once, 18(23%) patients missed twice only and 7(9%) patients missed more than twice. Patients treated were mostly Singaporean (85%), male (64.3%), Chinese (67.1%), and age greater than 65 years old (32.9%). However, Malays (40.4%) were likely to miss their appointments. Further analysis, showed 55.6% of patients between 10–19 years old missed their appointments, more than twice that of patients in other age range. Unfortunately, a large proportion couldn't be contacted via telephone to elucidate reason for default. However, common reasons for defaulting were readmission to hospital (25.6%), patients forgetting appointments (11.5%), migration (11.5%) and death (3.8%). Patients older than 65 years old were likely absent due to readmission to hospitals (44%) and foreigners, tended to be absent due to migration. Of patients who missed appointments the first time, letters were sent to 29 patients and 14(48.3%) returned for follow-up. Of patients who missed appointments the second time, recall letters were sent to 10 patients and 4(40%) returned.
Conclusion From our profile, Malay ethnicity and patients between 10–19 years have a higher risk of default. Success rate with recall letter was around 50%. Implementation of pre-TB treatment education could improve patients' understanding of the disease and importance of compliance to treatment and perhaps reduce defaulter rates.

1-D4: COPD 1

PS153

THE INCLUSION OF MANUAL THERAPY IN A PULMONARY REHABILITATION PROGRAM FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A RANDOMIZED CONTROLLED PILOT TRIAL

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Background and Aim of Study The primary source of exercise limitation in people with chronic obstructive pulmonary disease (COPD) is dyspnoea. Part of the cause for this has been attributed to changes in chest wall mechanics, with a decrease in chest wall mobility contributing to the decrease lung function. As manual therapy (MT) is known to increase joint mobility, administering MT to people with COPD introduces the potential of reversing this process, even if only for the short term. The aim of this trial was to investigate the effect on lung function of including MT in a pulmonary rehabilitation (PR) program for patients with COPD.
Methods 33 participants with COPD, aged between 55 and 70 years (mean = 65.5 years ± 4), were randomly assigned to three groups: PR only, soft tissue manual therapy (ST) and PR, and ST and spinal mobilisation (SM) and PR. Outcome measures were recorded at 0, 8, 16 and 24 weeks.
Results A clinically significant increase was reported in forced vital capacity (FVC) between the three groups at 24 weeks ($p = 0.03$). For the ST+SM+PR Group versus PR only the increase was 0.44 litres (SE: 0.16; $p = 0.02$). In the six minute walking test (6MWT), despite a significant difference between groups at 16 weeks ($p = 0.01$), individual group increases were not significant. No major or moderate adverse events were reported following the administration of 131 ST and 272 SM interventions.
Conclusion The increase in FVC is a unique finding. Although the underlying mechanisms responsible for this outcome are not yet understood, the most likely explanation is a synergistic effect resulting from the combination of interventions. These results support the call for further investigation into the use of MT for COPD.

PS154

ABSTRACT WITHDRAWN

PS155

OUTCOME OF PULMONARY REHABILITATION FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background As per the chronic obstructive pulmonary disease (COPD) Management Network of the Ishinomaki District, our hospital manages pulmonary rehabilitation (PR) of COPD patients of this area.
Methods Sixteen consecutive male COPD patients (mean age, 73 ± 6 years old) were enrolled. The COPD patients were diagnosed by a pulmonologist at a general hospital, and were referred to our hospital for PR. We assessed symptoms, respiratory muscle strength and flexibility, breathing pattern and 6-minutes walk distance, and prepared individually suitable rehabilitation programs. Every 1–2 weeks, the patients underwent PR which involved light-, moderate, and heavy-intensity exercises. Their symptoms, respiratory muscle strength and flexibility, breathing method learning, exercise tolerance, activities of daily living (ADL), mental state, spirometry, and blood gas analyses were monitored.
Results Seventy-five percent of the patients were GOLD Stages II and III, and equal number were grades 1 and 2 on MRC Breathlessness Scale. Thirty percent scored above 5 on the BODE Index. Before PR, the mean FEV_1 was 52.5 ± 24.3% predicted (GOLD Stage II), FEV_1/FVC was 40.8 ± 12.3%, and 6-minute walk distance was 311 ± 109 m. The above parameters were unchanged after 27 ± 13 months of PR. ADLs were preserved (Group P) or ameliorated (Group A) in 75% of the patients, and deteriorated (Group D) in 25%. Before PR, Group A had a significantly lower 6-minute walk peak heart rate (HR) (90.5 ± 6.6) than Group P (105 ± 10, $p = 0.028$). Group D had significantly lower rate of good training comprehension (33.3%) than Group P (85.7%, $p = 0.044$). PR improved ADL. Six-minute walk peak HR and good training comprehension were associated with good PR outcome.
Conclusion PR was useful for preservation and improvement in ADL of COPD patients.

PS156

COMPARISON OF TAICHI EXERCISE AND TREADMILL WALKING AT 60% OF MAXIMAL LOAD

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The physiological value of Tai Chi (TC) as a useful mode of pulmonary rehabilitation in COPD remains poorly understood, especially in comparison with the generally accepted threshold of 60% of maximal load which is considered necessary for pulmonary rehabilitation. we compared the physiological work, judged by oxygen uptake, esophageal pressure swing and diaphragm electromyography, entailed by TC compared with that entailed by constant rate treadmill walking at 60% of maximal load. Quadriceps fatigue after both these tasks was assessed. Eleven patients (age 62 ± 8 years) with a range of COPD severity (FEV1 61 ± 27 % of predicted) were studied. The intensity of workload entailed by TC did not differ from treadmill walking at 60% VO2max but only TC elicited quadriceps fatigue (mean fall in Tw Q 12.6%, $P < 0.01$).
Conclusions TC constitutes a physiologically sufficient stimulus to exercise load to be useful for pulmonary rehabilitation which may be culturally more acceptable in some parts of the world.

PS157

PHYSIOLOGICAL AND SYMPTOM-BASED ASSESSMENT OF THE THERAPEUTIC EFFECTS OF INDACATEROL IN COPD PATIENTS

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Objective To assess the therapeutic effect of indacaterol in COPD patients by physiological and symptom-based approach.
Methods We assessed the temporary effects of single dose of indacaterol (150 μg) in COPD patients using oscillometry and spirometry (before and 15, 60 and 180 minutes after inhalation), and also assessed improvement of symptoms using COPD assessment test (CAT) more than two weeks after treatment of indacaterol.
Results First, we evaluated the temporary effects up to 180 minutes physiologically. In seven patients, FEV1 showed significant increase and maximum improvement at 15 minutes after inhalation ($p < 0.05$ vs. baseline). Respiratory impedance improved similarly with spirometry, but only frequency dependence of resistance consistently improved over time and showed maximum improvement at 180 minutes ($p < 0.01$ vs. baseline). We also assessed add-on effect of indacaterol to regular therapy (mostly LAMA) in the same way. FEV1 showed significantly and maximum improvement at 15 minutes ($p < 0.05$ vs. baseline), though respiratory impedance did not show significant changes. Next, we assessed changes of FEV1 and CAT score more than two weeks after add-on treatment. A total of 21 patients, which include former subjects ($n = 10$), were investigated. Both FEV1 and CAT score showed significant improvement (1.05 L [0.89, 1.21] to 1.13 L [0.96, 1.31], 19.4 [16.3, 22.4] to 15.8 [13.0, 18.7], respectively. $p < 0.01$ for each). Twelve patients achieved CAT score improvement over MCID (1.6 units). Even in patients who were added indacaterol to tiotropium ($n = 8$), FEV1 and CAT score ($p < 0.01$ and $p < 0.05$, respectively) significantly improved compared with pretreatment values.
Conclusion Physiological indices improved in different time course by single dose of indacaterol. This result may reflect characteristics of indacaterol that is early onset and long duration of bronchodilation. In clinical settings, regular treatment of indacaterol represented significant benefit even in add-on therapy in COPD patients.

PS158

COPD ASSESSMENT TEST AS A PREDICTIVE FACTOR OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim of Study COPD assessment test (CAT) is a useful tool to evaluate health-related quality of life (HRQOL) of COPD outpatient. Although the ECLIPSE study showed that HRQOL is a predictive factor of acute exacerbation in addition to a history of prior exacerbations, it is little known whether CAT score predicts acute exacerbation of COPD. We aimed to investigate the influence of CAT scores on incidence of acute exacerbation of COPD.
Methods We enrolled 287 COPD outpatients in our hospital and observed them for 1 year. We measured body mass index (BMI), CAT scores, pulmonary function tests and a history of at least one acute exacerbation in the previous year, then we analyzed correlation between incidences of acute exacerbation for the next year. Acute exacerbations were defined as events that led a care provider to prescribe antibiotics or corticosteroids (or both) or that led to hospitalization.
Results Exacerbations occurred in 27% of all patients in 1 year. In univariate analysis, BMI, CAT scores, a history of exacerbation within the previous year, VC (%pred), FEV_1 (%pred) and FEV_1/FVC indicated significant correlations between incidence of acute exacerbation for the next year. In multivariate analysis, only CAT scores (HR = 1.06, $p = 0.006$) and a history of exacerbation within the previous year (HR = 4.76, $p < 0.0001$) were good predictive factors of acute exacerbation.
Conclusion In addition to prior exacerbations, CAT scores can predict acute exacerbation of COPD.

PS159

DIRECT EVIDENCE OF FORCED EXPIRATORY AIRFLOW LIMITATION AT THE INTRA-MEDIASTINAL AIRWAY IN EMPHYSEMA PATIENTS BY THE USE OF 4D-CT

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Rationale Functional disorder of the pulmonary emphysema has been believed due to dynamic compression of peripheral small airways caused by decrease of parenchymal elastic recoils. However, direct evidences of the proposed mechanism have never been shown. We have analyzed end-inspiratory and end-expiratory 3D-CT data sets, and proposed a hypothesis that overinflated lungs compressed the inra-mediastinal airway (IMA, intra-thoracic trachea, main bronchi, and right lobar bronchi) at the beginning of forced expiration and would let IMA collapse due to Bernoulli's effect in emphysema patients (presented in APSR2006). However, breath-hold static images could not reflect dynamic behaviors during breathing.
Objectives We evaluated the morphological and volumetric changes of IMA during maximum forced expiration by 4D-CT, and investigated its relationship to the value of $FEV_{1.0}$.
Method Five emphysema patients and a normal subject underwent 4D-CT by multi-detector row CT during maximum forced expiration over 6 sec at supine posture. Voxel size was $0.7 \times 0.7 \times 1.0$ mm^3 and time interval was 0.35 sec. Volumes of intra-thoracic trachea and bilateral main bronchi are measured through expiration, and the relative volume to the volume just before the beginning of forced expiration was calculated for each frame.
Results The IMA of all emphysema patients were extremely narrowed immediately after the beginning of forced expiration and slightly recovered later. The membranous part of IMA was invaginated inside. There was no apparent shape change in the normal subject. The 2 sec-relative volume were highly correlated to $FEV_{1.0}$ ($r^2 = 0.93$).
Conclusion These 4D-CT images have revealed that low values of $FEV_{1.0}$ in emphysema patients are caused by dynamic collapse of IMA due to Bernoulli's effect. Current concepts of respiratory mechanics, pulmonary function tests, and COPD should be urgently reconsidered.

PS160

PLACEBO CONTROLLED STUDY OF ROFLUMILAST IN BANGLADESHI COPD PATIENTS

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Background Roflumilast an oral, selective phosphodiesterase-4 inhibitor has been shown to improve lung function in COPD patients. We investigated whether Roflumilast along with conventional therapy would improve lung function in Bangladeshi COPD patients.
Methods A single blind, randomized, placebo controlled study was carried out in the department of Respiratory medicine at National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka, Bangladesh. 130 patients were recruited initially and randomly distributed into Group-A where patients got conventional therapy (Inhaled Salmeterol + Fluticasone and Tiotropium) and Roflumilast (0.5 mg once daily) and Group- B where patients got placebo with conventional therapy. Study duration was 3 months. Patients developing exacerbations and requiring emergency treatment were excluded from the study. 46 patients in group-A and 50 patients in group-B completed the study. A spirometry and CAT (COPD assessment test) score was performed in each case at the beginning and monthly for 3 months. Difference of mean FEV1 and CAT- score from baseline between two groups was measured to assess the Roflumilast activity. The primary outcome variable was change in mean FEV1 and secondary outcome variable was change in mean CAT score from base line.
Results Clinical characteristics of the study population in terms of cough, dyspnoea, wheeze, sputum production, loss of weight and appetite were not statistically significant. In group A, mean FEV1 increased and mean CAT score changed at all three visits. The change was statistically significant.
Conclusion COPD patients who received Roflumilast along with conventional therapy experience better lung function and symptomatic improvement than conventional therapy alone.

1-E1: COPD 2

PS161

ROLE OF A NEW LONG ACTING BETA-2 AGONIST (INDACATEROL) IN MANAGEMENT OF COPD PATIENTS

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Background and Aim of Study Bronchodilator therapy is the corner-stone in managing chronic obstructive pulmonary disease (COPD). Newer and more effective bronchodilators are long been sought for. Indacaterol is an inhaled ultra-long-acting beta-2 agonist providing 24 hours efficient bronchodilatation with once daily dosing in patients with COPD. It has shown promising results in some recent studies. This quasi-experimental study reviewed the efficacy of Indacaterol along with other conventional treatments used in COPD.
Methods Purposively selected 30 elderly (50 years or above) ex-smoker male COPD patients, not adequately controlled (Forced Expiratory Volume in 1st second – FEV1 < 50% of predicted value) with conventional treatments were given Indacaterol (150 mcg of dry powder inhalation at bedtime) in addition to their ongoing pharmacotherapy. Their COPD Assessment Test (CAT) scoring was measured at the beginning and after 6 months of using Indacaterol.
Results The mean of post-Indacaterol CAT score (19.7 ± 3.12) was found to be decreased over pre-Indacaterol CAT score (21.8 ± 3.13) significantly ($p = 0.0117$; 95% CI = 0.48–3.7). This indicates a substantial improvement in the treatment outcomes of COPD patients.
Conclusion Indacaterol, a novel ultra-long-acting beta-2 agonist, may be considered as an effective therapeutic agent for the treatment of COPD.

PS162

A 26-WEEK RANDOMISED, DOUBLE-BLIND STUDY DEMONSTRATING THE EFFECT OF ONCE-DAILY INDACATEROL IN A PREDOMINANTLY CHINESE POPULATION WITH COPD

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Background and Aim of the Study This study investigated the efficacy and safety of indacaterol, a once daily (o.d) inhaled ultra-long-acting β_2-agonist (LABA), for the treatment of moderate-to-severe COPD in a predominantly Chinese population.
Methods This 26-week, double-blind study, randomised patients to indacaterol 150 or 300 μg or placebo o.d. The primary variable was trough forced expiratory volume in 1 second (trough FEV_1; an average of 23 h 10 min and 23 h 45 min post-dose) at Week 12. Health status (St George's Respiratory Questionnaire, SGRQ), dyspnoea (transition dyspnoea index, TDI), and safety were also evaluated over 26 weeks.
Results Of the 563 patients randomised, 561 (89.8% Chinese) received study treatment and 482 completed the study. At Week 12, trough FEV_1 improved significantly for both indacaterol doses vs placebo ($p < 0.001$), with indacaterol-placebo differences exceeding the pre-specified minimal clinically important difference of 0.12 L (0.15 and 0.13 L for indacaterol 150 and 300 μg, respectively). TDI score at Week 26 was superior to placebo for both indacaterol doses (0.82, 1.15 points; $p < 0.01$), as was the percentage of patients with clinically relevant improvement (≥1 point; 74.1%, 78.6% vs 55.5%; $p < 0.05$). At Week 26, both doses provided ≥4-point improvements from baseline in SGRQ score that were numerically greater than placebo (unadjusted means: –9.6, –8.8 vs –7.0 points). A similar pattern was seen in the percentage of patients with clinically relevant improvements in SGRQ score (65.0%, 61.5% vs 60.6%). Incidences of adverse events were comparable across the treatment groups.
Conclusion Indacaterol provided effective bronchodilation in predominantly Chinese population, with significant improvements in breathlessness and health status.

PS163

ARTERIAL BLOOD GAS ANALYSIS CHARACTERISTIC IN HOSPITALIZED ACUTE EXACERBATION OF COPD AND ITS RELATIONSHIP IN HOSPITAL MORTALITY

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Background and Aim of Study Arterial blood gas analysis shows various indicator in patients with acute exacerbation of COPD (AECOPD) has been evaluated. Aim of this study is to investigate the characteristic of arterial blood gas analysis and its relationship with mortality.
Methods In a retrospective cohort study, we analyzed medical records of 36 male adults hospitalized with AECOPD in Persahabatan Hospital from March 2011 to February 2013. Arterial blood gas parameters such as pH, pCO_2, pO_2, HCO_3 and SaO_2 were analyzed on admission and during hospital stay.
Results A total of 36 hospitalized AECOPD patients (mean age 66.61 ± SD 9.13; BMI 19.20 ± SD 3.24) were included. There was no significant association between age, Brinkman Index, BMI and BUN with mortality rate. The acid-base balance rate on admission were normal 44.44% (n = 16), acidosis 27.78% (n = 10), and alkalosis 27.78% (n = 10), hyperoxia 52.8% (n = 19), hypoxia 33.3% (n = 12), hypercapnia 44.4% (n = 16), hypocapnia 16.7% (n = 6). The acid-base balance on follow up was normal 50% (n = 18), acidosis 33.33% (n = 12), alkalosis 16.67% (n = 6), hyperoxia 25% (n = 9), hypoxia 52.8% (n = 19), hypercapnia 44.4% (n = 16), hypocapnia 16.7% (n = 6). The mortality rate was 22.22% (n = 8). There was significant mean difference in pO_2 level on admission (109.40 ± SD 51.69 vs 95.71 ± SD 30.21, $p < 0.05$), pCO_2 level on follow up (68.81 ± SD 39.14 vs 45.98 ± SD 8.38 $p < 0.05$) and SaO_2 level on follow up (82.36 ± SD 15.56 vs 93.98 ± SD 8.38, $p < 0.05$) between death and survive patients. There was no correlation between pO_2 level on admission and pCO_2 level on follow up.
Conclusion Arterial blood gas parameters have significant relationship with mortality in hospitalized AECOPD patients. The alteration of pO_2, pCO_2 and SaO_2 might help clinicians in patient management to decrease hospital mortality rate.

PS164

EVALUATION OF COPD ASSESSMENT TEST (CAT) AND ACUTE EXACERBATION DURING PILGRIMAGE IN INDONESIAN PILGRIMS

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Background As a global health problem, COPD may contribute to significant health problems during pilgrimage for moslems. Indonesian Ministry of Health documented acute exacerbation of COPD (AECOPD) as the second leading causes of death in pilgrims with 12.3% of total mortality in 2008. Identifying individuals with higher risk to have AECOPD prior to their embarkation is essential. Therefore, the use of CAT scores in assessing risk of acute AECOPD in this special population merits further investigation.
Methods This is a cohort study recruiting 61 COPD patients at Jakarta embarkation point where patients completed CAT. Subjects and their pilgrims groups' doctors were given diary cards to record any symptoms of exacerbation during pilgrimage. On arrival at disembarkation point, subjects underwent history taking, health examination and all diary cards were collected. AECOPD were determined from the diary cards and individual health record book carried by every pilgrim.
Results All patients completed the study. Most subjects were male (57; 93.4%) with a mean age for this study is 58.8 ± 8.5 years. Thirty five patients (57.4%) suffered from AECOPD during pilgrimage. CAT scores range from 0–25 with a mean of 8.2 ± 5.5. Subjects within low impact group (CAT score < 10) comprised 63.9% of subjects while the remaining 36.1% were in medium to high impact group (CAT score 10–30). Mean CAT score in exacerbation group were significantly higher than in non-exacerbation group (10.2 ± 5.2 vs. 5.4 ± 4.8, $p = 0.00$, independent *t*-test).
Conclusions This study indicates that the use of CAT may be a valuable tool in identifying individuals at risk of AECOPD prior to pilgrims' embarkation.

PS165

ANEMIA AND EOSINOPENIA IN PATIENTS HOSPITALIZED FOR COPD EXCACERBATION AND ITS RELATIONSHIP WITH MORTALITY RATE AND REHOSPITALIZATION

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Background Chronic obstructive pulmonary disease is multisystemic inflammation with high morbidity and mortality. Comorbid anemia was common in patients with chronic disease and eosinopenia as marker of inflammation has been evaluated. This study investigate the prevalence association of anemia, eosinopenia with mortality rate and rehospitalization in patients with COPD excacerbation.
Methods A retrospective study analyzed medical record 59 male adult hospitalized for COPD excacerbation in Persahabatan hospital from January 2011 to December 2011. Hemoglobin (Hb) and eosinophil on admission were assesed. Patients were classified as anemic (Hb < 13 g/dl) or non-anemic and eosinopenic (eosinophil count < 50 cell/mm^3) or non-eosinopenic. We calculate the prevalence of anemia, eosinopenia and compared with mortality rate and rate of rehospitalization in 1 year.
Results A total of 59 patients hospitalized for COPD excacerbation (mean age 66.51 ± SD 8.63; Hb 13.65 ± 1.84; FEV1% predicted 46.9 ± 18.41) were included. Prevalence of anemia was 28.8% (n = 17) and eosinopenia 32.2% (n = 19). There was no significant association between age, brinkman index, BMI, FEV1% predicted, cardiovascular and diabetes mellitus comorbid with anemia and eosinopenia. One year mortality rate was 28.8% (n = 17) and rate hospitalization ≥ 2x per year in survived patient was 28.6% (n = 12). Independent predictors of one year mortality were eosinopenia ($p < 0.05$) and FEV1% predicted ($p < 0.05$). One year mortality rate was significantly different ($p < 0.05$) between eosinopenia group (52.6% vs 17.5%; RR 3.01; 95%CI 1.36–6.67) and non-eosinopenia. Anemic patients had higher risk rehospitalization ≥ 2x/year than non-anemic patients (54.5% vs 19.4%; $p < 0.05$ 0.05; RR 2.82; 95%CI 1.15–6.92).
Conclusion Eosinopenia might be a useful predictor to predict mortality and anemia to predict rehospitalization in patients with COPD excacerbation. As it was routinely given in blood count in all patients admitted to hospital, there was no extra cost for this beneficial test.

PS166

LUNG FUNCTION STATUS AND ITS RELATIONSHIP WITH NUMBER OF EXACERBATIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background and Aim of the Study Chronic Obstructive Pulmonary Disease (COPD) is a major cause of mortality and morbidity around the world. Majority of COPD patients experience at least one exacerbation per year, and the frequency of exacerbations increases with disease severity. Increased number of exacerbations is reported to have a more rapid decline in FEV_1. The aim of this research is to evaluate the incidence of exacerbations and the changes in lung function in our patients who are on regular follow up.
Method We conducted a cross-sectional study on a cohort of COPD patients who are on regular follow up at Asthma/COPD outpatient clinic in our hospital from 2011 until 2013. Patients were interviewed and spirometry was performed, which was then compared with spirometry data of 2011. Retrospective analysis of their medical records was done for exacerbation events in the last two years which lead them to seek medical care.
Results Total of 32 patients (M = 31, F = 01) were evaluated. Fifteen percent (n = 5) were below 60 years of age and 27 (84.4%) above 60 years of age. Disease severity as per GOLD were; mild disease 21.9%, Moderate 71.9% and severe 6.25%. A total of 129 exacerbations were recorded (average 2.02 exacerbations/patient/year). Patients with infrequent exacerbations 56.25% (n = 18) had an average 124.5 ml decrease in FEV_1 value and patients with frequent exacerbations 43.75% (n = 14) had a decline of FEV_1 average 187.25 ml/year.
Conclusion Patients with a higher number of exacerbations had greater decline in FEV_1.
Key Words COPD; exacerbation; lung function; FEV_1.

PS167

CLINICAL SIGNIFICANCE OF MEASUREMENT OF HEALTH STATUS USING COPD ASSESSMENT TEST IN COPD PATIENTS TREATED WITH INHALED LONG-ACTING BRONCHODILATORS

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Background For effective management of COPD, a comprehensive approach is needed to relieve symptoms, improve exercise tolerance, health status and to prevent complications and exacerbations. Although the health status is conventionally assessed by SGRQ and other questionnaires, the new COPD assessment test (CAT) is currently available for the measurement of health health status in COPD patients.
Methods We examined the effects of long-acting bronchodilators on pulmonary function and health status in 28 male COPD patients. We also examined the relationships between the pulmonary function variables and the degree of health status using by CAT. The patients were treated with one or two months of inhaled long -acting bronchodilators. The assessment was performed before and after the treatment.
Results The pulmonary function indices including FVC and FEV1 were significantly increased by one or two months of inhalation of long -acting bronchodilators in the patients. The CAT score was also decreased from 14.8 to 9.3 in the patients. The degree of the improvement of CAT is not correlated with delta FEV1(post-inhaled FEV1-preinhaled FEV1), but weakly correlated with delta FEV1/baseline FEV1.
Conclusion Most of the patients with COPD improved health status by inhaled long-acting bronchodilators. However, the degree of improvement of health status is very weakly correlated with pulmonary function.

PS168

HEALTH STATUS PROPERTY AND ITS RELATION TO PULMONARY FUNCTION AND DYSPNEA IN COPD PATIENTS

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Background The health status is an important aspect of the purpose of COPD treatment. The new COPD assessment test (CAT) is currently applicable for the measurement of health status in COPD patients. Howver, the relathinships between health status score and pulmonary function and dyspnea score have not been fully elucidated.
Methods We examined pulmonary function, and assessed health status and dyspnea in 45 male COPD patients. The Health status was assessed by CAT. The dyspnea was assessed by the Medical Research Counci dyspnea grade scoring (MRC). The profile of CAT scoring was evaluated. The relationships between CAT score and spirometric indices and MRC scores were also examined.
Results The CAT scores ranged from 0 to 27 in the patients with COPD. The mean CAT sores was 12.1. The scores are weakly correlated with FEV1, but well correlated with dyspnea scores as indicated as MRC grades.
Conclusion The health status in COPD patients is associated with the severity of dyspnea on exertion, but little with static pulmonary function.

PS169

THE USE OF MEF50/MEF25 MAY OVER-ESTIMATE THE PRESENCE OF SMALL AIRWAY DISEASE: THE TAKAHATA STUDY

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Background Maximal expiratory flows (MEFs) depend on the elastic recoil pressure in the alveoli, airway resistance and bronchial collapsibility. MEFs at lower levels of vital capacity [MEFs at x% FVC (MEFx)] would indicate the patency of peripheral airways. In Japan, a ratio of MEF50 to MEF25 (MEF50/MEF25) greater than 4.0 is used as an index of injury to the small airways in subjects without airflow limitation. However, there have been no epidemiological investigations relating to this index. The aim of this study was to evaluate the impact of cigarette smoking on MEFs in a general population, and to assess the validity of using this index to evaluate injury to the small airways.
Methods Subjects aged 40 years or older (n = 2,917), who had participated in a community-based annual health-check in Takahata, Japan, were enrolled in the study. MEF75, MEF50 and MEF25 were measured in these subjects.
Results No difference in MEF50/MEF25 was observed between smokers and never-smokers. In both genders, MEF50/MEF25 was slightly, but significantly, elevated with aging of the population. In addition, 36.5% of subjects who participated in this health-check had MEF50/MEF25 values greater than 4.0. In smokers, as compared with never-smokers, percentage predicted MEFs (%MEFs) decreased according to the aging of the population, except in the case of %MEF25 in females. In males, but not in females, %MEFs decreased significantly with an increase in cigarette consumption.
Conclusions The use of this criterion may over-estimate the presence of small airway disease, because many healthy subjects aged 40 years or older have MEF50/MEF25 values greater than 4.0.

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ABSTRACT WITHDRAWN

1-E2: COPD 3

PS171

THE EFFECTIVENESS OF NEW INSPIRATORY MUSCLE TRAINING

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Aim The purpose of this study was to investigate the effectiveness of a new method of inspiratory muscle training (IMT) in which IMT was carried for 30 breaths under different loarding pressures.
Methods Thirty-three healthy young students were randomly divided into three groups: group 1, IMT with 60% maximum inspiratory pressure (PImax); group 2, IMT with 40% PImax; and group 3, IMT with 20% PImax. Subjects in all groups performed IMT for 30 breaths per session twice a day for 4 weeks using POWERbreathe™ (Gaiam, UK). Pulmonary function, inspiratory muscle force, and inspiratory muscle endurance (incremental inspiratory threshold loading: ITL) were evaluated before, and at 2 and 4 week after IMT commenced.
Results Inspiratory muscle force and inspiratory muscle threshold loads were significantly improved at 2 and 4 weeks after IMT began compared with pre-training values in all groups ($p < 0.01$). There was significantly more improvement in inspiratory muscle force in the group 1 compared with group 3 at 4 weeks ($p < 0.05$). Otherwise the improvement showed no significant differences among training groups.
Conclusions This study suggests that 30-breaths IMT might be effective at 20% or more PImax loading pressure. Furthermore, this study suggests that the higher the loading pressure the greater the generated inspiratory muscle forces.

PS172

MULTIDETECTOR-ROW COMPUTED TOMOGRAPHY ASSESSMENT OF ADDING BUDESONIDE/FORMOTEROL TO TIOTROPIUM IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background In patients with chronic obstructive pulmonary disease (COPD), multidetector-row computed tomography (MDCT) showed that tiotropium dilated the inner diameters in airways from the third to the sixth generation of the bronchi. Here we aimed to evaluate the morphological effect by adding a budesonide/formoterol combination to tiotropium in COPD patients using three-dimensional MDCT.
Methods Pulmonary function tests, St. George's Respiratory Questionnaire (SGRQ) and MDCT imaging studies were performed at the beginning and after budesonide/formoterol combination treatment for 12 weeks in 14 patients with COPD.
Results The median age was 73.5 years and the mean forced expiratory volume in 1 second (FEV1) as a percentage of the predicted value was 57.2 ± 18.3 %. The average luminal area and wall area percentage in the third, fourth and fifth generations were correlated with the SGRQ total score. Budesonide/formoterol induced insignificant pulmonary function changes and significant symptoms improvement. CT images showed an increased inner luminal area and decreased wall area after budesonide/formoterol treatment. Average luminal area was significantly increased from 24.3 ± 9.7 to 26.0 ± 9.9 mm^2 in the third generation, 13.0 ± 6.5 to 14.7 ± 7.3 mm^2 in the fourth generation, 8.0 ± 4.8 to 9.4 ± 4.9 mm^2 in the fifth generation and 5.6 ± 2.7 to 6.7 ± 3.6 mm^2 in the sixth generation ($p < 0.01$). The wall area percentage significantly decreased from 51.5 ± 9.2 to 49.1 ± 9.7 % in the third generation, 56.1 ± 9.7 to 53.0 ± 11.1 % in the fourth generation, and 62.3 ± 9.9 to 57.6 ± 9.8 % in the fifth generation ($p < 0.05$). Emphysema volume/CT-derived total lung volume was unchanged with treatment.
Conclusion MDCT demonstrated budesonide/formoterol-induced bronchodilation in the non-small airway. CT imaging can evaluate drug therapeutic effect and may provide additional insights into pharmacotherapy for COPD.

PS173

CORRELATION OF NUTRITIONAL STATUS USING SUBJECTIVE GLOBAL ASSESSMENT (SGA) ON PULMONARY FUNCTION PARAMETERS IN PATIENTS WITH COPD

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Nutritional Status greatly affects the patient. Subjective Global Assessment is well validated screening tool for malnutrition. It is the aim of this study to determine the correlation of Nutritional Status using SGA on Pulmonary Function Parameters of newly diagnosed and already diagnosed COPD patients according to GOLD criteria seen at the Philippine Heart Center. This is a Cross Sectional Study. Patients 40 years old and above diagnosed with COPD are included. Nutritional status were assessed using anthropometric indices such as weight, height, Body Mass Index (BMI), Mid Arm Circumference (MAC) and Subjective Global Assessment. The association of anthropometric parameter with pulmonary function was determined using Pearson correlation analysis. Analysis of variance was used to determine relationship of malnutrition and pulmonary function. A p-value of < 0.050 was considered significant. One hundred fourty-five COPD patients participated in the study. Forced Vital Capacity (FVC) decreases as the patient became malnourished. The difference proved to be significant ($p = 0.000$). Forced Expiratory Volume in 1 second (FEV1) showed the same significant decrease as the patient became malnourished ($p = 0.000$). The FEV1/FVC ratio diminished from a well nourished patient to a severely malnourished patient which proved to be likewise significant ($p = 0.000$). Among the anthropometric measurements performed, weight and mid arm circumference have positive correlation with FEV1 ($p = 0.016$; $p = 0.000$) and FEV1/FVC ratio ($p = 0.001$; $p = 0.001$). BMI was noted to be positively correlated with FEV1/FVC ratio ($p = 0.001$). However, no correlation was noted on both leukocyte count and albumin with PFT parameters. Nutritional Status assessed using Subjective Global Assessment correlates significantly with FEV1, FVC, FEV1/FVC ratio of COPD patients. Body weight, MAC and BMI were found to have positive correlation with PFT results of COPD patients. SGA, weight, MAC, BMI can be a gauge to monitor the severity of COPD without doing frequent PFT especially among difficult, critically ill COPD patients.

PS174

THE UTILITY OF TIOTROPIUM AMONG PATIENTS WITH COPD: AN UPDATE OF A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS (UTAC UPDATE)

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Background Tiotropium is a recently developed inhaled anticholinergic, used at once-daily dosing in the management of COPD. Previous studies have hinted that long-term use may lead to an increased risk for cardiovascular mortality. In 2010, the US-FDA issued a statement indicating the cardiovascular safety of Tiotropium based on the UPLIFT trial (2008), the largest and longest placebo-controlled trial on Tiotropium. However, there is still question on Tiotropium's cardiovascular safety, especially in comparison to active treatment, particularly, inhaled long-acting beta-agonists.
Objectives We determined the efficacy of long-term tiotropium use on clinical endpoints such as mortality, exacerbations, and hospitalizations compared to inhaled LABAs among patients with stable moderate to severe COPD.
Methodology RCTs were identified from electronic databases such as PubMed, Cochrane Library, Ovid, Herdin, Clinicaltrials.gov and Google Scholar. Relevant studies and reviews were also hand-searched. RCTs among patients with COPD comparing Tiotropium monotherapy with inhaled LABAs with at least 6 months follow-up were selected. Data on all-cause mortality, mortality from pulmonary and from cardiovascular causes, rates of hospitalizations and exacerbations were identified. The date of last search is September 7, 2012. Two independent investigators evaluated and extracted relevant data, which were analyzed using Cochrane Review Manager 5.1.
Results From 495 titles and abstracts, 5 clinical trials with a total of 10,759 patients met inclusion criteria. Tiotropium did not reduce all-cause mortality (RR 0.83 95%CI 0.40–1.70), mortality from respiratory causes (RR 0.70 95%CI 0.40–1.25), and mortality from cardiovascular causes (RR 1.57 95%CI 0.86–2.85). Tiotropium significantly decreased the risk for exacerbations (RR 0.91 95%CI 0.85–0.98), and exhibited a trend towards decreased hospitalizations (RR 0.78 95%CI 0.61–1.00).
Conclusions Tiotropium did not reduce all-cause mortality, mortality from pulmonary causes, and mortality from cardiovascular causes compared to inhaled LABAs. Tiotropium significantly decreased the risk for exacerbations, and showed trend towards possible decreased hospitalizations.

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ARE THERE GENDER-RELATED DIFFERENCES IN PATIENTS HOSPITALIZED FOR COPD

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Introduction Although, the incidence of COPD is increasing in women, the knowledge regarding the gender differences in acute COPD exacerbations is limited. Our study aimed to determine if gender is a risk factor that has effects on clinical characteristics of the COPD patients with acute exacerbation.
Methods We included COPD patients whom admitted to a tertiary reference center in Southern Marmara Region and hospitalized with acute exacerbation in the last three years. Medical records of the study participants screened retrospectively.
Results A total of 393 patients hospitalized for acute COPD exacerbation were included. Of these 84.2%were males, and 15.8% were females. Female patients were younger than the males (63.4 ± 13.1 years old vs. 67.4 ± 10.4 years old, $p < 0.05$, mean age ± SD for females and males respectively). Routine laboratory tests on admission did not differ between males and females. On arterial blood gas examination HCO3 and PaCO2 levels were found to be higher in female COPD patients than the males (27.3 mmol/L (min: 11-max: 48) vs. 25.9 mmol/L (min: 2.2-max: 44.3), $p < 0.05$, for HCO3) and (49.4 mmHg (min: 28-max: 102) vs. 45 mmHg (min: 24–max: 142), $p = 0.55$, for PaCO2). Diabetes mellitus (F/M: 46.9%/25.8%, $p < 0.05$), hypertension (F/M: 59.5%/35.9%, $p < 0.05$), and anemia (F/M: 45.8%/19%, $p < 0.05$) were more prevelant in females with COPD exacerbation. Multimorbidities were more frequent in females than the male patients (36% vs 15.1%, OR: 19.06, $p < 0.05$). Gender was not an effecting factor on mortality in patients with acute exacerbation.
Conclusion Female COPD patients were tend to be more hypercapnic than the males on admission for hospitalization with acute exacerbation. As comorbidities such as diabetes mellitus, anemia and hypertension were more prevalent in females, we assume that the female sex may be a risk factor for having comorbidies in COPD patients requiring hospitalization for acute exacerbation.

PS176

COMORBIDIES IN PATIENTS HOSPITALIZED FOR ACUTE EXACERBATION OF COPD

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Introduction Comorbidies such as diabetes mellitus, hypertension and cardiac disease are commonly reported in patients with chronic obstructive pulmonary disease (COPD). This study aimed to determine the frequency of comorbid conditions and the multimorbidities in hospitalized patients with acute COPD exacerbation.
Methods We included COPD patients whom admitted to a tertiary reference center in Southern Marmara Region and hospitalized with acute exacerbation in 2012. Medical records of the study participants were screened retrospectively and comorbid diseases were analyed.
Results A total of 75 patients hospitalized for acute COPD exacerbation were included. Of these 88% were males, and 12% were females with a mean age of 68.8 ± 10.2. The prevalence of diabetes mellitus, hyperlipidemia, hypertension and coronary artery diseaese were 14.7%; 6.7%, 26.7, and 22.7% respectively. The multimorbidities were more frequent in females than the male patients with COPD exacerbation (55.6% vs 6.1%, OR: 19.06, $p < 0.05$). In routine laboratory blood tests on admission serum creatinin levels were higher in COPD patients with multimorbidities than the ones with no comorbid condition (1.1 (min: 0.7-max: 1.8) vs. (0.8 (min: 0.5–max: 8.0), $p < 0.05$). On the other hand, the red cell distribution width were lower in COPD patients with multimorbidities when compared with the ones having no comorbid condition (15.0 ± 2.1 vs 17.5 ± 4.5, $p < 0.05$).
Conclusion Comorbidities are common in patients hospitalized for COPD exacerbation. Female sex is a significat risk factor for having multimorbidies in COPD patients requiring hospitalization for acute exacerbation.

PS177

PERCEPTION OF SYMPTOM VARIABILITY IN CHINESE COPD PATIENTS

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Background/Aims Studies in western countries have shown COPD is associated with significant diurnal symptom variability, notably in the morning. However, it is unknown whether this occurs in Chinese COPD patients with moderate or greater airflow limitation.
Methods In a non-interventional, cross-sectional study conducted at 10 hospitals in China involving 323 COPD patients (mean age 65.4) with mostly moderate (n = 152), severe (n = 127) or very severe (n = 42) airflow limitation (GOLD 2011 classification), patients' perceptions of the daily variability of COPD symptoms and the impact of symptoms on their morning activities, sleep quality and quality-of-life (QoL) were assessed via investigator-applied questionnaires. MMRC and CAT questionnaires were also applied for assessment.
Results Variability in COPD symptoms during a day was noted in 48.9% of patients overall, and 55.1%/54.8% respectively of severe/very severe airflow limitation patients. The most frequent times when patients were most distressed by COPD symptoms were the morning on waking (33.5% of patients), later in the morning (20.9%), and in the evening (22.2%); in patients with very severe airflow limitation, 56.5% were most distressed on waking. Clinical symptom questionnaires indicated that the major activities adversely affected by COPD symptoms were negotiating stairs (83.6% of patients), physical activity/exercise (89.5%), and shopping (50.8%). Sleep quality was rated by 34.4% of patients as poor. Scores on both the MMRC and CAT questionnaires were significantly correlated with the impact on patients' morning activities ($p < 0.0001$).
Conclusion COPD symptoms in Chinese patients with moderate or greater airflow limitation exhibited diurnal variability, and impacted on their daily living and morning activities and sleep quality. Morning symptoms and morning activity impact due to COPD should be paid more attention by clinical physicians.
This study was funded by AstraZenca China and medical writing was supported by Content Ed Net.

PS178

EFFICACY AND SAFETY OF ONCE-DAILY QVA149 COMPARED WITH THE FREE COMBINATION OF ITS MONO-COMPONENTS: THE BEACON STUDY

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Introduction QVA149 is a once-daily dual bronchodilator containing a fixed-dose combination of the long-acting β_2-agonist (LABA) indacaterol and long-acting muscarinic antagonist (LAMA) glycopyrronium (NVA237) for the treatment of chronic obstructive pulmonary disease (COPD). The BEACON study evaluated the efficacy and safety of QVA149 compared with the concurrent administration of it mono-components indacaterol and glycopyrronium (IND+GLY).
Methods This multicenter, double-blind, parallel group, active controlled study randomized (1:1) patients with moderate-to-severe COPD to once-daily QVA149 (110 μg indacaterol/50 μg glycopyrronium) and placebo or concurrent administration of indacaterol (150 μg) and glycopyrronium (50 μg) via the Breezhaler® device for 4 weeks. The primary objective was to demonstrate the non-inferiority of QVA149 versus IND+GLY for trough forced expiratory volume in one second (FEV_1) after 4 weeks (non-inferiority margin = –100 mL). Secondary objectives included FEV_1 area under the curve from 0 to 4 hours ($AUC_{0–4h}$) at Day 1 and Week 4, symptom scores, rescue medication use, safety and tolerability.
Results Of the 193 randomized patients, 187 (96.9%) completed the study. QVA149 demonstrated non-inferiority versus IND+GLY for trough FEV_1 at Week 4 (treatment difference = –0.005 L (95% Confidence interval (CI): –0.051, 0.040). The treatment differences for FEV_1 $AUC_{0–4h}$ between QVA149 and IND+GLY at Day 1 and Week 4 were 0.02 L (95%CI: –0.005, 0.054) and –0.01 L (95% CI: –0.059, 0.034), respectively. Both treatment groups had a similar reduction in symptom scores and recuse medication use from baseline. The incidence of adverse events was similar between QVA149 (25.6%) and the IND+GLY (25.2%) groups. No deaths were reported in the study.
Conclusion Once-daily QVA149 improved lung function, reduced symptom scores and rescue medication use and had a similar safety and tolerability profile compared with the free combination of its mono-components.

1-E3: COPD 4

PS179

HIGH PREVALENCE OF STREPTOCOCCOUS PSEUDOPNEUMONIAE IN SPUTUM OF PATIENTS WITH ACUTE EXACERBATION OF COPD

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Introduction Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a common condition that leads to unscheduled health care utilization and impaired health status among patients.
Methods This study assessed the infective etiologies related to AECOPD with molecular techniques including viruses such as bocavirus, human metapneumovirus and novel bacteria like Streptococcous pseudopneumoniae. We also studied paired sputum samples for the same panel of viruses for subjects with positive nasophargneal aspirate (NPA). The relationship between the identification of micro-organisms and short term clinical outcomes of the patients such as hospital length of stay, need for non-invasive ventilation and mortality at 3 months were assessed.
Results 323 episodes of AECOPD and 30 control COPD subjects at stable state were studied. Overall, about 20% of the subjects had positive NPA. The commonest viruses identified from the NPA of AECOPD patients were rhinovirus, coronavirus and respiratory syncytial virus. For the control subjects, the commonest organisms detected in NPA specimens were atypical organisms like Mycoplasma pneumoniae (6.5%) and Chlamydia pneumoniae (9.7%). 63.4% of AECOPD patients and 20.8% of control subjects had positive sputum bacterial test. Streptococcus pseudopneumoniae was identified in 29.4% of subjects with AECOPD. Among subjects with positive NPA results, 43.3% showed positive results in paired expectorated sputum. Comparisons of the subjects with same organisms identified in both NPA and sputum versus those in NPA only found similar demographic characteristics and short term clinical outcomes.
Conclusion The role of the high prevalence of Streptococcous pseudopneumoniae in sputum of AECOPD patients and atypical organisms like mycoplasma and chlamydia in NPA of stable COPD subjects needs further investigation.

PS180

SERUM URIC ACID: AN ALTERNATIVE TEST TO ASSESS DEGREE OF SEVERITY OF COPD

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Background Hypoxemia, as a consequent of alveolar hypoxia, increases along with the severity of COPD. Tissue hypoxia triggers the degradation of purine. Serum uric acid (UA), the final product of purine degradation, has been shown to be increased in the hypoxic state. Therefore, serum UA may reflect the severity of hypoxia. We assessed whether the presence of higher values of serum UA is associated with the degree of severity of COPD.
Methods The research was conducted in the outpatient pulmonary clinic of Soetomo Hospital, Surabaya, East Java, Indonesia. We included 38 consecutive patients with COPD. Patients were in clinically stable condition and without other significant comorbid conditions. The degree of severity was then compared with oxygen saturation and values of serum UA.
Results A weak correlation was found between hypoxemia and the degree of severity of COPD ($r = -0.375$, $p = 0.020$). There was no patient with level of saturation less than 80%. Correlation between serum UA value and the degree of severity of COPD presented no significant ($r = -0.177$, $p = 0.288$).
Conclusion Severity of COPD that is characterized by decrease of lung function (FEV1) did not result in increased levels of serum uric acid in patients with COPD.

PS181

THE ROLE OF TNF ALPHA SERUM IN NUTRITIONAL STATUS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Background Systemic inflammation may contribute to cachexia in COPD patients. TNF-α is one of the important biomarker in systemic inflammation. Aim this study was to analyze correlation between systemic inflammation and nutritional status of chronic obstructive pulmonary disease patients.
Methods This case-control study was conducted in May up to June 2013. The respondents were stable COPD GOLD I-IV patients, aged 40–80 year. Case was defined as COPD patient with poor nutritional status, control was defined as COPD patient with good nutritional status. Nutritional status was measured using body mass index (BMI), percentage ideal body weight, lean body mass and fat-free mass. TNF-α serum was measured using enzyme immunoassay. The correlation between nutritional status and level of TNF-α serum were analyzed with Univariat and multivariat analysis.
Result Mean of TNF-α serum level in case group was higher than control group ($49{,}68 \pm 19{,}23$ pg/ml vs $22{,}22 \pm 7{,}65$ pg/ml, $p = 0{,}000$). Level of TNF-α serum had correlation with BMI ($r = 0{,}594$; $p = 0{,}000$), percentage ideal body weight ($r = 0{,}595$; $p = 0{,}000$), lean body mass ($r = 0{,}594$; $p = 0{,}000$) and fat-free mass ($r = 0{,}594$; $p = 0{,}000$). The odds ratio was 28 (CI 95%, 4,43–176,78; $p = 0{,}000$).
Conclusion TNF-α serum was correlated with decrease of nutritional status in COPD patients.
Keywords TNF-α, Tumor necrotic factor, systemic inflammation, nutritional status, COPD.

PS182

PHYSICIAN KNOWLEDGE AND PERCEPTION OF COPD MANAGEMENT IN KOREA AND JAPAN: CONTINUING TO CONFRONT COPD (C2C) PHYSICIAN SURVEY 2012–2013

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Background and Aim of Study Few surveys have focused directly on physicians' perspectives on treating COPD. The C2C Physician Survey aimed to describe physician beliefs and behaviors related to COPD diagnosis and treatment, including knowledge of Revised GOLD 2011 Strategy, in 12 countries including Japan and Korea.
Methods Sampled physicians were identified from in-country professional association databases, including a total of $n = 103$ in Korea (74% general practitioners [GP], 26% chest physicians [CP]) and $n = 101$ interviews in Japan (70% GP, 30% CP). Standardized, translated questionnaires were conducted by telephone, face-to-face, or online from January to May 2013.
Results Awareness of the GOLD 2011 Strategy was 73% overall in Korea and 54% overall in Japan; knowledge was higher among CPs compared to GPs (Korea 96% vs. 36%; Japan 80% vs. 42%). Spirometry (Korea 86%; Japan 85%) and chest x-ray (Korea 91%; Japan 97%) were commonly used to establish a COPD diagnosis, while use of patient-reported outcomes (Korea 58%; Japan 47%) was lower in both countries. Sixty-five percent of Korean physicians and 47% of Japanese physicians reported that they discuss smoking cessation with their patients at every visit. Perceived patient adherence to prescribed treatment regimen was low, with only 13% of Korean physicians and 17% of Japanese physicians indicating that at least three-quarters of their patients always complied with their treatment regimen. Both Korean (47%) and Japanese (57%) physicians indicated medication cost as the most common barrier to accessing and adhering to an optimal regimen.
Conclusion Awareness and application of the GOLD 2011 Strategy were high among respiratory specialist physicians in Korea and Japan, and an opportunity to improve general practitioner delivered care of COPD patients was identified. Sponsored by GSK.

PS183

SURVEY OF SUBJECTIVE SYMPTOMS AND THE ACTUAL CONDITION OF PATIENTS RECEIVING TREATMENT FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Objectives We aimed to understand the symptoms, actual daily behavior, and degree of satisfaction of the patients receiving treatment for chronic obstructive pulmonary disease (COPD).
Method A questionnaire survey targeting 500 patients in 27 medical institutions specializing in pulmonary medicine was carried out between April and June 2013. We included patients aged ≥ 40 years patients who were visiting a medical institution after being diagnosed with COPD via pulmonary function testing. Further, all patients provided consent for participation in the survey. The treating doctors provided data on the pulmonary function, number of exacerbations, and treatment regimens of their patients.
Results Most patients were treated using long-acting inhalational drugs, and the patients indicated a relatively high degree of satisfaction with the treatment. Cough, sputum, and exertional dyspnea, depending on the disease severity, were frequently observed. Most patients reported that cough was the most troublesome, and was accompanied by sputum, during about 2 h after awakening. Exertional dyspnea was also reported to be the most severe on awakening, which continued for about 2 h, and in the afternoon. Patients reported a greater number of exacerbations than did their doctors, which indicated that the doctors probably did not completely understand the suffering of their patients.

PS184

EVALUATION OF PROPERTIES OF THE COPD ASSESSMENT TEST (CAT) VS SGRQ IN PREDICTING SEVERITY OF COPD BY GOLD CRITERIA

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Background The COPD assessment test (CAT) was developed to assist patients and their clinicians assess and quantify the symptoms and impacts of COPD and enable better communication between patients and physicians about these consequences of their disease. It was already validated to other countries as well in the Philippines and also has strong correlation to SGRQ.
Methods The study was a cross-sectional, 254 stable COPD patient were included in the study. CAT and SGRQ questionnaires administered as random basis. Data was described as mean ± sd or frequency (no.) and percent distribution. Kappa test was used to determine significance of agreement of cut-off points of scoring system with severity of COPD as diagnosed by spirometry.
Results The results obtained showed significant impairment in health status that was related to COPD severity. The COPD severity increases the CAT and SGRQ scores also increases significantly (CAT ($p = 0$), SGRQ ($p = 0.001$)). However, there was no significant agreement of cut off scores in CAT with COPD severity. (Kappa test: 0.17 $p = 0.009$).
Conclusion CAT showed significant association in health related impact to COPD severity with good correlation to SGRQ scoring system.

PS185

RISK FACTORS ASSOCIATED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE EARLY READMISSION

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Background and Aim of Study 31-day readmission rate is deemed to be an important indicator of the quality of medical care in China. The objectives of this study were to identify the readmission rate of acute exacerbation for chronic obstructive pulmonary disease (COPD) and to evaluate its associated risk factors.
Methods We retrospectively reviewed patients with acute exacerbation of COPD (AECOPD) to hospital between January 2011 and November 2012. The early readmission group and non-early readmission group were determined by whether patients were readmitted within 31 days after discharge. Logistic regression analysis was performed to identify risk factors for early readmission following an AECOPD.
Results There were 692 patients with 925 admissions during the 23-month period, 63 (6.8%) admissions were defined as early readmission. Multivariate analysis showed that chronic pulmonary heart disease (odds ratio (OR) 2.14, 95% confidence interval (CI) 1.26–3.64, $p = 0.005$), hypoproteinemia (OR 2.02, 95% CI 1.03–3.95, $p = 0.040$) and the level of PaCO2 (OR 1.03, 95% CI 1.00–1.06, $p = 0.027$) were the risk factors for early readmission of AECOPD.
Conclusion Readmission rate for AECOPD was high. AECOPD patients with chronic pulmonary heart disease, hypoproteinemia, and high level of PaCO2 are at risk for readmission with 31 days of hospital discharge, and medical care of these patients warrants much greater attention.

PS186

LOW LUNG VOLUME IS ASSOCIATED WITH VISCERAL ADIPOSE TISSUE INFLAMMATION

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Background Chronic obstructive pulmonary disease (COPD) has been recognized as a systemic inflammatory disease. Although visceral adipose tissue inflammation is known to be associated with various lifestyle diseases, such as diabetes mellitus and atherosclerosis, its contribution to the systemic inflammation of COPD remains unclear. The aim of this study was to evaluate the association between lung function and visceral adipose tissue inflammation.
Methods This study included 82 patients who underwent surgical resection due to an early stage of abdominal cancer, such as gastric and colon cancer. Visceral adipose tissue was obtained during the operation with informed consent. We quantified inflammatory cells in the adipose tissues, and evaluated its association with clinical parameters including lung function. This study was approved by an institutional ethics committee.
Results The number of visceral adipose tissue macrophage (ATM) did not show a significant correlation with FEV1% (FEV1/FVC), and was not different between patients with ($n = 20$) and without airflow limitation ($n = 62$). However, there was a significant negative correlation between ATM and % predicted VC ($r = -0.30$, $p = 0.006$). In addition, there was a significant positive correlation between ATM and body mass index (BMI). The levels of CRP was significantly higher in patients with low % predicted VC. Multivariate analyses demonstrated that % predicted VC and BMI were independently associated with the number of visceral ATM.
Conclusion The adipose tissue inflammation may contribute to the systemic inflammation of advanced COPD with low lung volume, independently from BMI.

1-E4: COPD 5

PS187

PREOPERATIVE PULMONARY DYSFUNCTION AND COMORBIDITIES IN PATIENTS UNDERGOING SURGERY

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Background Chronic obstructive pulmonary disease (COPD) is known to be associated with various comorbidities and unfavorable conditions during post-operative period. However, there are limited data on the association between subclinical airflow limitation (AL) and comorbidities. The aim of this study was to evaluate the frequency of preoperative pulmonary dysfunction among various diseases, and to assess the associations of pulmonary dysfunction with clinical parameters including comorbidities and the period of hospital stay.
Methods This study included 839 patients who had undergone surgical operation due to breast (n = 256), lung (n = 233), colorectal (n = 122), gastric (n = 256), or cardiovascular disease (n = 77). We retrospectively reviewed their clinical records such as age, sex, body mass index, smoking, underlying diseases, hospital days, and comorbidities such as hypertension, hyperlipidemia, hyperuricemia, and diabetes. We evaluated associations between these clinical parameters and pulmonary dysfunction.
Results The preoperative AL was observed in 240 (28.6%) among the patients, whereas only 32 (3.8%) had subjective symptoms and had been diagnosed as having COPD. The % predicted VC was significantly lower in patients with cardiovascular disorder than others. There were different frequencies of AL among patients with cardiovascular (45.5%), breast (7.0%), lung (40.3%), colorectal (32.0%), and gastric disorder (35.8%). Age and male gender were independently associated with the presence of AL. Among comorbidities, only hypertension (58.0% in patients with AL, 39.0% without AL) was significantly associated with AL, independently from age and sex. In addition, significantly longer hospital days were observed in patients with AL (23 days) than patients without AL (17 days) ($p < 0.0001$).
Conclusion Preoperative AL is frequently observed, and is mostly present as a subclinical dysfunction. Preoperative AL is significantly associated with hypertension, and the prolonged hospital days.

PS188

EVALUATION OF CARDIOVASCULAR RISKS IN PATIENTS WITH COPD USING HIGH-SENSITIVITY C-REACTIVE PROTEIN, CAROTID INTIMA-MEDIA THICKNESS AND DETECTION OF PLATELET HYPERAGGREGABILITY

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Background and Aim of Study Cardiovascular events such as acute myocardial infarction and stroke are the major comorbidities and the leading cause of death in patients with COPD. Atherosclerotic changes are largely responsible for these events. In the present study, we evaluated the cardiovascular risks in COPD patients by detecting platelet hyperaggregability and measuring high-sensitivity C-reactive protein (hs-CRP) which is a marker of systemic inflammation and carotid max intima-media thickness (Max-IMT).
Methods The study included 26 stable COPD patients (stage2–4) and 26 healthy controls. We measured carotid artery Max-IMT using ultrasound imaging, and hs-CRP in venous blood sampling. Regarding hyperaggregability, we analyzed frequency of occurrence of natural platelet aggregates in venous blood using an Abbot CELL-DYN SAPPHIRE hematology analyzer.
Results Platelet aggregates were positive in 4 of 26 (15.4%) in COPD patients, but only 1 of 26 (3.8%) in healthy controls. The average value of hs-CRP was 0.136(±0.139, SD) mg/dL in COPD patients and 0.047(±0.063) mg/dL in controls. The average value of the Max-IMT was 1.10(±0.40)mm in COPD patients and 0.96(±0.32)mm in controls. There was a tendency to thickening in the COPD group. Plaque was detected in 91% of the COPD group, but in 54% of the healthy controls.
Conclusion The results of the present study indicate that patients with stage 2–4 COPD have a significant risk of thrombosis due to atherosclerotic changes, and suggest that early detection of platelet hyperaggregability by the present method are useful for prevention of cardiovascular events.

PS189

SYSTEMIC REVIEW AND META-ANALYSIS OF PULMONARY SPECIFIC THERAPY FOR EXERCISE CAPACITY IN COPD

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Background Some patients with chronic obstructive pulmonary disease (COPD) have pulmonary hypertension (PH) that adversely affects survival. We performed a systematic review and meta-analysis to assess whether PH-specific therapies have an effect for patients with stable COPD.
Methods Data sources were Medline (from 1948 through October 2011), EMBASE (from 1980 through 20 November 2012), Cochrane Central Register of Controlled Trials, Koreamed and references from relevant publications. Randomized prospective trials that compared PH specific therapy in COPD for more than 6 weeks with placebo were included. Two reviewers independently extracted the data. The outcomes were the exercise capacity as 6 minute walking and adverse events of treatment.
Results Four randomized controlled trials involving 109 subjects were included in the analysis. Among the four trials two involved bosentan, one involved sildenafil and one involved beraprost. The studies varied in duration of treatment from 3 months to 18 months. In a pooled analysis of four trials, exercise-capacity was not significantly improved with PH-specific treatment for COPD (risk ratio −5.09, 95% CI −13.00 to 2.82). COPD patients with overt PH significantly improved the exercise capacity (mean difference 111.63, 95% CI 63.31 to 159.94) but COPD patients with PH unknown did not (mean difference 26.61, 95% CI −24.31 to 77.52). There was no significant difference in hypoxemia between PH-specific treatment and placebo groups (mean difference 2.55, 95% CI −3.68 to 8.77).
Conclusion PH specific treatments have a significant effect in improving exercise capacity in COPD patients with overt PH.

PS190

REPEATED EDUCATIONAL CAMPAIGNS ABOUT CHRONIC OBSTRUCTIVE PULMONARY DISEASE FOR GENERAL PRACTITIONERS AND THEIR EFFECTIVENESS

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Background Chronic obstructive pulmonary disease (COPD) is one of the common causes of death. However, limited number of patients is properly treated in Japan. One of the reasons is that some of the patients are not recognized and diagnosed by general practitioners (GPs).
Hypothesis Repeated educational campaigns about COPD for GPs could change their knowledge of diagnosis and treatments of COPD.
Methods Various educational campaigns about COPD had been organized in the cooperation with Shiga Prefectural Medical Association between 2005 and 2010. Surveys were performed using custom made unsigned questionnaires in 2005, 2006, and 2010.
Results The number of collected questionnaires were 298 out of 711 in 2005, 269 out of 731 in 2006, and 321 out of 856 in 2010. Throughout the period, the number of doctors who prescribed inhaled long-acting muscarinic antagonist (LAMAs), which is recommended as a first-line treatment by the guideline of the Japanese Respiratory Society, was significantly increased ($p < 0.001$). However, there was no significant change in the rate of having a spirometer in possession and recognition of the guidelines. When we focused on the survey results from the doctors specialized in internal medicine, the recognition of the guidelines was significantly increased ($p < 0.01$) despite no change in the rate of having a spirometer in possession. Furthermore, multivariable analysis of the 3rd survey result revealed that doctors who specialized in internal medicine, examined many patients with COPD, and recognized the guidelines prescribed more LAMAs significantly. On the other hand, doctors who did not specialize in internal medicine and examined few patients with COPD did not even know the guidelines.
Conclusions Not only educational campaigns but also comprehensive regional medical liaison between hospitals and clinics would be needed. Educational campaigns would be more beneficial when GPs' background was taken into consideration.

PS191

ATOPIC FACTORS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background Early initiation of inhalational corticosteroid therapy is useful in certain COPD patients, but associations of COPD signs with atopic factors are not clearly defined.
Methods Sixty-eight COPD patients who received medical care in our hospital from 2010 through 2013 were classified in the following 3 groups: (1) BA+COPD: Patients diagnosed with asthma complicated with COPD on the basis of smoking history and laboratory findings. (2) COPD+BA: Patients diagnosed with COPD complicated with asthma on the basis of response to treatment. (3) COPD: Patients diagnosed with COPD alone. Lung capacity, $\%FEV_1$ after β_2-agonist inhalation, peripheral blood eosinophil count, and serum total IgE and antigen-specific IgE antibody levels as well as the presence of emphysematous lesions were analyzed.
Results There were no significant age differences among the groups. %FEV1 and serum total IgE level in the BA+COPD group were significantly higher than those in the COPD group. The percentage of patients with positive specific IgE antibodies for more than one antigen was 78%, 57%, and 52% in the BA+COPD, COPD+BA, and COPD groups, respectively. Positive rates were higher in the BA+COPD than in the COPD group for house dust, a tick, a cockroach, a midge, and a moth, and higher in the COPD+BA than in the COPD group for house dust. Positive rates for Candida and aspergillus were similar among groups (approximately 20%).
Conclusion An asthmatic patient with dyspnea may be diagnosed with COPD. I suggest that environmental antigen sensitization may occur in the atopic factor-positive COPD patient with age, and that the possibility of complicating asthma must be considered.

PS192

ACUTE EXACERBATIONS OF COPD IN THE PILGRIMS FROM JAKARTAEMBARKATION 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.
Purpose Knowing the proportion and risk factors for AECOPD in the Jakarta Embarkation pilgirm during hajj 2011 and 2012.
Methodology Studies using cross-sectional design, which is implemented when pilgrims through the Hajj in Saudi Arabia during during Hajj year of 2001 and 2012.
Methods This is a cross-sectional 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. The proportion of AECOPD during Hajj 2011 and 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%). In the bivariate and multivariate analyzes found significant relationship between acute respiratory tract infection and comorbidity factors on the incidence of AECOPD.
Conclusion This study found a high proportion of AECOPD in Jakarta Embarkation pilgrims. We found Significant relationship between acute respiratory tract infection and comorbidity factors on the incidence of AECOPD.
Key Words Acute exacerbation of COPD, Pilgrims of Jakarta Embarkation.

PS193

CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS THE RISK FACTORS OF POST-OPERATIVE LUNG COMPLICATIONS IN THE PATIENTS WITH UNRUPTURED AORTIC ANEURYSMS

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The impacts of chronic obstructive pulmonary disease (COPD) in patients with aortic aneurysms are still unclear. The aim of the present retrospective study is to investigate the influences of COPD in patients who underwent the graft replacement operations for unruptured aortic aneurysms in Japan. The effects of airflow obstruction and post-operative physical therapy on the post-operative mortalities and lung complications were investigated in 109 patients. The patients were performed a spirometry before open thoracic or abdominal operations for unruptured aortic aneurysms under general anesthesia. Diagnosis and staging of COPD were in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. The ratio of COPD was 53.2% (58/109). The risk factors (risk ratio, p value) of post-operative lung complications were significantly increased in COPD (2.2, $p < 0.0001$), COPD GOLD stages II and III (9.3, $p < 0.0001$), open thoracic operation (1.7, $p < 0.05$), and aneurysm's diameters of 60 mm and over (2.3, $p < 0.05$), respectively. The frequency of post-operative lung complications in COPD patients was also significantly higher than that in non-COPD patients ($p < 0.05$). The post-operative physical therapy did not affect the outcomes after operations. Our results demonstrated that approximately 50% of patients with unruptured aortic aneurysm had the undiagnosed COPD. A spirometry should be needed to diagnose COPD for predicting post-operative lung complications of patients with unruptured aortic aneurysm.

PS194

THE BENEFITS OF PULMONARY REHABILITATION IN COPD; EXAMINATION BY A NEW GOLD CLASSIFICATION

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Background and Aim of Study The GOLD 2011 document proposed a new classification system for COPD combining airflow limitation, risk of exacerbations, and symptoms. Although the benefits of pulmonary rehabilitation (PR) in COPD are well recognized, PR is not recommended in patients with group A in the GOLD document. We aimed to examines the association of the new ABCD classification and the effects of the PR in patients with COPD.
Methods Outpatients who participated in a 10-weeks PR program at Tosei General Hospital were enrolled from July 1997 to July 2012. The patients were categorized into groups A, B, C, and D according to the GOLD 2011. PR program that consists of high intensity exercise training (60–80%peak work rate), resistance training, and inspiratory muscle training pressure load was 30% of the patient's PImax. Dyspnea (Baseline dyspnea index: BDI), exercise capacity (6-min walk distance: 6MWD), health status (the St George's Respiratory Questionnaire; SGRQ), and respiratory muscle strength (PEmax and PImax) were measured at baseline and after PR program.
Results 141 outpatient (68.2 ± 8.0 years of age; %FEV1:42.2 ± 16.2%) were included in the study. The patients' numbers in four groups A, B, C, and D were 18, 23, 26, and 74, respectively. The group A patients significantly improved BDI ($+0.8 \pm 0.2$, $p = 0.011$), 6MWD ($+23.3 \pm 5.6$ m, $p = 0.0023$), PEmax ($+10.8 \pm 4.8$ cmH2O, $p = 0.0249$), PImax ($+13.9 \pm 3.5$ cmH2O, $p = 0.0007$) after the PR program. The SGRQ did not improve after the PR program (-3.4 ± 7.8, $p = 0.0883$). Significant improvements in BDI, 6MWD, SGRQ, PEmax, and PImax occurred in the groups B, C and D following the PR program.
Conclusion These results suggest that all groups of COPD patients including the group A benefit from PR.

1-F1: INTERSTITIAL LUNG DISEASE 1

PS195

RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN IN THE TREATMENT OF ACUTE EXACERBATIONS OF IDIOPATHIC PULUMONARY FIBROSIS

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Background and Aim of Study Acute exacerbations (AE) of idiopathic pulmonary fibrosis (IPF) is considered to be a nearly fatal condition during the clinical course of IPF, as it is unresponsive to most conventional therapies. The aim of this study is to evaluate the efficacy of recombinant human soluble thrombomodulin (rhsTM) for AE of IPF.
Subjects and Mehtods We conducted a retrospective study of IPF cases who developed AE and were treated with corticosteroids (CS) combined with rhsTM. The subjects in the rhsTM-treated group comprised 15 patients with a mean age of 72.3 years. The clinical features and prognosis of the rhsTM-treated group was compared to those of the control group consisted of 25 IPF patients who had developed AE but not received rhsTM.
Results CS pulse therapy followed by CS maintenance treatment were conducted in all cases after the onset of AE. Patients in the rhsTM-treated group received combination therapy of CS and a rhsTM (380 IU/kg for 30 min, iv. once daily) for 6 days. Two-months survival after the onset of AE is 93.3% in the rhsTM-treated group and 24.0% in the non-rhsTM-treated group ($p < 0.001$) The median survival after the first onset of AE was 308.3 days in the rhsTM-treated group and 137.7 days in the non-rhsTM-treated group. Therefore the prognosis of the rhsTM-treated group therefore was significantly better than that of non-rhsTM-treated group.
Conclusions This study indicate that rhsTM combined with CS therapy may have beneficial effect in patiants with AE of IPF.

PS196

EFFICACY OF PIRFENIDONE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Rationale Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, fibrotic, and fatal lung disease without proven beneficial therapy. Recently pirfenidone (5-methyl-1-phenyl 2-[1H]-pyridone), an anti-inflammatory, antioxidant and antifibrotic agent, has been demonstrated to improve clinical course of IPF in several clinical trials. However, the time beginning pirfenidone for the therapy is still unclear and controversial. Thus, objective of this study is to investigate the clinical feature of patients with IPF, who were treated with pirfenidone for more than 6 months.
Methods This study was done retrospectively to investigate 11 patients with IPF or usual interstitial pneumonia (UIP) with connective tissue disease (CTD), except for case of acute exacerbation. All patients were required for definitive or probable UIP pattern in high-resolution computed tomography in accordance with the international consensus statement. Ten patients with IPF and 1 patient with CTD were treated with pirfenidone (1200 mg/day) and compared several indices as follows, severity, pulmonary function test (PFT), oxygen saturation by pulse oximetry (SpO2), and serum KL-6 levels, between baseline and treatment at 6 months.
Results At baseline, age and restrictive disorder in PFT of patients were older and more severe, respectively, than previous studies. At 6 months of treatment, there were no alteration in vital capacity (VC) (from 1905.0 ± 477.9 mL to 1994.0 ± 608.5 mL, %VC (from 58.4 ± 12.1 to 59.2 ± 16.6), severity, SpO2, and KL-6 levels (from 1448.8 ± 756.0 U/mL to 1322.3 ± 776.4 U/mL) from baseline. However, comparing alteration in the indices in term between 6~9 months before and 6 months after baseline, pirfenidone attenuated progression of restrictive disorder in PFT and elevation of KL-6 levels. One patient was improved from 4 to 1 of severity. No serious adverse events were seen.
Conclusion Treatment with pirfenidone may stabilize and improve clinical course of IPF when the introduction is done earlier.

PS197

EFFICACY OF PIRFENIDONE COMBINED WITH N-ACETYLCYSTEINE TREATMENT IN PATIENTS WITH ADVANCED IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study Treatment with pirfenidone may decrease the rate of decline in vital capacity and may increase the progression-free survival time. To assess the combined effects of inhaled N-acetylcysteine (NAC) and pirfenidone in patients with advanced IPF.
Methods Eligible patients had a clinical and radiologic diagnosis of advanced IPF (stages of severity with 3&4). Patients who exhibited a relative decline in FVC of 5% or more within the preceding six months were enrolled. The outcome was evaluated from the date of the 6-month follow-up PFT. Relative declines in FVC of more than 5% were defined as ineffective group, while those less than 5% were defined as effective group. We compared the clinical features and efficacy of the combined therapy with inhaled NAC and pirfenidone: NAC group ($n = 14$) with that of pirfenidone alone: non-NAC group ($n = 9$).
Results Twenty three patients, 59–82 years of age, with IPF who received pirfenidone therapy were reviewed. Nine of 14 patients (64%) in the NAC group were effective at the 6-month follow-up PFT. On the other hand, three of nine patients (33%) in the non-NAC group were effective. The median change in FVC at six months was –290 mL in the NAC group and –510 mL in the non-NAC group. The relative change in FVC at six months was –13% in the NAC group and –22% in the non-NAC group. The median survival period was 674 days in the NAC group and 401 days in the non-NAC group ($p = 0.88$). The use of combined NAC therapy was correlated with a favorable outcome.
Conclusions Even though the advanced IPF patients with a more progressive status, patients treated with pirfenidone combined with NAC therapy exhibited favorable outcomes. Additional studies are needed to confirm the efficacy of this combined therapy for IPF.

PS198

EFFECTS OF INTERVAL EXERCISE IN INTERSTITIAL LUNG DISEASE PATIENTS

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Background and Aim of Study There are little data on the effect of interval exercise in patients with interstitial lung disease (ILD). The aim of this study was to evaluate the feasibility and the effectiveness of interval exercise (IE) on the exercise capacity in patients with ILD.
Methods Patients with ILD completed a four weeks of in-patient pulmonary rehabilitation (PR) at Tosei General Hospital from January 2005 to December 2012 were recruited. All patients first were recommended to enroll in the constant load exercise (CLE) group, and patients who could not perform the CLE protocols participated in the IE group. IE protocols were 30 second work periods interspersed with 30 second rest periods for 40 min/day. Patients who can carry out CLE (CLE group) exercised for 20 min/day. Target intensity was > 80–100% of baseline peak work rate in the IE group, and 80% in the CLE group. All patients evaluated the pulmonary function tests, 6 minute walk distance (6MWD), constant work rate test, quadriceps force, baseline dyspnoea index (BDI) on baseline and after PR program.
Results Twenty-seven ILD patients (CLE in 12, IE in 15) were studied. After PR program, 6MWD increased significantly compared with baseline value both in the IE group (from 291.5 ± 119.8 m to 347.7 ± 143.3 m, $p = 0.048$) and in the CLE group (from 309.6 ± 129.0 m to 347.0 ± 114.4 m, $p = 0.023$). Constant work rate test (IE, 177.0 ± 71.8 sec to 396.8 ± 302.6 sec, $p = 0.003$; CLE, 196.3 ± 90.9 sec to 422.0 ± 464.4 sec, $p = 0.006$), quadriceps force (IE, 56.8 ± 17.1 Nm to 64.2 ± 20.8 Nm, $p = 0.002$; CLE, 71.3 ± 21.4 Nm to 76.2 ± 21.5 Nm, $p = 0.031$) and BDI (IE, 4.9 ± 1.8 to 5.5 ± 1.8, $p = 0.039$; CLE, 2.8 ± 1.8 to 3.6 ± 2.4, $p = 0.024$) improved significantly in both groups. SGRQ improved significantly in IE group (IE, 66.3 ± 14.2 to 60.1 ± 15.4, $p = 0.003$; CLE, 71.3 ± 10.6 to 65.9 ± 14.2, $p = 0.195$).
Conclusion IE produced improvements in exercise tolerance in ILD patients who could not perform CLE.

PS199

EFFECTS OF IN-PATIENT PULMONARY REHABILITATION FOR ADVANCED IDIOPATHIC PULMONARY FIBROSIS

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Background and Aim of Study Idiopathic pulmonary fibrosis (IPF) is a progressive and devastating disease. Recent studies showed the beneficial effects of pulmonary rehabilitation (PR) for IPF, however, data for patients with advanced IPF are limited. The aim of this study was to examine the effects of PR for advanced IPF.
Methods Patients with advanced IPF completed a four weeks of in-patient PR at Tosei General Hospital from January 2001 to December 2012 were recruited. In-patients PR program were recommended because they could not perform out-patient PR program. A four weeks in-patient PR program consisted of high intensity exercise training(60–80%peak work rate) using cycle ergometer. In addition, they also performed resistance training. Dyspnea (Baseline dyspnea index : BDI),quadriceps force,exercise capacity (6-min walk distance: 6MWD) and health related QOL (SGRQ) were measured at baseline and after four weeks of PR.
Results Twenty-eight IPF patients (19 males; 69 ± 8 years of age; FVC % predicted, 53 ± 17%; DLCO % predicted, 31 ± 15%) were studied. Following PR, significant improvements were observed in BDI (3.6 ± 1.9 to 4.2 ± 2.1, $p = 0.001$), quadriceps force (67.5 Nm $\pm$ 21.0 Nm to 71.7 Nm $\pm$ 24.2 Nm, $p = 0.007$), 6MWD (300.9 m $\pm$ 129.7 m to 327.4 m $\pm$ 149.0 m, $p = 0.028$), and SGRQ Total (69.8 ± 11.5 to 64.3 ± 15.2, $p = 0.014$).
Conclusion In-patient PR program improved dyspnea, quadriceps force and exercise capacity and HRQOL in patients with advanced stage of IPF.

PS200

THE USEFULNESS OF A 30-SECOND CHAIR STAND TEST FOR EVALUATING EXERCISE CAPACITY IN PATIENTS WITH MILD-TO-MODERATE INTERSTITIAL LUNG DISEASE

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Background and Aim of Study Although a 30-second chair stand test (CS-30) has been used as a measurement test for assessing the strength of lower extremities in adults, the usefulness in interstitial lung disease (ILD) is unknown. The aim of this study was to elucidate the usefulness of a CS-30 in mild-to-moderate ILD.
Methods Nineteen consecutive patients with ILD who underwent a 6-min walk test (6MWT) and CS-30 as evaluations in clinical practice were included (17 of idiopathic pulmonary fibrosis and 2 of connective tissue disease related ILD). The data was reviewed retrospectively and a comparison was made between 6MWT and CS-30.
Results Of 19 patients, 15 were male. The age was 73 ± 9 years old. The modified Medical Research Council (MRC) dyspnoea score was 2.3 ± 0.7. The PaO2 was 87 ± 13 Torr. The percent predicted FVC, TLC, and DLCO were 80 ± 16%, 78 ± 14%, and 70 ± 22%, respectively. The 6MWT data was as follows; walk distance (6MWD): 450 ± 101 m, maximum heart rate (HRmax): 118 ± 17 bpm, maximum respiratory rate (RRmax): 42 ± 8 bpm, minimum SpO2 (SpO2 min): 87 ± 6%, and maximum modified Borg dyspnoea score (MBSmax): 6.4 ± 1.6. In contrast, the CS-30 data was as follows; number of times (CS-30T): 16 ± 4, HRmax: 103 ± 15 bpm, RRmax: 31 ± 5 bpm, SpO2 min: 92 ± 4%, and MBSmax: 4.7 ± 1.2. In comparison of these parameters between the two tests, the CS-30T was significantly correlated with the 6MWD ($\rho = 0.80$, $P < 0.001$). However, the HRmax, the RRmax, and the MBSmax were significantly lower ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively) and the SpO2 min was significantly higher ($P < 0.001$) in the CS-30. The number of patients who desaturate severely (SpO2 min < 85%) was significantly smaller in the CS-30 (2 vs 6, $P = 0.04$). The decrease in SpO2 during the tests was significantly smaller in the CS-30 (5.1 ± 2.5% vs 9.9 ± 4.5%, $P < 0.001$).
Conclusion The CS-30 is a useful test to evaluate exercise capacity in patients with mild-to-moderate ILD because of its alleviated desaturation.

PS201

CHARACTERISTICS OF INSPIRATORY AND EXPIRATORY REACTANCE IN IDIOPATHIC PULMONARY FIBROSIS

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Background Forced oscillometry is a non-invasive method to measure respiratory resistance and reactance. In this study, we investigated the characteristics of resistance and reactance obtained with an impulse oscillation system (IOS) in patients with idiopathic pulmonary fibrosis (IPF).
Method IOS and spirometry were performed in 35 IPF patients, 40 chronic obstructive pulmonary disease (COPD) patients, and 27 healthy volunteers. Respiratory resistance and reactance were assessed as measurements averaged over several tidal breaths (whole-breath analysis) and as measurements separately averaged during inspiration and expiration (inspiratory-expiratory analysis).
Results Whole-breath IOS analyses in IPF patients showed increased resistance at 5 Hz (R5) and decreased reactance at 5 Hz (X5) compared with controls, although these features were also found in the COPD groups. However, the changes in X5 between inspiration and expiration were found to vary between IPF and COPD groups. Expiratory X5 was more negative than inspiratory X5 in COPD patients. In contrast, inspiratory X5 was found to be more negative than expiratory X5 in IPF patients. In IPF patients, within-breath changes in X5 (deltaX5), defined as expiratory X5 minus inspiratory X5, was significantly higher than those in the other groups. Furthermore, deltaX5 was inversely correlated with vital capacity, diffusing capacity of carbon monoxide and composite physiologic index (CPI) in IPF patients.
Conclusions This study suggests that an increased X5 magnitude during inspiration compared with that during expiration is a characteristic feature of IOS measurements in IPF patients, which is clearly different from those in COPD patients. This within-breath X5 change in IPF might be associated with its severity and physiological abnormality, although further studies are needed to investigate its cause.

PS202

QUANTIFICATION OF LUNG PERFUSION BLOOD VOLUME AND XENON VENTILATION BY DUAL-ENERGY CT IN PATIENTS WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Aim The aim of the study is to investigate the clinical feasibility of the quantification of lung perfusion blood volume (PBV) and xenon ventilation by dual-energy CT in differentiation of patients with combined pulmonary fibrosis and emphysema (CPFE) associated with idiopathic pulmonary fibrosis (IPF) and IPF alone.
Subjects and Methods Seventeen CPFE patients (12 males, 5 females; mean age, 74.9 years) and 17 IPF alone patients (12 males, 5 females; mean age, 75.4 years) underwent dual-energy CT (SOMATOM Definition; Siemens Healthcare, Forccheim, Germany) during April 2012 and March 2013. The subjects inhaled 35% stable nonradioactive xenon to take a single deep breath. After performing xenon ventilation CT, intravenous injection of contrast material was administered. Xenon-enhanced and pulmonary CT angiographic images were derived by using three-material decomposition technique. Furthermore, the percentage of areas enhanced by xenon and adjusted PBV CT values were calculated in the upper, middle, and lower lung fields relatively by the following formulae: volume enhanced by xenon gas/volume of each lung field x 100 and PBV CT value/enhanced CT value in pulmonary artery x 100.
Results The percentage of areas enhanced by xenon in both lungs calculated as CPFE/IPF = 71.9 ± 15.8%/77.5 ± 13.5% relatively. In particular, the percentage of areas enhanced by xenon in upper predominant defect pattern of CPFE was significantly higher than that in diffuse defect pattern of CPFE. The honeycomb lesions in IPF alone showed significantly increased the percentage of areas enhanced by xenon/adjusted PBV CT values ratio compared with those in CPFE. In addition, the ratio of each lung field in diffuse defect pattern of CPFE was more decreased than that in IPF alone.
Conclusions Quantification of lung perfusion blood volume and xenon ventilation by dual-energy CT is feasible for differentiating of patients with CPFE and IPF alone.

1-F2: INTERSTITIAL LUNG DISEASE 2

PS203

RETROSPECTIVE ANALYSIS OF THE PATIENTS WITH LYMPHANGIOLEIOMYOMATOSIS

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Background Lymphangioleiomyomatosis (LAM) is a progressive rare lung disease that exclusively affects women of childbearing age. Recent studies have revealed that measurement of serum vascular endothelial growth factor (VEGF)-D level is useful for the diagnosis of LAM. Serum VEGF-D level may serve as a biomarker of disease severity, disease progression, or treatment response in LAM. In this study, we analyzed patients of LAM retrospectively.
Subjects and Methods We analyzed 87 sporadic LAM (38.4 (22.5–64.2) years old) and 13 TSC-LAM Patients (36.7 (25.2–58.4) years old) retrospectively in this study. There are 7 patients who underwent lung transplantation and 7 patients passed away. One patient was overlapped between lung transplantation groups and passed away group. Serum proteins levels were evaluated with clinical data by using multivariate analysis.
Results Seven patients passed away because of respiratory failure and one patient by severe seizure attack. These patients were complicated with pneumothorax, chylothorax, angiomyolipoma, lymphatic diseases, and so on. Patients with the history of treatment with gonadotrophin-releasing hormone analogues (n = 8) and/or sirolimus (n = 5) were included in these patients. Median age of onset and first medical examination were 29.0 and 34.9 years old, respectively. The age of death in this 14 cases (lung transplantation and passed away) were 41.0 (32.0–57.3) years old, and life expectancy after diagnosis was 4.4 (0.3–14.9) years. And 5 years survival rate after visiting our hospital was 92 %. Among biomarkers, serum VEGF-D was the most sensitive biomarker for monitoring the prognosis compared to KL-6, SP-D, SP-A and ACE. Furthermore, serum VEGF-D level decreased immediately with sirolimus treatment.
Conclusion LAM is a systemic disease with the poor prognoses. Serum VEGF-D level is useful biomarker for clinical diagnosis but not enough for prognosis factor of LAM. However, serum VEGF-D level is a good indicator of mTOR treatment.

PS204

DIAGNOSTIC METHODS AND UTILITY OF TRANSBRONCHIAL LUNG BIOPSY IN THE DIAGNOSISOF LYMPHANGIOLEIOMYOMATOSIS

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Background and Aim of Study Clinical diagnosis of lymphangioleiomyomatosis (LAM) can be made if high-resolution CT (HRCT) revealed characteristic appearance of multiple and thin-walled cysts distributing throughout both lungs and excluded other cystic lung diseases. However, the diagnosis by pathologic examination is still recommended if feasible. Surgical lung biopsy, including video-assisted thoracic surgery (VATS), is useful for the diagnosis of LAM, but it is so invasive especially for patients with severely impaired pulmonary function. Transbronchial lung biopsy (TBLB) is less invasive than VATS, but may result in low diagnostic yield if sufficient amount of LAM lesions were not included in the biopsied lung tissues. The purpose of our study was to examine the variety of diagnostic methods utilized in our LAM cohort and utility of TBLB in the diagnosis of LAM.
Methods We retrospectively reviewed clinical records of 244 LAM patients in our hospital.
Results The diagnosis of LAM was established by either pathologic examinations in 187 patients (76.6%), clinical diagnosis in 51 patients (20.9%), or other methods in 6 patients (2.5%). Of 187 patients with pathologic diagnosis, 119 (63.6%) had surgical lung biopsy, 32 (17.1%) were TBLB, 28 (15.0%) were abdominal surgery for retroperitoneal lymphangioleiomyomas, 4 (2.2%) were excised lung, and 4 (2.2%) were cytologic examination. The diagnostic yield of TBLB was 90% and there was no complication of pneumothorax after TBLB. The reason for our high diagnostic yield by TBLB seemed to be our careful selection of LAM patients who showed diffuse cystic changes in HRCT.
Conclusion TBLB appears to be safe and efficient method for establishing the diagnosis of LAM. Surgical lung biopsy, especially VATS, is an effective method for treatment of pneumothorax as well as the diagnosis in LAM patients with pneumothorax.

PS205

UIP PATTERN OF CHRONIC HYPERSENSITIVITY PNEUMONITIS: DIFFERENTIATION FROM IDIOPATHIC PULMONARY FIBROSIS

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Background The pathologic findings of chronic hypersensitivity pneumonitis (CHP) have many varieties of patterns, and often present UIP patterns. Therefore the distinction of CHP presenting UIP pattern (CHP-UIP) from idiopathic pulmonary fibrosis (IPF) is often difficult. The purpose of this study is to clarify high-resolution CT (HRCT) findings that can be useful to differentiate CHP-UIP from IPF.
Method This study included 50 patients with CHP-UIP and 48 patients with IPF. Two groups of observers independently assessed the HRCT findings, evaluated the extent of each abnormal CT finding, and then made a first-choice diagnosis. When the diagnosis was CHP-UIP, they noted what was inconsistent with IPF.
Results Correct diagnoses were made 78–80% in CHP-UIP, and 52–54% in IPF. There was no difference in the extent of ground-glass opacities, consolidation, honeycombing, and emphysema of both groups. The features that best differentiated CHP-UIP from IPF was excess of micronodules (hazard ratio 12.0 (95% CI;2.2–65.4), $p = 0.004$).
Conclusion Although HRCT findings of CHP-UIP closely resemble to those of IPF, the excess of micronodules in HRCT can be useful finding to differentiate CHP-UIP from IPF.

PS206

MYELOPEROXIDASE ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY (MPO-ANCA) ASSOCIATED LUNG DISEASE: CLINICAL, RADIOLOGICAL AND BRONCHOALVEOLAR LAVAGE FLUID FINDINGS

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Background and Aim of Study Characteristics of MPO-ANCA associated lung disease have not been well understood. The aim of this study was to assess the clinical, radiological and bronchoalveolar lavage (BAL) fluid findings of MPO-ANCA associated lung disease.
Methods We retrospectively reviewed 26 patients (18 females and 8 males, median age 71 years) who showed elevated MPO-ANCA levels more than double for the standard value in our hospital (>40 EU) and performed chest computed tomography in our department (respiratory medicine and nephrology) between 1996 and 2011. BAL was performed in 10 of 26 patients before treatment. BAL fluid findings were compared with idiopathic pulmonary fibrosis (IPF) group (n = 24) and idiopathic nonspecific interstitial pneumonia (I-NSIP) group (n = 15).
Results The frequency of the clinical symptom was: fever 46%, dyspnea or cough 31%, sputum or leg edema 23%, hemosputum 12% and hematuria 4%. Sixteen patients (62%) had renal dysfunction at diagnosis. The criteria of microscopic polyangitis was fulfilled in 15 patients (58%). CRP was positive in 24 patients (92%), and serum KL-6 and SP-A levels were positive in 64% and 92%, respectively. The findings of chest computed tomography were: interstitial pneumonia 46% (usual interstitial pneumonia pattern 23% and NSIP pattern 19%), bronchiectasis 19% and multiple nodules 8%. BAL fluid showed increasing percentage of neutrophils in MPO-ANCA associated lung disease (14.4%) compared with IPF (3.8%) and I-NSIP (1.7%). BAL fluid IL-8 levels significantly correlated with the percentage of neutrophils in BAL fluid of patients with MPO-ANCA associated lung disease. All 26 cases were treated by corticosteroid w/wo immunosuppressant, and relatively have a good prognosis.
Conclusion The clinical symptoms and radiological findings of MPO-ANCA associated lung disease were various. BAL fluid findings were characterized by increasing percentage of neutrophils and this suggests that neutrophils play a pivotal role in MPO-ANCA associated lung disease.

PS207

CLINICAL ANALYSIS OF LUNG MANIFESTATIONS IN SJÖGREN'S SYNDROME

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Background Although pulmonary involvement of Sjögren's syndrome (SS) has been reported, its clinical characteristics have not been clear in detail.
Aim of Study The goal of this study was to clarify the characteristics of pulmonary manifestation in patients with SS.
Methods We reviewed patient with SS admitted to our hospital from 2007 to 2011, and retrospective analysis was performed.
Results We had 37 patients with SS including 26 primary (pSS) and 11 secondary Sjögren's syndrome (sSS). Only 11 patients had mucous membrane drying symptoms. Anti-SSA and SSB antibodies in serum were positive in 32 and 13 patients, respectively. Thirty three patients had consistent findings of fluorescent dye examination and/or lip biopsy with SS. Interstitial pneumonia (IP) was the main pulmonary manifestation, and 10.2% of IP patients with unknown etiology on admission were diagnosed as having SS by careful clinical evaluations. Histopathological analysis revealed a variety of histological findings such as non-specific IP, and cellular bronchiolitis. Grand glass attenuation was the major HRCT pattern with lower and peripheral predominant distributions, and analysis of bronchoalveolar lavage fluid showed increase number of lymphocytes and neutrophils. Five-year survival rate was about 80%, and prognosis in patients with pSS seemed to be better compared with sSS patients.
Conclusions IP is the major pulmonary manifestation of SS, and prognosis of SS patients with pulmonary diseases is not so poor. However, for more understanding of this disease, careful clinical evaluations including lip biopsy are necessary even for patients without sicca symptoms because of under-diagnosis of SS.

PS208

RILUZOLE-INDUCED LUNG INJURY IN TWO PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Riluzole has recently become the first drug proven effective in the treatment of amyotrophic lateral sclerosis (ALS). We report two rare cases of lung injury caused by riluzole therapy in patients with ALS. Chest radiographs showed bilateral lower lobe, dorsal-dominant ground glass opacity and/or consolidation. A drug lymphocyte stimulation test (DLST) of peripheral blood or of bronchoalveolar lavage cells was positive for riluzole. Histopathological examination of lung biopsy specimens revealed lung injury without fungoid granuloma, vasculitis, or diffuse alveolar damage. To the best of our knowledge, this is the first report of riluzole-induced lung injury with a positive DLST results.

PS209

SARCOIDOSIS LIKE FINDINGS IN A CROHN PATIENT TREATED WITH INFLIXIMAB

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Sarcoidosis and Crohn's disease are both granulomatous disorders and in some cases thought to be a different spectra of the same disease. Crohn's pulmonary manifestations are mostly drug induced eosinophilic pneumonia, fibrosis and subclinical pulmonary function abnormalities. Some case reports indicated that anti-TNF therapy can paradoxically cause sarcoidosis-like reactions. Our case is a 49 year-old white man who had been suffering from crohn's disease for 6 years and had needed tumour necrosis factor-alpha (TNF-α) treatment for perianal pericecal fistula. In routine control for anti-tnf treatment thorax CT scan showed centrale ground glass pulmonary infiltrates and a nodule in left apicoposterior segment. Bronchoalveolar lavage mycobacterial and bacterial cultures were negatif so we started isoniazid prophylaxis with infliximab therapy. After three months control torax CT scan showed regression of infiltrates. The patient had no respiratory complaints so follow-up was planned. After two years due to new infiltrates in X-ray, a new CT showed bilateral tree-in-bud and pulmonary infilitrates and mediastinal lymph nodes of 8×13 mm. Tracheal aspiration culture was negative for tuberculosis so with nonspecific antibiotherapy infliximab treatment continued. Control CT scan showed regression in left lung fields and new infiltrates in right lung fields. Neither eosinophilia nor any specific antibodies were found in the peripheral blood. Alveoler lavage revealed CD4/CD8 ratio of 9,2. In our case there is a diagnostic confusion about pulmonary infiltrations, mediastinal lymph nodes and alveoler lavage results. Crohn's disease alone can immitate sarcoidosis in bronkoalveoler lavage or can be concominant with sarcoidosis. In addition anti-TNF therapy can paradoxically cause sarcoid-like granulomatosis. The clinical discussion is whether withdraw infilximab therapy or to continue followup because the patient is asemptomatic and has no pulmonary function loss.

PS210

CLINICAL AND RADIOLOGICAL CHARACTERISTICS OF RAPIDLY PROGRESSIVE INTERSTITIAL PNEUMONIAE

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Background and Objective An effective treatment has not been established for rapidly progressive interstitial pneumoniae (RPIP) and outcomes are poor. Furthermore, the predictive factors for prognosis are unkown. The aim of the present study was to assess the clinical and radiological characteristics, and the prognostic predictors for survival in RPIP. We have defined RPIP as interstitial lung disease presenting as acute respiratory failure, with bilateral infiltrative shadows on chest high-resolution CT (HRCT), and unrelated to chronic respiratory disease or alternative causes of interstitial pneumonia due to underlying diseases.
Study Subjects and Methods Fifteen RPIP patients (male:11, female:4) with a mean age of 69.9 years were studied retrospectively. All patients were treated at our institution in the period August 2007 to September 2012. We compared the clinical features and HRCT findings between 4 survivors and 10 non-survivors. In addition, we have assessed the prognostic predictors for survival during 60 days after the onset of RPIP.
Results Here were no significant differences between survivors and non-survivors in age, sex, P/F ratio (110+–99 v.s 169+–85), serum KL-6, serum SP-D, APACHE score (11.2+–1.6 v.s 12.6+–4.7), lung injury score (3.3+–1.3 v.s 2.7+–1.1) and the therapeutic regimen and ground-glass attenuation, consolidation, honeycombing on HRCT. The HRCT findings such as architectual distortion and traction bronchiolectasis were more extensive in non-survivors than those in survivors. Ten of 15 (66%) patients died due to progression of RPIP during hospitalization. The median survival period was 838.6 days in survivors and 21 days in non-survivors.
Conclusions Ithough the mortality of patients with RPIP is high, long-term survival can be expected in patients who recovered from the status of refractory respiratory failure. HRCT findings were potentially helpful for predicting the prognosis in RPIP.

PS211

TWO CASES OF RAPIDLY PROGRESSIVE INTERSTITIAL PNEUMONIA ASSOCIATED WITH CLINICALLY AMYOPATHIC DERMATOMYOSITIS SUCCESSFULLY TREATED WITH EARLY INTENSIVE THERAPY

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Rapidly progressive interstitial pneumonia (RPIP), which is resistant to therapy and have a poor prognosis, is occasionally accompanied by clinically amyopathic dermatomyositis (CADM). Effective treatment of RPIP associated with CADM has not yet been determined. The anti-CADM-140 antibody is frequently detected in RPIP associated with CADM, and thought to be a useful serological marker. In addition, the serum ferritin level is thought to predict disease activity and prognosis. We encountered two Japanese patients with RPIP accompanied by anti-CADM-140 antibody positive CADM. These patients complained of fever, rapidly progressive dyspnea and characteristic cutaneous manifestations (Gottron sign, heliotropic rash and mechanic's hand), but mild muscle weakness. Chest high resolution computed tomographic scans (HRCT) revealed reticular opacities and air-space consolidation in both lungs with basilar predominance. The serum ferritin levels were elevated in both patients. The diagnosis of RPIP accompanied by CADM was made clinically. Intensive therapy was initiated with pulsed methylprednisolone, followed by high-dose oral administration of prednisolone, pulsed cyclophosphamide, and cyclosporine immediately. At early time point, high-dose intravenous immunoglobulin (IVIG) and direct hemoperfusion with polymyxin B-immobilized fiber column (PMX-DHP) were also administrated. This intensive combined therapy rescued the two patients without respiratory failure. Chest HRCT image and pulmonary function test gradually improved, and the anti-CADM140-antibody titers and serum ferritin levels decreased in parallel. Early intensive therapy including IVIG and PMX-DHP could be an effective therapy for life-threatening RPIP associated with CADM.

PS212

BAL FLUID CONCENTRATIONS OF CYTOKINES IN PATIENTS WITH NSIP, UIP, COLLAGEN VASCULAR DISEASE ASSOCIATED WITH INTERSTITIAL PNEUMONIA, AND SARCOIDOSIS

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Background Inflammatory cytokines have been reported to play important roles in the pathogenesis of interstitial lung diseases. However, their individual roles in idiopathic interstitial pneumonitis (IIP) and in the other types of interstitial pneumonitis (IP), including collagen vascular disease associated interstitial pneumonitis (CVD-IP), remain unknown. In this study, we measured the bronchoalveolar lavage (BAL) fluid levels of several cytokines in patients with IIP and CVD-IP.
Methods Cell subpopulations in BAL fluid were counted, and BAL fluid levels of IL-2, -6, -7, -8, -17, IFN-gamma, TNF-alpha, and TGF-beta1 were measured using a bead suspension array or an enzyme-linked immunosorbent assay (ELISA) kit in 16 patients (8 men, 8 women) with idiopathic nonspecific interstitial pneumonitis (NSIP), 5 patients (3 men, 2 women) with idiopathic usual interstitial pneumonitis (UIP), 5 patients (3 men, 2 woman) with rheumatoid arthritis in CVD-IP (RA), and 5 patients (3 man, 2 women) with dermatomyositis in CVD-IP (DM), and 13 patients (3 men, 10 women) with sarcoidosis.
Results BAL cell subpopulations had high amounts of lymphocytes in NSIP and sarcoidosis, and neutrophils in RA. Levels of IL-7 were significantly higher in DM than in RA. IL-7 in DM was significantly correlated with lymphocytes. The levels of TNF-alpha were highest for RA, compared with other IPs, and sarcoidosis. In addition, the levels of IL-17 were highly detectable in RA, but not in NSIP, UIP, or sarcoidosis.
Conclusions Differences in the cell types of BAL fluid and the level of each cytokine between patients with IIP and CVD-IP might reflect pathogenesis and be useful for diagnosis.

2-A1: OTHERS 1

PS213

CHARACTERISTICS OF MEDIASTINAL TUMORS IN PERSAHABATAN HOSPITAL IN JANUARY 2012-JULY 2013

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Background and Aim of the Study Mediastinal tumors, both benign and malignant, are found in mediastinal cavity. Aim of the study was to know the characteristics of mediastinal tumors who underwent thoracotomy in Persahabatan Hospital, Jakarta, Indonesia.
Methods This study is a descriptive retrospective study. Data were taken from hospital medical records of 30 cases of mediastinal tumor underwent thoracotomy in the ward of Thoracic Surgery, Persahabatan Hospital in January 2012-July 2013.
Results Due to incomplete medical records information, only 21 cases were included in the study. Subject was mostly young individuals with average age of 27.28 years and male was 12 (57.14%). The location of tumor were more dominant in the anterior mediastinum (19 subjects, 90.47%) and 2 subjects in the posterior mediastinum. Among anterior mediastinal tumor, post thoracotomy diagnosis were lymphoma (7/19), Teratoma (6/19), Thymoma (4/19), germ cell tumor – yolk sac tumor (1/19), and fibrosing mediastinitis due to tuberculosis (1/19). Ganglioneuroma and thymoma were among the posterior mediastinum tumor. The surgical approach was diagnostic open biopsy (7/21), debulking of tumor mass, extended thymectomy. Myasthenia gravis as shown by positive Harvey Masland test was found in 4 subjects, and interestingly all were male, with pathological diagnostic range from lymphoma (1/4), thymoma (2/4), and mediastinitis fibrosis (1/4). Pre operative bronchoschopy showed compression of trachea in 8/21 patients. Among the routine tumor marker evaluation (CEA, LDH, β-HCG, AFP), LDH was increased in 9/21 patients (lymphomas 3/9, teratoma 3/9, thymoma 2/9, germ cell tumor) and AFP was increased only in 1/21 patients (teratoma).
Conclusions Characteristics of patients with mediastinal tumor are very important as a baseline for future studies. Further study is needed to evaluate the survival, predictive factor, role of tumor markers evaluation and myasthenia gravis complication.

PS214

LUNG LEUKOSTASIS: A SERIAL CASE REPORT FROM THREE PATIENTS WITH CHRONIC MYELOCYTIC LEUKEMIA

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Lung leukostasis: a serial case report from three patients with chronic myelocytic leukemialka Trisnawati, Eko Budiono, Sumardi, Bambang Sigit Division of Pulmonology, Department of Internal Medicine Faculty of Medicine Gadjah Mada University/DR. Sardjito Hospital, Yogyakarta, Indonesia

Introduction Leukostasis is a fatal complication in leukemia. Brain and lung are most commonly involved organs in leukostasis. In the lung, the clinical presentation similar to acute respiratory distress syndrome (ARDS). Being a medical emergency, early recognition of leukostasis and initiation of therapy prevents mortality.
Result All of 3 patients in this article we disscussed had been diagnosed with chronic myelocytic leukemia (CML) before. They came to hospital emergency department because of dyspneu. From blood count, all of the patients got hyperleukocystosis, with leukocyte count 576.000/mm^3, 308.000/mm^3, 380.000/mm^3, respectively. All expertised of X-ray by radiologist were the same result: lung infiltrates. From blood gases analysis, first patient has SaO2: 45,9%, PaO2: 28,6 mmHg, AaDO2: 117,4 mmHg; second patient has SaO2: 65,1%, PaO2: 23,1 mmHg, AaDO2: 115 mmHg; third patient has SaO2: 76,6%, PaO2: 56,5 mmHg, AaDO2: 114,9 mmHg. They all were asssesed as lung leukostasis. First patient underwent a fine needle aspiration and the histological result was leukemic cells (myeloblast and mylocyte) infiltrated in lung. After they had been gotten cytoreduction (leukapheresis and hydroxyurea) they clinically and labolatory got better.
Conclusion Although hydroxyurea and leukapheresis have been proposed to rapidly reduce leukocytes count and possibly related symptoms, few data support their true value in decreasing early mortality. In absence of specific guidelines for the management of symptomatic hyperleukocytosis such as lung lekostasis, leukapheresis when feasible, should be considered in the day-to-day practice.
Keyword lung lekostasis, leukapheresis, blood gas analysis, mortality.

PS215

FEASIBLE USE OF BIPOLAR TISSUE SEALING SYSTEM FOR THORACOSCOPIC THYMECTOMYDEPARTMENT OF SURGERY

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Introduction We had mainly used monopolar electric scalpel though heat diffusion by this instrument might have possibility to mistakenly damage surrounding tissue and vessels. In addition, during the operation of thoracoscopic thymectomy, it was difficult to choose what device should be used because of its narrow working space. Introduction of bipolar tissue sealing system has made a great progress and solve these problems.
Patients and Methods We have mainly used ENSEAL TRIO it can control heat diffusion into lateral tissue that enables safe manipulation in the area neighboring blood vessels and nerves; it can appropriately seal tissue with even and high compression through the entire length of the jaw; it can seal and cut the tissue with one motion; it can give better visualization and manipulation in narrow operative field with its curved jaw shape.
Results ENSEAL TRIO experience of thoracoscopic thymectomy demonstrated high feasibility without operative method change, intraoperative side injuries, and postoperative complications.

PS216

PULMONARY LYMPHAGNGIOLEIOMYOMATOSIS IN ELDERLY PATIENTS: A CASE REPORT AND REVIEW OF LITERATURE

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Introduction Lymphangioleiomyomatosis is a rare pulmonary disorder characterized by proliferation of smooth muscle diffusely throughout the lung parenchyma. Most patients present during their reproductive years, and survival is generally less than 10 years. While pulmonary lymphangioleiomyomatosis (PLAM) in elderly patients is very rare and some cases have been sporadically reported, the pathophysiologic mechanism and epidemiology of PLAM in elderly patients is still unknown. We present our case and review all previously reported cases of PLAM in elderly patients, published since 1960. Three case reports and one review article, a total of 6 elderly patients with PLAM have been demonstrated, including our case which we report here. Case reportA 76-year old woman complained of dyspnea of exertion and cough for previous 5 years. Spirometry did not reveal restrictive ventilatory impairment, FEV1 was 1.36 L and forced vital capacity was 1.79 L (84.4% predicted). Chest computed tomography (CT) showed diffuse thin-walled cystic air spaces throughout both lungs. Video-assisted thoracic surgery (VATS) was performed, and microscopic findings of thin-walled cyst showed proliferation of smooth muscle cells. Immunohistochemical staining revealed that aSMA-antigen was positive, although HMB antigen was negative. She was diagnosed as PLAM.
Results A total of 6 patients were included in the review of previously published cases. The age of the patients was 65 to 76 years. All patients were female. The most common symptoms on initial visit was dyspnea on exertion (5 of the 6, 83%). In terms of treatment, none received any hormone therapy. Two of the 4 patients (50%) survived.
Conclusion PLAM could occur in elderly patients after menopause even if it is very rare. Physicians should consider PLAM if women present dyspnea of exertion despite they are in a postmenopausal state. The severity of PLAM in elderly women might be better than the one in menopausal women.

PS217

S-1 MONOTHERAPY FOR ADVANCED THYMIC CARCINOMA

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Background Thymic carcinoma is a rare malignant tumor. No definitive chemotherapeutic regimens have been established in the advanced disease, especially in the second line setting, and thus its prognosis is still disappointing. The thymidylate synthase (TS) expression level in the thymic carcinoma were lower compared with lung squamous cell cancer, suggesting a potential sensitivity of thymic carcinoma to S-1.
Methods We evaluated the efficacy and toxicity of S-1 monotherapy as salvage in three patients with relapsed thymic carcinoma from April, 2011 to July, 2013. The initial dose of S-1 was determined based on the body surface area (BSA), and the drug was taken orally twice daily for two weeks.
Results One patient achieved partial response, whilst two patients had stable disease. Median progression-free survival time was 2.8 months in the three patients, one of whom obtained disease control in 17 months. Hematological toxicity was mild, whereas gastrointestinal toxicity and general fatigue were observed.
Conclusion Oral S-1 monotherapy seems effective and safe in the salvage setting in patients with advanced thymic carcinoma. A multicenter phase II trial has been launched.

PS218

A CASE OF SERUM CEA ELEVATION WHICH MARKED DIAGNOSIS OF PULMONARY ALVEOLAR PROTEINOSIS

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A 61-year-old man was indicated by health check that serum CEA elevated, and visited other hospital. He was seen in our hospital because of suspect of intestinal pneumonia in chest CT scan,or other malignancy diseases. He had a history of colon cancer at age of 56 which was resected by endoscopic mucosal resection. He was suspected of recurrence of colon cancer. But, no findings suggestive of malignancy were obtained with total colon fiber scopy. Chest CT scan showed ground-glass pattern,thickened interlobular septa in both lower lobes. Blood exam showed elevation of KL-6, LDH. He had bronchoscopic examination with susupect of intestinal pneumonia. Bronchoalveolar lavage showed white turbidity as like as water that has been used to wash rice. Because Anti-GM-CSF autoantibody was significantly increased in serum and bronchoalveolar lavage,we diagnosed him as autoimmune pulmonary alveolar proteinosis. He had got outpatient treatment without worsening of respiratory status for about 6 months. Serum CEA is usually used as a marker of malignant disease. While it is reported that serum KL-6 followed by CEA are correlated with disease progress of autoimmune pulmonary alveolar proteinosis. In this case, we could diagnose him as pulmonary alveolar proteinosis by bronchoscopic examination with serum CEA elevation and serum other marker.

PS219

PENTRAXIN-3 IN FEBRILE NEUTROPENIA IN LUNG CANCER PATIENTS

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Background and Aim of Study Pentraxin-3 (PTX3) is newly discovered inflammatory biomarker in various inflammatory conditions. This study was designed to measure plasma PTX3 levels in febrile neutropenia (FN) lung cancer patients and to examine its usefulness.
Methods Consecutive 14 FN patients during chemo/chemoradiotherapy were enrolled. On the onset day (day1), plasma was taken and treatments for FN were started following guidelines. On the day3 and day7 plasma were also taken. As control subjects, 28 untreated lung cancer patients without infections and 48 healthy controls were enrolled and plasma was also taken on the enrolled day. We measured CRP and PTX3 levels by ELISA and examined its correlation with clinical parameters of FN in lung cancer.
Results Plasma CRP levels on day1 in FN lung cancer patients (FN/LC, 8.11 ± 6.42) were significantly increased compared with those of healthy controls (HC) and chemo/chemoradiotherapy naïve lung cancer patients (CN/LC) ($p < 0.05$). However, CRP levels of CN/LC (0.27 ± 0.11) were significantly higher compared with those of HC (0.06 ± 0.06) ($p < 0.05$). In contrast, plasma PTX3 levels on day1 in FN/LC (6.14 ± 5.28) was significantly increased compared with those of HC and CN/LC ($p < 0.05$). PTX3 levels of FN/LC (0.80 ± 0.72) were not significantly higher compared with HC (0.77 ± 1.06). PTX3 levels in FN/LC reached a peak immediately in day1. However, CRP levels in FN/LC reached a peak slowly in day3. However, PTX3 levels in day7 and CRP levels in day3 were significantly correlated with fever period.
Conclusion PTX3 has the potential to be a useful biomarker for FN in lung cancer patients.

PS220

THORACOSCOPIC SURGERY USING ABSORBABLE FELT TO PREVENT THE RECURRENCE OF PNEUMOTHORAX

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Aims To prevent the postoperative prolonged air leakage or the recurrence of pneumothorax, staple-line reinforcement is often needed for the patients of pneumothrax with emphysema. Polyglycolic acid (PGA) felt is an absorbable artificial material. Suture-line covering method with PGA felt after the lung resection by video-assisted thoracic surgery (VATS)) is considered to be one of the most useful methods. The purpose of this study is to evaluate the merit and demerit of this method for spontaneous pneumothorax surgery.
Methods PGA felt (NEOVEIL, GUNZE, Tokyo, Japan) covering procedures were as follows. After the lung resection with autosutures, we tied 2 sections of staple line using 1–0 silk and threaded the sheet of PGA through the access port. PGA felt was fixed by 1–0 silk ligatures. Since April 2001, VATS with PGA large size felt (10×10 cm) wrapping were performed for 80 patients with pneumothrax (Group A) and PGA small size (10×5 cm) for 24 Patients(Group B). VATS without wrapping were 56 cases (Group C). We compared those groups to check the clinical course and complications.
Results The average of postoperative drainage period was 1.5 days in group A (range 1 to 3), 1.4 days in group B (range 1 to 2), and 1.9 days in group C (range 1 to 6). The rate of prolonged air leaks (more than or equal to 5 days)was 0% in group A and B, and 3.6 % (2 cases)in group C. Patients treated PGA felt had shorter periods of postoperative drainage. Rate of recurrence is 0% in group A, 4.1% in group B and 8.9 % in group C. There was no other complication and no mortality.
Conclusions VATS with PGA felt is useful method that may reduce the air leakage, postoperative drainage periods and the recurrence rate.

PS221

EARLY DETECTION OF MEDIASTINAL TUMORS USING LOW-DOSE SPIRAL COMPUTED TOMOGRAPHY

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Background Chest radiographic screening is a commonly used conventional method for the detection of lung and mediastinal tumors. However, more than half of the tumors detected by chest radiography are those that have already progressed to the advanced stage. Recent studies have shown that low-dose spiral computed tomography (CT) is effective for the early stage detection of lung cancer, and this facilitates better resectability and long-term survival. The present study was performed to evaluate the usefulness of chest radiography and spiral CT in the diagnosis of mediastinal tumors.
Methods Approximately, 50000 consecutive asymptomatic individuals had undergone a health check-up at our institution from April 2012 to March 2013. Of these individuals, 44663 had undergone chest radiography or low-dose spiral CT. The presence of mediastinal tumors was investigated in these individuals.
Results Four mediastinal tumors were detected (1 thymoma, 1 teratoma, 1 liposarcoma, and 1 neurofibroma with Recklinghausen's disease). One case was detected using both chest radiography and CT, whereas the other 3 were detected using chest CT only. In these 3 cases, no abnormal opacity was observed on chest radiographs. The tumors in all 4 cases were successfully resected, and to date, no tumor recurrence has been observed.
Conclusion Thus, we propose that screening using low-dose spiral CT is more useful than chest radiography and might contribute to the early detection and treatment of mediastinal tumors.

PS222

A NOVEL CLINICAL ROLE FOR ANGIOPOIETIN-1 IN MALIGNANT PLEURAL MESOTHELIOMA

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Background Malignant pleural mesothelioma (MPM) is an aggressive malignant tumor associated with asbestos exposure with limited response to conventional therapy, so diagnosing MPM early is very important. We have previously reported that angiopoietin (Ang)-1 was correlated with bleomycin-induced pulmonary fibrosis.
Methods We investigated the association of Ang-1 with the development of MPM which originate from mesenchymal cells similar to lung fibroblasts.
Results We demonstrated that Ang-1 stimulated the cell growth and migration of MPM cells in in vitro studies. We also demonstrated that patients with MPM had significantly higher serum levels of Ang-1 in comparison to a population who had been exposed to asbestos but had not developed MPM. The patients with advanced stage MPM showed higher levels of Ang-1 than the early stage MPM patients and the Kaplan-Meier method revealed a significant correlation between serum Ang-1 levels and survival.
Conclusions We propose the possibility that Ang-1 plays an important role in MPM tumor growth and our data suggest that the serum concentration of Ang-1 could be useful as prognostic factor.

PS223

MESOTHELIOMA CELL PROLIFERATION THROUGH AUTOCRINE ACTIVATION OF PDGF-ββ RECEPTOR

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Background/Aims Growth factors play a critical role in proliferation for a variety of cancer cells. The present study was conducted to understand the signaling cascades underlyingPDGF-D/PDGF-ββ receptor-mediated proliferation of mesothelioma cells.
Methods Cell growthand cell cycle were analyzed in human non-malignant Met5A cells and malignant mesotheliomacells such as MSTO-211H, NCI-H28, NCI-H2052, and NCI-H2452 cells.
Results Growth of allthe cells used here was not affected by PDGF-D, regardless of concentrations (1–30 ng/ml) ortreatment time (48–72 h). Spontaneous growth of those cells was significantly inhibited byknocking-down PDGF-D or PDGF-ββ receptor, without affecting cell cycling. The cell growth wassignificantly inhibited by the Akt inhibitor MK2206 and the ROCK inhibitor Y27632 for all the celltypes, by the PDK1 inhibitor BX912 for NCI-H28 cells alone, and by the Rac1 inhibitor NSC23766 for NIC-H2052 cells alone, while the PI3 kinase inhibitor wortmannin had no effect. The cellgrowth, alternatively, was significantly attenuated by MAP kinase kinase inhibitor PD98059 or theERK1/2 inhibitor FR180204 for all the cell types.
Conclusion The results of the present studyshow that PDGF-D promotes mesothelioma cell proliferation by targeting ROCK or MAP kinasethrough autocrine activation of PDGF-ββ receptor.

2-A2: OTHERS 2

PS224

CLINICAL CHARACTERISTICS OF INTERSTITIAL PNEUMONIA IN MICROSCOPIC POLYANGIITIS

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Background and Aim of Study The association of pulmonary abnormalities in microscopicpolyangiitis (MPA) has not been well documented. Especially, interstitial pneumonia (IP) was frequently seen in MPA. The aim of this study was to assess the clinical characteristics of IP in MPA.
Methods Twenty-eight patients diagnosed as having IP in MPA (18 males and 10 females with a mean age of 73.0 years, MPO-ANCA; range, 11–3160 EU; mean, 519 EU) were studied during the period 2001 through to 2011. The clinical features, chest CT scan images and prognoses were evaluated retrospectively.
Results Among 28 patients with IP, 21 were associated with two or more organ's lesions corresponding to MPA (MPA-IP group) and 7 were pulmonary limited vasculitis (PLV group). Patterns of IP were UIP pattern in 14, non-UIP pattern in 9 and CPFE in 5, respectively. The mean MPO-ANCA titer was higher in MPA-IP (599 EU) than that in PLV (278 EU). The causes of death in 15 out of 28 patients were respiratory infection in 7, diffuse alveolar hemorrhage in 3, acute exacerbation of IP in 3, sepsis in 1 and heart failure in 1, respectively. The 5 years survival rate from diagnosis of MPA was 53.0% in MPA-IP and 42.8% in PLV with no significant difference. However, the 5 years survival rate in the low ANCA titer group (<145 EU) was better than that in high titer group (>145 EU) (85.7% vs 35.7%).
Conclusion In patients with high ANCA titer group showed poor prognosis in our study. The survival in IP with MPA were as worse as idiopatic pulumonary fibrosis in our institution.

PS225

VALIDATION OF RAPID EMERGENCY MEDICINE SCORE AS A PROGNOSTIC SCORING SYSTEM FOR ADULT NONSURGICAL EMERGENCY PATIENTS IN INDONESIA

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Background and Aim of the Study Identifying the mortality risk of emergency patients is essential as a consequence of increasing number of admission with diverse severity of disease. Rapid Emergency Medicine Score (REMS) has been developed to predict the mortality of nonsurgical emergency patients and to help doctors in making clinical decision rapidly based on objective data. We evaluated the performance of REMS in predicting the mortality of nonsurgical emergency patients in Cipto Mangunkusumo Hospital (CMH), a tertiary referral center in Indonesia.
Methods We performed a prospective cohort study on nonsurgical patients who attended to Emergency Department (ED) of CMH between October and December 2012. Age, body temperature, mean arterial pressure, heart rate, respiratory rate, peripheral oxygen saturation, and Glasgow coma scale were obtained at admission to calculate the REMS. The outcome was in-hospital mortality. Calibration was evaluated with Hosmer-Lemeshow test and discrimination was evaluated with area under the receiver operating characteristic curve (AUC).
Results A total of 815 nonsurgical patients attended to ED during the study. As many as 741 (90.9%) patients were followed until the outcome occured. In-hospital mortality was observed in 145 patients (19.6%). Hosmer-Lemeshow test showed a good calibration (p = 0.665). The AUC of REMS was 0.77 (95% CI 0.723; 0.817).
Conclusion Rapid Emergency Medicine Score is a good prognostic scoring system for adult nonsurgical emergency patients in Indonesia. Key Words: Rapid emergency medicine score, nonsurgical, mortality.

PS226

EFFECT OF A NEGATIVE PRESSURE AT INTERCUFF SPACE IN DOUBLE CUFFED ENDOTRACHEAL TUBE

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Objective We designed a prototype endotracheal tube with double cuffs and a small intercuff hole connected to a negative pressure port. The hypothesis of this study was that a negative pressure between double cuffs prevents fluid leakage past the double cuffs.
Methods We obtained two cuffs from Standard endotracheal tubes and attached them to a tube (8.0 mm internal diameter (ID)). We made a 1 mm-sized hole between the cuffs, which is connected to an external port for applying the negative pressure in the intercuff space. PVC trachea with a 20 mm-sized internal diameter was intubated with ETT. We spilled continuously the blue-dyed water on the upper cuff and applied a negative pressure in the intercuff space though the port for 10 minutes. And then we measured the volume of dripped water below the lower cuff. And the leakage tests were performed at 7 different negative pressures(–40, –50, –60, –70, –80, –90 and –100 mmHg) using an external port at 4 different intracuff pressures (15, 20, 25 and 30 cmH_2O).
Results The mean volume of fluid leaked over 10 minutes is at least –90 mmHg pressure, we prevented completely the water from leaking, regardless of the 15 cmH_2O intracuff pressures in the artificial trachea.
Conclusions The double cuffed endotracheal tube with –90 mmHg pressure in intercuff space completely prevented the water from leakage at all intracuff pressures (15–30 cmH_2O) in a 20 mm-sized artificial trachea in vitro.

PS227

A COMPARISON OF SIZE SELECTION STRATEGIES OF SLIPA WITH REGARD TO PATIENT HEIGHT VS. THYROID CARTILAGE WIDTH

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Background Streamlined Liner of the Pharynx Airway (SLIPA) is a disposable supraglottic airway. There are two strategies to select the size of SLIPA. This study compared the utility of two strategies in selecting the optimal size.
Methods One hundred forty-two patients were randomly divided into two groups with size selection by height (H) and the maximal width of the thyroid cartilage (T). The investigator lifted the jaw and pushed the device until the heel lodged in the nasopharynx. And then, the investigator made note of the oropharyngeal leakage pressure (OLP) and the degree of insertion difficulty. In cases of an OLP under 15 cmH2O, the investigator manipulated the apparatus to try to properly position it. If air still leaked, another attempt was made using a SLIPA one size larger until an OLP over 15 cmH2O was achieved in up to three attempts. After insertion, the investigator measured the inspiratory and expiratory tidal volume (TVinsp and TVexp, respectively). Postoperatively, the presence of blood or regurgitated fluid on the device was evaluated.
Results OLP for group T was higher than that of group H (P = 0.009). The need for manipulation and the leak fraction [(TVinsp-TVexp)/TVinsp] was higher in group H than in group T (P = 0.008 and 0.034, respectively). The degree of insertion difficulty, number of trials and incidence of blood and regurgitated fluid on the device were similar between the two groups.
Conclusions The width of thyroid cartilage is a more appropriate strategy than patient's height for selecting the optimal SLIPA size. However, both strategies are clinically applicable.

PS228

EFFICACY OF STRUCTURED FAMILY MEETING ON THE WILL OF TRACHEOSTOMY IN PATIENTS WITH PROLONGED MECHANICAL VENTILATION IN A LOW-TRACHEOSTOMY-RATE COUNTRY

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Background and Aim of Study The utility of tracheostomy to expedite weaning and prevent complications in patients with mechanical ventilation is suggested. The optimal timing of tracheostomy is debated and usually not a strong option to the patients and family in Taiwan, a culturally low-tracheostomy-rate country. The aim of this study is to build up the structured family meeting and determine its efficacy on the will of tracheostomy, rate of ventilator weaning, hospitalization length and mortality rate in patients with prolonged mechanical ventilation (PMV).
Methods This retrospectively observational study is implemented from January, 2010 to March, 2013. Structured family meeting is built up and held to those who fulfill all of the following criteria: 1. Patients who were admitted to the respiratory care center (RCC), a subacute ventilator dependency setting, 2. Patients with endotracheal tube intubation and unwilling to receive tracheostomy in intensive care units (ICUs).
Results A total of 102 patients were enrolled. 57.8% (59/102) patients were male and 42.2% (43/102) patients were female. 42.2% (43/102) patients underwent tracheostomy after implementation of structured family meeting. Patients who came from medical ICU is the only predictor of the will of tracheostomy (Odds ratio = 4.029; $p = 0.013$). Patients who underwent tracheostomy had longer RCC length and hospital length than patients with unwilling to receive tracheostomy (37.2 ± 18.2 v.s. 23.9 ± 16.3, $p = 0.000$; 71.5 ± 23.4 v.s. 58.7 ± 18.9, $p = 0.003$, respectively). The rate of ventilator weaning and mortality rate within one-month after discharge in patients who underwent tracheostomy were similar with patients with unwilling to receive tracheostomy (72.1% v.s 57.6%, $p = 0.196$; 11.6% v.s. 20.3%, $p = 0.370$, respectively).
Conclusion The structured family meeting increased the will of tracheostomy in patients with PMV in a culturally low-tracheostomy-rate country.

PS229

MEASUREMENT AND ANALYSIS OF THE COMMON FOOD ALLERGENS SPECIFIC IGE

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Background and Aim of Study To discuss and analyse the correlation of the positive rate of common food allergen-specific immunoglobulin E (sIgE) with suspected food allergy patients in our hospital.
Methods Using fluorescence enzyme-linked immunosorbent assay to detect the serum sIgE antibody of the patients, including 7 kinds of food allergens (milk, egg white, egg yolk, peanut, soy, shrimp and crab) from July 2006 to January 2013.
Results 528 patients were detected milk and egg white sIgE, the positive rate of milk sIgE was 35.2%, the positive rate of egg white was 33.7%, 26.9% were both positive, $R = 0.758 (P < 0.01)$. 282 patients were detected egg white and egg yolk sIgE, the positive rate of egg white sIgE (59.6%) was much higher than the yolk sIgE (9.2%). The positive rate of the milk and egg white sIgE decreased with the age. The degree in level 4 or above of milk and egg white sIgE was only 0.4%in positive patients. We detected serum sIgE of shrimp and crab in 64 patients, 16 cases was positive of the shrimp, 17 cases of the crab was positive, both positive in 16 cases, $R = 0.973$ ($P < 0.01$). In the simultaneous detection of 34 patients' serum sIgE of peanut and soybean, peanut was positive in 4 cases, soybean was positive in 3 cases, both positive in 2 cases, $R = 0.879$ ($P < 0.01$).
Conclusion Egg white is the major allergen of egg allergy. The relevance of shrimp and crab, peanuts and soybeans is extremely high, probably because of their homology; egg white and milk is not homologous food, but their positive rate has significant correlation, indicating the synergistic reaction.

PS230

A CASE OF MOUNIER-KUHN SYNDROME WITH TRACHEAL WEB

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Background Tracheal web is a rare congenital abnormality of the trachea and is often misdiagnosed as refractory asthma. Mounier-Kuhn syndrome (MKS) is also a rare disorder characterized by a marked dilatation of the trachea and main bronchi, sometimes with diverticulosis and tracheobronchomalacia. However, the etiology is uncertain.
Case Report 47-year-old woman referred to our hospital because of persistent cough and wheezing. She was diagnosed as asthma 10 years ago and had some episodes of pneumonia and 200 pack-year smoking history until 10 years ago. The pulmonary function tests showed a flat pattern of flow volume curve with marked limitation of peak flow. The chest CT scan revealed trachobronchomegaly (diameter, 67 mm) and web-like tracheal stenosis. The tracheal web obstructed almost 90% of the inside diameter of the trachea 5 cm below the vocal cords, although the collapse of the trachea on expiration was unclear. According to these evidences, this patient was diagnosed as MKS with tracheal web.
Discussion Despite the congenital tracheal web, there were no asthmatic symptoms in infancy because the congenital dilation of trachea was present in birth. Tracheobronchomegaly in this case was due to a congenital abnormality rather than an atrophy of the connective tissue of trachea. Also, she gave birth safely to two children 25 years ago asymptomatically, and asthmatic symptoms appeared 10 years ago. It is considered that the web-like tracheal stenosis is in progress. The resection of this web might be considered to be a reasonable treatment. The lack of the significant tracheal collapse on expiration, which is one of the main features of MKS, might suggest the prevention of the tracheal collapse by the tracheal web in this case. Thus, the choice of the future treatment to her, should be made deliberately.

PS231

RELATIONSHIPS BETWEEN SMOKING STATUS AND COGNITIVE FUNCTION IN COMMUNITY-DWELLING ELDERLY MEN

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Background and Aim Smoking is associated with increased risks for various diseases. On the other hand, dementia becomes a social burden as an elderly population increases. The present study aimed to clarify relationships between smoking status and cognitive function in community-dwelling elderly men.
Methods A comprehensive geriatric health survey of all residents, aged 65 years and over, of a village along the Sea of Japan was carried out between August and September 2012. Self-administered questionnaires were distributed by mail, and the subsequent responses were validated through home-visit and face-to-face interviews by trained interviewers who simultaneously performed the Mini-Mental Status Examination (MMSE). On the analysis, the subjects were divided into 3 groups, the current smoker, former smoker and non-smoker. The MMSE score was compared according to the smoking status and age.
Results Of the 1103 subjects who participated in this survey (participation rate: 91.9%), 416 male subjects were analyzed. These were 93, 234, and 89 subjects in the current smoker, former smoker and non-smoker groups, respectively. The current smokers aged 80 years and over were the fewest ($p < 0.001$). The MMSE scores were not significant different among any smoking status and age groups. In the MMSE average scores, however, tendencies were found that current smoker aged < 70 and 70–79 years had the lowest compared to the former and never smokers, whereas those aged 80 years and over were the highest.
Conclusion In this study we could not find any association between the MMSE scores and smoking status.

PS232

OPTIMAL VENTILATOR SETTING IN THORACOSCOPIC BLEB RESECTION UNDER LOW TIDAL TWO-LUNG VENTILATION ANESTHESIA

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Background Most video-assisted thoracoscopic surgery (VATS) requires general anesthesia with one-lung ventilation. According to our previous studies, thoracoscopic bleb resection (TBR) could be performed under low tidal volume (Vt), two-lung ventilation without any technical problem. Usually low Vt requires higher respiration rate (RR) to meet patents' metabolic needs, producing fast-moving operation field which is unfavorable. We evaluated the most feasible ventilator setting for TBR with low Vt in the respect of gas exchange.
Methods Patients who received scheduled TBR were included according to inclusion and exclusion criteria. General anesthesia was provided and TBR was performed under two-lung ventilation with low Vt setting (5 ml/kg). RR was varied 15, 18 and 22 cycles/min according to protocol. Surgery was performed without CO_2 gas insufflation. During anesthesia period, vital sign, arterial blood gas analysis (ABGA), values associated mechanical ventilation were monitored and recorded.
Results Total 48 patients were finally included in statistical analysis. Operation and anesthetic time, number of used endoplate were not significantly different between 3 groups. There was no patient presented hypoxemia or hypercarpnia. Minute ventilation was significantly lowered in RR 15 group ($P < 0.001$), the results of ABGA were in physiologic range.
Conclusion Tow-lung ventilation with low Vt and 15 cycles/min RR was acceptable for TBR even though decreased minute ventilation. With this ventilation setting, optimal surgical field was guaranteed and arterial blood gases were remained within normal range.

PS233

CARING BY TEAMWORK OF ONE STOP SERVICE FOR ASTHMATIC PATIENTS AT THE ADULT ASTHMATIC CLINIC OF BURIRAM HOSPITAL

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Asthma is chronic disease and numbers of asthmatic patients increase continually. Thailand has asthmatic patients more than four million. Mortality rate of asthmatic patients was 5% in each year and Public health of ministry has policy 3 D of service so Department out of patients of Buriram Hospital improved caring by teamwork of One Stop Service at the Adult Asthmatic Clinic by every service this hear altogether and teamwork has 12 development of activities. This study was descriptive research, studies result of caring 256 asthmatic patients who consistently admitted at the Adult Asthmatic Clinic during 1 January 2011 to 31 December 2012. Used statistics to the analysis were Paired t-test, percentage and mean. The results showed that Admittion decreased 60% and ER-visit decreased 62.50 %, peak flow expiratory rate more than 80% increased form 82.67% to 89.35% and significance by statistics, ($p < 0.05$). After One Stop Service was implemented, the averaged time spent at Adult Asthmatic Clinic decreased 1.04 hours, payment of caring decreased 89,853.50 bath and satisfaction rate was 94.25% and enlarge 23 hospitals networks where can take care asthma patient, so this caring was asthma controll, service convenient quickly, high satisfaction and decreased payment of caring, so this service should be cover other asthmatic patients who don't admitted in Asthmatic Clinic and especially the old patients or don't have care givers, so this service should be cover other chronic diseases example hypertension, stroke.

PS234

ACCURACY OF HANDHELD SPIROMETRY AS A COMPARABLE DIAGNOSTIC TOOL TO PULMONARY FUNCTION TESTING

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Background Assessment of patients with pulmonary illnesses requires objective measurement. However not all areas have standard spirometry. Portable electronic spirometers have been developed, but need further evaluation. The objective of this study is to evaluate the handheld spirometer as a diagnostic tool in comparison to standard pulmonary function testing.
Methodology A cross-sectional study conducted at the Philippine Heart Center. Patients 19 years old and above, who underwent standard pulmonary function testing were requested to undergo handheld spirometry upon return. Results were interpreted independently.
Results A total of 395 subjects were included. There was a significant difference in the values of the FVC, FEV1 and FEV1/FVC between handheld spirometer and standard PFT (p 0.0001). However, there was good agreement between the two devices as to diagnosis of normal, obstructive and restrictive lung disease (kappa 0.984, p 0.008). There was also good agreement between the two devices as to classification of mild, moderate and severe for both obstructive (kappa $0.839 + 0.044$) and restrictive lung disease (kappa $0.898 + 0.028$). The handheld spirometer was noted to be accurate in diagnosing obstructive lung disease (kappa 1.0, sensitivity 100%, specificity 100%, PPV 100%, NPV 100%), but slightly less accurate in diagnosing restrictive lung disease (0.968, sensitivity 97.9%, specificity 100%, PPV 100%, NPV 95.9%).
Conclusion The values of FVC, FEV1 and FEV1/FVC obtained using the handheld spirometer may vary significantly from standard PFT, but the handheld spirometer can diagnose normal, restrictive and obstructive lung disease, and classify disease severity as to mild moderate and severe, with good agreement with standard PFT. The handheld spirometer was found to be accurate in diagnosing obstructive lung disease and slightly less accurate in diagnosing restrictive lung disease. It may substitute the use of standard spirometry in areas lacking standard PFT and for patients with difficulty ambulating.

2-A3: LUNG CANCER 3

PS235

CLINICAL CHARACTERISTICS OF 64 LUNG CANCER PATIENTS WITH PLEURAL PLAQUES

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Background Asbestos exposure will increase the risk of lung cancer, mesothelioma and pleural disorders, including asbestosis, pleural plaques, pleural thickening, and pleural effusions. Pleural plaques are the most frequent response to asbestos exposure, appearing even with low-dose, often intermittent, exposures. Therefore, radiographic evidence of pleural plaques in lung cancer patients indicates the history of asbestos exposure.
Methods Between 2003 and 2012 in our hospital, there were 1190 patients in whom pleural plaque was confirmed by computed tomography (CT) scanning. Among those patients, 64 were histologically diagnosed as primary lung cancer.
Results There were 63 men. The frequent histologic types of the cancers were adenocarcinoma (23 patients) and squamous cell carcinoma (22 patients), followed by small cell carcinoma (8 patients). 16 patients had Stage 1A disease, 8 patients had stage 1B disease, 3 patients had stage 2B disease, 8 patients had stage 3A disease, 6 patients had stage 3B disease and 21 patients had stage 4 disease. The median overall survival was 23.0 months and 1 year, 2 year and 5 year survival rate of all the patients were 56.0%, 49.0% and 23.7%, respectively. Based on the primary treatment, 28 patients received surgery, 4 patients received radiation therapy, 5 patients received chemoradiotherapy, 19 patients received chemotherapy and 6 patients received best supportive care. The median overall survival of the patients treated by surgery, radiation therapy, chemoradiotherapy, chemotherapy, and best supportive care, were 96.0 months, 40.9 months, 6.3 months, 8.4 months and 3.0 months, respectively.
Conclusion Among the lung cancer patients associated with pleural plaques alone, early stage patients showed favorable prognosis. Therefore, the early detection of lung cancer may contribute to a better outcome in the population which has pleural plaque alone, not accompanied with asbestosis.

PS236

CLINICAL FEATURES AND OUTCOMES IN LUNG CANCER WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Background The syndrome of combined pulmonary fibrosis and emphysema (CPFE) has been proposed as important phenotype of pulmonary fibrosis, defined by the coexistence of emphysema in the upper pulmonary area and pulmonary fibrosis in the lower area. CPFE may be at significantly increased risk of lung cancer compared with isolated emphysema or pulmonary fibrosis each. However, the clinical feature of lung cancer with CPFE is not clear.
Patients and Methods The medical records for a series of consecutive patients with a definitive diagnosis of primary lung cancer and IIPs were reviewed. One hundred fifty one patients who could re-evaluate pretreatment Computed Tomography (CT) scan of the chest were retrospectively analyzed.
Results The eighty eight (58.3%) of lung cancer with IIPs met the criteria of CPFE. All patients were Japanese, the ratio of men to women (92% vs 73%; $P < 0.002$) was higher among lung cancer patients with CPFE than among lung cancer patients with isolated IIPs. In the choice of initial treatment, no difference was observed between the isolated IIPs group and the CPFE group. Incidences of AE related to initial invasive treatment for patients with isolated IIPs and for those with CPFE were 11.3% and 19.1%, respectively. The median overall survival of lung cancer patients with CPFE (20.3 months) was less than that of lung cancer patients with isolated IIPs (23.7 months), but there was no significant difference.
Conclusion The prognosis of lung cancer with CPFE might be worse than that of lung cancer with isolated IIPs. However, we considered that the impact of emphysema is limited in lung cancer with IIPs.

PS237

LUNG VOLUME ASSESSMENT ON 3D-CT AND PREDICTED POSTOPERATIVE PULMONARY FUNCTION FOR LUNG CANCER PATIENTS

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Background and Aim of Study The radical cure treatment of lung cancer is a surgical operation. The evaluation of a postoperative pulmonary function is important for estimating the risk of complications and long-term disability after pulmonary resection, especially for elderly patients. Number of segments method is often used to estimate the predicted postoperative pulmonary functions. However, that method does not consider the actual volume of resected lobe. Currently, 3D-CT can divide and calculate the lung volume for every lobe. The aim of this study is to reveal the differentiation between 1) actual values examined after lobectomy, 2) estimated postoperative values calculated with traditional number of segments method, and 3) estimated postoperative values calculated with resected lobular volume obtained by 3D-CT on $FEV_{1.0}$ (PO $FEV_{1.0}$, ePO_{seg} $FEV_{1.0}$, ePO_{CT} $FEV_{1.0}$), predicted $FEV_{1.0}$ (PO $\%FEV_{1.0}$, ePO_{seg} $\%FEV_{1.0}$, ePO_{CT} $\%FEV_{1.0}$) and predicted DLco (PO %DLco, ePO_{seg} %DLco, ePO_{CT} %DLco), respectively.
Methods We calculated the lobar volume and the emphysematous lobar volume < –950 HU of each lobe using slice-by-slice method with Zaiostation2® software program.
Results 8 patients were enrolled for this study (mean age 71.9 years). All patients were classified into GOLD2, and were diagnosed as adenocarcinoma (2 patients), squamous cell carcinoma (3) and non-small cell lung cancer (2). Both PO $FEV_{1.0}$ and ePO_{CT} $FEV_{1.0}$ are significantly larger than ePO_{seg} $FEV_{1.0}$, but, there is no statistically significant between PO $FEV_{1.0}$ and ePO_{CT} $FEV_{1.0}$. There is no significantly difference between ePO_{seg} $\%FEV_{1.0}$. and ePO_{CT} $\%FEV_{1.0}$, and those are significantly smaller than PO $\%FEV_{1.0}$. There is no significantly difference between ePO_{seg} %DLco. and ePO_{CT} %DLco, and those are significantly smaller than PO %DLco.
Conclusion In COPD patients with moderate air flow limitation, the predicted postoperative pulmonary function calculated with number of segments method or 3D-CT might be underestimated compared with actual measurement.

PS238

SVC SYNDROME AS A PROGNOSTIC FACTORS FOR EXTENSIVE STAGE SMALL CELL LUNG CANCER

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Background and Objectives Despite a high cheomosensitivity, the long term survival of extensive stage small cell lung cancer is poor. But the individual prognosis is variable. We want to evaluate prognostic factors in extensive stage of small cell lung cancer.
Methods We retrospectively analyzed clinical and laboratory characteristics of 129 patients who were diagnosed extensive stage small cell lung cancer. Clinical and laboratory characteristics were analyzed.
Results The median survival time is 196 days (95% confidence interval[CI], 162 to 229 days). Univariate analysis found that gender, body mass index(BMI), performance status(PS), the presence of superior vena cava(SVC) syndrome, diabetes or anemia were associated survival(all P-value < 0.05). Multivariate Cox regression analysis indicate that survival time was independently associates with BMI(<18.5) (hazard ratio [HR];6.56, 95% CI 2.83–15.21; $p = 0.000$), the presence of SVC syndrome([HR];3.54, 95% CI 1.50–8.36; $p = 0.004$) and the presence of anemia([HR];1.83, 95% CI 1.01–3.34; $p = 0.047$).
Conclusions In this study, lower BMI, the presence of SVC syndrome and the presence of anemia were poor prognostic factor for survival.

PS239

CLINICAL FEATURES OF PATIENTS WITH NSCLC WHO HARBOR EGFR MUTATION AND PRESENT WITH MILIARY INTRAPULMONARY OR DISSEMINATED CARCINOMATOSIS

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Background It is reported that EGFR mutation is frequent in non small cell lung cancer (NSCLC) patients who are presenting with miliary intrapulmonary carcinomatosis. We often encountered disseminated carcinomatosis as well as intrapulmonary carcinomatosis. This study aims to investigate the clinical characteristics of patients with miliary intrapulmonary or disseminated carcinomatosis.
Methods Patients with advanced NSCLC who harbor EGFR mutation and presented with miliary intrapulmonary or disseminated carcinomatosis were enrolled respectively, from September 2005 to January 2011. EGFR mutations in exons 18–21 were confirmed by pyroseqeuncing method after genomic DNA was extracted from paraffin-embedded tissue specimens. Clinical characteristics, responses to treatment and outcome were collected from medical records.
Results The most frequent mutation was in-frame deletions in exon 19 (68.7%). A L858R and G719A were detected in 19 (29.7%) and 1 (1.7%) patient, respectively. Patients with miliary intrapulmonary or disseminated carcinomatosis were more common in female (80.0% vs. 55.1%), non smoker (80.0% vs. 53.1%), and 19 deletion mutation (86.7% vs. 63.3%), however there were no significant difference statistically. They showed relatively shorter PFS to EGFR TKIs (median 9.7 vs, 12.8 months) and poorer overall survival (median 15.9 vs. 29.0 months) compared to patients without miliary metastasis. In multivariate analysis, higher metabolic tumor volume (MTV) in PET-CT was confirmed to be an independent predictor of shorter OS, when considered together with stage, gender and smoking status.
Conclusions The data indicate that NSCLC presenting miliary intrapulmonary or disseminated carcinomatosis were more common in female, adenocarcinoma, non-smoker and 19 deletion mutation was comparatively frequently detected, however there were no statistically significant differences. PFS to EGFR tyrosine kinase inhibitors and overall survival was less in patients with miliary intrapulmonary or disseminated carcinomatosis compared to patients without miliary metastasis. Poor clinical course might be associated with high tumor burden represented by MTV or total lesion glycolysis.

PS240

RISING THE PROPORTION OF LUNG ADENOCARCINOMA IN A TERTIARY REFERRAL HOSPITAL OF SOUTH KOREA

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Introduction The aim of this study was to evaluate the recent epidemiology of lung cancer in a tertiary referral hospital of South Korea.
Methods Consecutive patients, who were newly diagnosed as lung cancer from June 2011 to December 2012 in Seoul National University hospital, were included in this retrospective study. The clinical and pathologic characteristics were reviewed.
Results All 979 of newly diagnosed lung cancer patients were included. The mean age at diagnosis was 65.6 ± 10.2 years old and 652 (66.6%) were males. Among 979 patients, 349 (35.6%) were never-smokers. In non-small cell lung cancer group (n = 887), stage IV was the most common (326, 36.8%). Adenocarcinoma was the major pathologic diagnosis (555, 56.7%). Compared to the data of previous national surveys, the proportion of adenocarcinoma was increasing from 30% in 1997 and 36.1% in 2005. The clinical characteristic of the patients with adenocarcinoma showed younger age (63.7 vs. 68.1, $P < 0.001$), predominance in female ($P < 0.001$), never smokers ($P < 0.001$), better performance status ($P < 0.001$) and early stage ($P = 0.005$).
Conclusions The proportion of the lung adenocarcinoma has been increasing.

PS241

OUTCOMES OF PATIENTS WITH LUNG CANCER ADMITTED TO THE MEDICAL INTENSIVE CARE UNIT

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Introduction Lung cancer is one of the common causes of cancer death. End of life care in advanced cancer patient would be needed. Admission to intensive care unit (ICU) in patients with cancer would make some distress in emotion and quality of life. The decision making is difficult to admit ICU in lung cancer patient. The predictive factors of outcome will be needed. We reviewed the clinical outcome and characteristics of patients with lung cancer who admitted ICU retrospectively.
Methods We retrospectively collected clinical data of patients with lung cancer who admitted ICU from January 2010 to November 2011. Causes of admission, use of mechanical ventilation, presence of do-not-resuscitate, mortality were included. Postsurgical care was excluded in analysis.
Results One hundred thirty one patients were admitted in ICU. For postoperative care ninety three patients were admitted in surgical ICU and excluded. We analyzed thirty eight patients of lung cancer. NSCLC patients were 34 (89%) and SCLC patients 4 (11%). 25 patients (66%) were inoperable stage (stage IIIB, IV). Causes of admission were acute respiratory failure (78%), cardiovascular disease (8%), gastrointestinal bleeding (8%) and neurologic disease (5%). The mortality of ICU was 53% (20/38). Seventeen patients and family noticed the code of do-not-resuscitation after ICU admission. Twenty nine (79%) patients were received mechanical ventilation and 25 of 29 patients were dead during ICU care.
Conclusion In advanced lung cancer patients, ICU care would not be needed in some conditions. The model of ICU mortality in lung cancer should be established for the purpose of well-dying care.

PS242

CHARACTERISTICS OF PATIENTS SUFFERING FROM LUNG MALIGNANCY IN KUCHING: A RETROSPECTIVE STUDY

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Introduction Incidence of lung malignancy is rising due to prevalence of smoking. Adenocarcinoma is the most common histological subtype worldwide and in Malaysia. Its treatments have evolved from the conventional chemotherapy to targeted therapy. EGFR mutation is an established predictive factor for the use of tyrosine kinase inhibitor (TKI). While EGFR mutation has been more commonly associated with Asians, its prevalence among different ethnic group among Asians has not be established.
Methods A retrospective study. All patients seen in respiratory unit between Nov 2011 to Feb 2013 whom were suffering from lung malignancy were included. Their characteristics were obtained from clinic cards.
Results A total of 93 patient was included in the analysis. Adenocarcinoma was found in 53% (n = 49) of the cases and squamous cell carcinoma in 25% (n = 23) of the cases. Overall, lung carcinoma suffers are more likely to be male (69%, n = 64) and smokers (56% n = 52). However, for subtype adenocarcinoma female (OR 2.48 $p = 0.048$) and non-smokers (OR 7.09, $p < 0.001$) were more common. 35 patient have their EGFR status available for analysis. It was detected in 57% (n = 20). Non-smokers have an OR of 11.3 ($p = 0.0035$) for EGFR mutation. Chinese have higher incidence of EGFR mutation compared to other race with OR of 8.25 ($p = 0.02$). Female has an OR of 3.2, ($p = 0.1317$). The most common mutation is deletion in Exon 19.
Conclusion Adenocarcinoma is now the most common histological subtype of lung carcinoma seen in Kuching population. Incidence of lung carcinoma is higher in smoker than in non-smoker. Our analysis shows that non-smoker and Chinese are significantly more common in patients with EGFR mutation.

PS243

RETROSPECTIVE STUDY OF COMBINATION CHEMOTHERAPY WITH CISPLATIN PLUS PEMETREXED AS FIRST LINE THERAPY FOR ADVANCED NON-SMALL CELL NON-SQUAMOUS LUNG CANCER

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Objective The objective of this study was to evaluate the efficacy and toxicity of cisplatin plus pemetrexed as first line therapy in patients with advanced non-small cell non-squamous lung cancer.
Methods 41 advanced non-small cell non-squamous lung cancer patients received cisplatin plus pemetrexed as first line therapy at our centor from September 2009 through 2011 were analyzed retrospectively.
Results Among these patients, the median age was 66 (range, 44–78). 31 were males and 10 were females. In the histological types, 39 were adeno carcinoma and 2 were non-small cell non-squamous carcinoma. Grade3/4 toxicities included leucopenia (12.2%), neutropenia (34.1%), anemia (7.3%), thrombocytopenia (4.8%), hyponatremia (24.4%), Hyperkalemia (4.9%), hiccup (2.4%), anorexia (22.0%), nausea (9.8%), vomiting (2.4%), diarrhea (2.4%), and infection with neutropenia (7.3%). In treatment effect, the response rate was 32.4% and the disease control rate was 78.4%. The median progression free survival time was 4.3 months and the median survival time was 22.1 months.
Conclusion Compared with past clinical investigation, the efficacy and toxicity of cisplatin plus pemetrexed as first line therapy in patients with advanced non-small cell non-squamous lung cancer was suggested.

PS244

HISTOLOGIC TYPES AND RADIOLOGICAL CHARACTERISTICS OF LUNG CANCER WITH USUAL INTERSTITIAL PNEUMONIA

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Background and Aim Usual interstitial pneumonia (UIP) has been considered to be associated with increased frequency of lung cancer. There are still some uncertainties in clinical, radiological, and pathological characteristics of lung cancer with UIP, especially in which histologic type of cancer is predominant. The aim of this study was to evaluate the predominance of histologic type of cancer and radiological characteristics in lung cancer with UIP.
Methods We investigated 50 patients of tissue confirmed lung cancer with typical UIP finding on high-resolution computed tomography (HRCT) for clinical, radiological, and pathological characteristics.
Results Clinically, forty four patients (88%) were male and average age were 70.5 ± 8.2 years. Forty seven patients (94%) had a history of smoking (current smoker: 32; ex-smoker: 15; 46.9 ± 24.2 pack-years). Pathologically, there were 11 small cell lung cancers (22%), 20 adenocarcinomas (40%), 14 squamous cell carcinomas (28%), and 5 other non-small cell lung cancers (10%). Most lung cancers were in the peripheral lung area (39 cases; 78%) and were located in the lower lung (30 cases; 60%). About two-thirds of the lung cancer arose in the honeycombed lesion on HRCT. In subgroup analyses of two major histologic types, adenocarcinoma or squamous cell carcinoma, for radiologic characteristics such as upper lung vs. lower lung, central area vs. peripheral area, and in vs. out of the honeycombed lesion, there were no statistically differences ($P > 0.05$).
Conclusion Most lung cancers with UIP were in honeycombed lesion in peripheral lung area of lower lung without predominance of histologic types, especially adenocarcinoma or squamous cell carcinoma. So squamous cell carcinoma, although known as central type of lung cancer, is considered as peripheral type of lung cancer in patients with UIP.
Key Words usual interstitial pneumonia; idiopathic pulmonary fibrosis; lung cancer; squamous cell carcinoma; peripheral type.

2-A4: LUNG CANCER 4

PS245

C609T POLYMORPHISM OF NADPH QUINONE OXIDOREDUCTASE 1 CORRELATES CLINICAL HEMATOLOGICAL TOXICITIES IN LUNG CANCER PATIENTS TREATED WITH AMRUBICIN

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Background Amrubicin hydrochloride (AMR) is a key agent for lung cancer. NADPH quinone oxidoreductase 1 (NQO1) metabolizes the quinone structures contained in both amrubicin (AMR) and amrubicinol (AMR-OH). We hypothesized that *NQO1* C609T polymorphism may affect AMR-related pharmacokinetics and clinical outcomes.
Methods The patients with lung cancer received AMR at a dose of 30 or 40 mg/m^2/day on day 1–3 at Osaka City University Hospital were enrolled. Plasma sampling was performed at the time points of 24 h after the third AMR injection. The concentrations of AMR and AMR-OH were determined by HPLC method. *NQO1* C609T polymorphism was assayed using real-time polymerase chain reaction methods.
Results A total of 35 patients were enrolled. The C/C, C/T, and T/T were observed in 12 (34.3%), 16 (45.7%), and 7 (20%) patients, respectively. A dose of 30 mg/m^2 was administered to 19 patients, and 40 mg/m^2 was administered to 16 patients. The mean plasma concentrations of AMR-OH on day 4 at a dose of 30 mg/m^2 and 40 mg/m^2 were 11.02 ± 3.83 and 16.18 ± 6.17 ng/ml, respectively ($p = 0.005$). In patients with AMR at a dose of 40 mg/m^2, the plasma concentrations of AMR-OH on day 4 exhibited a tendency toward a relationship with *NQO1* genotypes with values of C/C 20.5 ± 5.89, C/T 15.9 ± 5.43, and T/T 11.2 ± 4.47 ng/ml ($p = 0.066$). The C/C was related to decrease changes in WBC, hemoglobin, and platelet counts ($p = 0.01$, $p = 0.03$, and $p = 0.0005$, respectively). No significant correlations were observed between *NQO1* genotypes and clinical outcomes at a dose of 30 mg/m^2.
Conclusions *NQO1* C609T polymorphism had a tendency of correlation with the plasma concentrations of AMR-OH, and thereby had significant correlations with hematologic toxicities. *NQO1* genotype appears to be the candidate biomarker of hematological toxicities of AMR treatment at a dose of 40 mg/m^2.

PS246

SURFACTANT PROTEIN A SUPPRESSES PROGRESSION OF HUMAN LUNG ADENOCARCINOMA IN NUDE MICE VIA MODULATING HOST IMMUNE RESPONSE

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Background and Aim of Study Surfactant protein A (SP-A) is a large multimeric protein found in the lungs. In addition to its immunoregulatory function in infectious respiratory diseases, SP-A is also used as a marker of lung adenocarcinoma. Despite the finding that SP-A expression level in cancer cells had the relationship with patient prognosis, the function of SP-A in lung cancer progression is still unknown. The purpose of this study is to investigate the role of SP-A in lung cancer progression and metastasis using mouse model.
Methods Human SP-A gene was introduced into human lung adenocarcinoma cell line PC14PE6 (PC14PE6/SP-A). We intravenously inoculated PC14PE6/SP-A into nude mice and examined the effect of SP-A on tumor lung metastasis.
Results PC14PE6/SP-A cells produced significantly fewer lung metastatic colonies and pleural effusion compared to vector transfected cells in vivo. Immunohistochemical analysis showed that the number of CD68-positive tumor-associated macrophages (TAMs) was increased in the lung metastatic colonies produced by PC14PE6/SP-A cells. Further analysis demonstrated that the increased phenotype of TAMs was M1 anti-tumor macrophages. The gene expression of M1 markers, especially CCL5, was also up-regulated in PC14PE6/SP-A lung metastatic colonies. In addition, the number of natural killer (NK) cells and the gene expression of perforin 1 and granzyme B was increased in SP-A-expressing metastatic tumor. In vitro analysis showed that the exogenous SP-A treatment increased the expression of M1-related genes such as CCL5, CCL2, TNF-α, and IL-1β in mouse macrophages, whereas it did not have the direct effect on the expression of perforin 1 and granzyme B in NK cells.
Conclusion These results suggested that SP-A activated monocytes/macrophages to obtain M1 phenotype, and these increased M1 TAMs then activated NK cells to exhibit cell killing. SP-A may have a protective role in lung cancer progression through modulating host immune response.

PS247

LIPID ACCUMULATION IN PERIPHERAL BLOOD DENDRITIC CELLS OF PATIENTS WITH LUNG CANCER

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Background Dendritic cells (DCs) are professional antigen presenting cells and play a central role in the anti-tumor immunity. DCs up-took cancer specific antigen are essential for the activation of cytotoxic T cells and cancer-specific helper T cells, and they are involved in early anti-tumor immunity. As a cause of suppression of anti-tumor immunity in the cancer-bearing patients, the lipid accumulation-induced dysfunction of dendritic cells has been reported. Purpose: We examined that lipid accumulation and subsets of peripheral blood DCs in patients with lung cancer of various disease stages.
Methods Peripheral blood was obtained from untreated naive lung cancer patients and healthy volunteers. We analyzed the surface markers indicating subsets of DCs (CD1a for mDC1, BDCA-3 for mDC2, BDCA-2 for pDC) using flow cytometry. To evaluate the content of lipids in DCs, we used the lipophilic fluorescent dye (BODIPY 650/665).
Results In untreated naive lung cancer patients, the total number of peripheral blood DC was significantly lower than that in healthy individuals. In addition, we analyzed the total number of DCs in each stage of untreated naïve lung cancer. As the clinical stage of patients advanced, the total number of DCs was significantly decreased. Lipid accumulation in DCs measured by the fluorescence intensity was significantly elevated in patients with lung cancer as compared with healthy individuals. The accumulation was also increased as the stage advanced.
Conclusion These findings suggest that decrease of the total number of DCs in the peripheral blood and increase of lipid accumulation in DCs may be the possible cause of suppression of anti-tumor immunity in patients with advanced lung cancer.

PS248

EFFECT OF SIMVASTATIN ON GEFITINIB RESISTANCE IN NON-SMALL CELL LUNG CANCER WITH THE T790M MUTATION OF EPIDERMAL GROWTH FACTOR RECEPTOR

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Backgroud Although Non-small cell lung cancer (NSCLC) tumors with activating mutations in the EGFR are highly responsive to EGFR tyrosine kinase inhibitors (TKI) such as gefitinib, development of acquired resistance is almost inevitable. Statins have reported antitumor activity, but it is unknown whether simvastatin can reverse gefitinib resistance in NSCLC with the T790M mutation of EGFR. This study was designed to investigate overcoming gefitinib resistance through a mechanism-based approach using simvastatin.
Methods The effects of simvastatin on apoptosis and AKT/β-catenin signaling were examined by annexin V binding assay and immunoblot analysis. We tested the effects of LY294002, siRNA and overexpression for AKT in simvastatin treated gefitinib-resistant NSCLC cells. We also evaluated the role of survivin in simvastatin-induced apoptosis of gefitinib-resistant NSCLC.
Results Addition of simvastatin to gefitinib enhanced caspase-dependent apoptosis in NSCLC cells with the T790M mutation. Simvastatin also exerted a inhibitory effect on activation of AKT, leading to suppression of β-catenin activity and expression of its targets, survivin and cyclin D1. Both insulin treatment and AKT overexpression markedly increased p-β-catenin and surivivn level even in the presence of gefitinib and simvastatin. On the other hand, inhibition of AKT by siRNA or LY294002 treatment both caused inhibition of p-β-catenin and survivin. To determine the role of survivin in simvastatin-induced apoptosis, we showed that the proportion of apoptotic cells induced by survivin-siRNA and combination of gefitinib and simvastatin was greater than the theoretical addictive effects, whereas survivin up-regulation could confer protection against apoptosis induced by gefitinib and simvastatin.
Conclusion Survivin is a key molecule that renders the NSCLC cells with the T790M mutation resistant to apoptosis induced by gefitinib and simvastatin. Taken together, simvastatin may overcome gefitinib resistance in NSCLC with the T790M mutation via AKT/β-catenin signaling dependent down-regulation of survivin and inducing apoptosis.

PS249

BOVINE LACTOFERRIN INHIBITS LUNG CANCER GROWTH THROUGH SUPPRESSION OF BOTH INFLAMMATION AND EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR

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Lung cancers are among the most common cancers in the world, and the search for effective and safe drugs for the chemoprevention and therapy of lung cancer has become important. In this study, bovine lactoferrin (bLF) was used in both in vitro and in vivo approaches to investigate its activity against lung cancer. A human lung cancer cell line, A549, which expresses a high level of vascular endothelial growth factor (VEGF) under hypoxia, was used as an in vitro system for bLF treatment. A strain of transgenic mice carrying the human VEGF-A165 (hVEGF-A165) gene, which induces pulmonary tumors, was used as an in vivo lung cancer therapy model. We found that bLF significantly decreased proliferation of A549 cells by decreasing the expression of VEGF protein in a dose-dependent manner. Furthermore, oral administration of bLF at 300 mg/kg of body weight 3 times a week for 1.5 mo to the transgenic mice overexpressing hVEGFA165 significantly eliminated expression of hVEGF-A165 and suppressed the formation of tumors. Additionally, treatment with bLF significantly decreased the levels of proinflammatory cytokines, such as tumor necrosis factor-α, and antiinflammatory cytokines, such as IL-4 and IL-10. Levels of IL-6, which is both a proinflammatory and an antiinflammatory cytokine, were also reduced. Treatment with bLF decreased levels of tumor necrosis factor-α, IL-4, IL-6, and IL-10 cytokines, resulting in limited inflammation, which then restricted growth of the lung cancer. Our results revealed that bLF is an inhibitor of angiogenesis and blocks lung cell inflammation; as such, it has considerable potential for therapeutic use in the treatment of lung cancer.

PS250

UP-REGULATION OF MIR-92A BY STAT3 ONCOGENE PROMOTES INVASIVENESS OF LUNG CANCER CELLS

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Background Signal transducer and activator of transcription 3 (STAT3) activation is frequently found in human lung cancer and is associated with increased metastasis and reduced survival. The molecular mechanisms by which STAT3 enhances cancer invasion have not been well characterized.
Methods The expression of microRNAs and target genes was measured by real-time RT-PCR. Protein level was studied by Western blotting. Luciferase reporter assay was used to confirm the direct targeting of microRNAs. Gelatin zymography was used to study matrix metalloproteinase (MMP) activity. Transwell assay was used to investigate cell migration and invasion.
Results We find that STAT3 expression is negatively associated with the expression of an endogenous MMP inhibitor, Reversion-inducing Cysteine-rich protein with Kazal motifs (RECK) in a set of lung cancer cell lines. Enforced expression of STAT3 decreases the endogenous MMP inhibitor RECK protein but not mRNA level in H460 cells. Conversely, STAT3 inhibitor S3I-201 increases RECK protein in STAT3-activating H1299 cells. We demonstrate that STAT3 up-regulates miR-92a to repress RECK via post-transcriptional inhibition. RECK 3'UTR reporter activity assay suggests RECK is a direct repression target of miR-92a. Delivery of pre-miR-92a reduces RECK protein level while transfection of anti-miR-92a restores STAT3-induced down-regulation of RECK. Anti-miR-92a attenuates MMP activity, migration and invasion of H1299 cells and STAT3-overexpressing H460 cells suggesting miR-92a is critical for STAT3-induced invasiveness.
Conclusion we demonstrate that up-regulation of miR-92a by STAT3 is one of the mechanisms by which STAT3 promotes cancer invasion. In addition, we show that RECK is an important mediator of STAT3-induced cell invasiveness. Targeting of the STAT3/miR-92a axis by may be helpful for the treatment of lung cancer.

PS251

CLINICOPATHOLOGICAL AND PROGNOSTIC SIGNIFICANCE OF INTERLEUKIN-8 EXPRESSION AND ITS RELATIONSHIP TO KRAS AND EGFR MUTATIONS IN LUNG ADENOCARCINOMA

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The CXC chemokine interleukin-8 (IL-8) is an angiogenic growth factor and is overexpressed in various human cancers, including non-small cell lung cancer (NSCLC). We have recently shown that activating KRAS mutations induce IL-8 overexpression, which promotes cell proliferation and migration in NSCLC cells. In the current study, we evaluated clinicopathological and prognostic significances of IL-8 expression in lung adenocarcinomas and its relationship to mutations of KRAS or EGFR. IL-8 mRNA expression was examined by quantitative RT-PCR using 136 surgical specimens obtained from lung adenocarcinoma patients. We then evaluated the association between IL-8 expression, clinicopathological features, KRAS or EGFR mutation status, and survival. IL-8 expression was predominantly expressed in lung adenocarcinomas from elderly patients and those with pleural involvement or vascular invasion. The differential IL-8 expression by age was prominent in nonsmokers but not in smokers. In a nonsmoker subgroup, there was a positive correlation between IL-8 levels and age. IL-8 was predominantly expressed in lung adenocarcinomas with KRAS mutation compared to those with EGFR mutation or wild-type EGFR/KRAS. There was a positive correlation between IL-8 levels and age in a subgroup of KRAS-mutants or EGFR-mutants. Disease-free survival (DFS) and overall survival (OS) were significantly shorter in lung adenocarcinoma patients with high IL-8 expression than in those with low IL8 expression. Furthermore, lung adenocarcinoma patients with KRAS-mutant/high IL-8 had significantly shorter PFS and OS compared to those with wild-type KRAS/low IL-8. Cox regression analysis revealed that IL-8 expression is an independent prognostic marker in lung adenocarcinomas. Our findings suggest that IL-8 expression is associated with certain clinicopathological features including age and is an unfavorable prognostic marker in oncogenic KRAS-driven lung adenocarcinomas.

PS252

ANTITUMOR EFFECT OF A HUMANIZED ANTIBODY AGAINST AMINOPEPTIDASE N IN MOUSE TUMOR MODELS

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Background and Aim of Study Aminopeptidase N (APN) has been reported to play important roles in tumor cell invasion and tumor angiogenesis. It's expression is associated with poor prognosis in patients with colon, pancreatic and lung cancers. The aim of this study is to evaluate antitumor effect of a humanized anti-APN antibody in mouse tumor models.
Methods Subcutaneous tumor and tail vein metastasis models were established in immune deficient mice using B16 melanoma cells stably transfected with APN (APN-B16), and H1299 cells highly expressing APN. These tumor-bearing mice were intraperitoneally administered a humanized antibody against APN. Sizes of subcutaneous tumor were measured and numbers of tumor nodules on the lung surface were counted. Tumor sections were immunostained with CD31 antibody to assess microvessel density.
Results The administration of anti-APN antibody reduced the sizes of subcutaneous tumors and the numbers of lung surface nodules in the mice bearing APN-B16 and H1299. Microvessel density in the tumors was also reduced.
Conclusion This humanized anti-APN antibody can suppress growth of tumor highly expressing APN probably through inhibiting angiogenesis.

PS253

PGE2-EP3 SIGNALING INDUCES PRE-METASTATIC NICHE FORMATION IN MEDIASTINAL LYMPH NODE BY CXCR4/SDF-1 AXIS

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Background Lymph node metastasis is one of the major factors of the prognosis and is facilitated by lymphangiogenesis, however the precise of the mechanisms is not well understood. In the present study, we investigated the role of COX-2-derived Prostaglandin E2 (PGE2) and Prostaglandin E receptor on formation of pre-metastatic niche that facilitate the lymph node metastasis in Lung Cancer.
Methods Lewis lung carcinoma (LLC 3.0 x 105/ml) cell suspensions were orthotopically introduced into the lung parenchyma of wild type mice (WT) and EP3 receptor knock out mice (EP3KO) via a limited skin incision without thoracotomy followed by direct puncture through the intercostal space.
Results Mediastinal lymph node metastasis formations were significantly suppressed in COX-2 inhibitor (celecoxib, 100 mg/kg/day) treated mice and EP3KO. The expressions of SDF-1, CXCR4, were significantly suppressed in celecoxib treated mice and EP3KO ($P < 0.05$). CXCR4 antagonist (AMD 3100) decreased lymph node metastasis formation. Furthermore, the accumulation of CD11C+DC was suppressed in COX-2 inhibitor treated mice and EP3KO. In vitro, under EP1–4 agonist stimulation, the SDF-1 concentration in immature DCs was significantly enhanced in EP3 agonist compared to EP1, EP2 and EP4. WT transplanted with EP3KO-BM were significantly suppressed mediastinal lymph node metastasis formation compared to WT transplanted with WT mice.
Conclusion These results suggested that pre-metastatic niche formation in mediastinal lymph node was induced by bone marrow derived immature dendritic cells via PGE2-EP3 signaling by induction of CXCR4/SDF-1-axis. Thus, COX-2 inhibitors, CXCR4 antagonists and/or EP3 antagonists may become one of the options to suppress the lymph node metastasis.

PS254

EXPRESSION AND ROLE OF INTERMEDIATE FILAMENT NESTIN IN SMALL-CELL LUNG CANCER

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Background and Aim of Study Small-cell lung cancer (SCLC) is highly aggressive tumor. Clinical trials of SCLC treatments have been conducted since the mid-1980s, but have not achieved prolonged survival. To improve outcomes, new therapeutic strategies including novel molecular targets are desired. Nestin is a class VI intermediate filament protein expressed in stem/progenitor cells during the development of the central nervous system. Nestin is detected in various types of tumors and is involved in malignant processes. This study investigated the expression and function of nestin in SCLC.
Methods Expression of nestin and achaete-scute homolog 1 (ASH1) was studied in 21 lung cancer cell lines. To assess the function of nestin, a short hairpin RNA (shRNA) targeting nestin was transfected into two SCLC cell lines (DMS53 and SBC3), and cloned cells that showed apparent down-regulation of nestin were obtained. Nestin expression was also studied immunohistochemically in surgically resected SCLC primary tumors and metastatic SCLC tumors obtained from autopsy cases.
Results Nestin was expressed in nine of 10 SCLC cell lines. The nestin expression level was significantly higher in SCLC cell lines than in non-small-cell lung cancer cell lines ($P < 0.01$). There was a statistically significant positive correlation between the expression levels of nestin and ASH1 in SCLC cell lines. Nestin knock-down cells created by transfection with shRNA exhibited decreased invasion and cell proliferation capabilities. Furthermore, nestin was detected in SCLC tumor cells and tumor vessels in all clinical tumor specimens.
Conclusion Nestin is expressed in SCLC in association with neuroendocrine features and participates in malignant phenotypes, including cell growth. Therefore, nestin may be a promising therapeutic target for SCLC.

2-A5: ASTHMA 4

PS255

ASTHMA AND SEVERITY OF THE 2009 NOVEL H1N1 INFLUENZA: A CASE-CONTROL STUDY

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Objective Previous studies reported that the most common chronic condition found among hospitalized patients due to the novel 2009 H1N1 influenza was asthma. However, these studies did not include a concurrent control group. Thus, we investigated the association of asthma status and severity of H1N1 influenza.
Methods The study was designed as a multi-site case-control study. Cases were patients who had positive PCR for H1N1 influenza and were admitted to the ICU or general ward with a diagnosis of H1N1 influenza from January 1, 2009 to December 31, 2009. Controls were patients who had positive PCR for H1N1 influenza, but were not admitted to hospitals.
Results There were 91 cases, including 41 ICU patients and 50 inpatients, and 56 controls who met the matching criteria were available. Of the 91 cases, the mean age was 47.3 years and 59% were female. Of the 91 cases, 38% had any comorbid conditions. Of the 91 cases, 12 (13%) had asthma. Stratified analysis by comorbid conditions other than asthma showed that among those without any comorbid conditions, 8 of 56 cases (14%) and 2 of 49 controls (4%) had asthma, (OR: 3.92, 95% CI: 0.79–19.42, $p = 0.095$) whereas, among the 39 subjects with one or more comorbid conditions, one of 7 controls (14%) had asthma and 4 of 35 (11%) cases had asthma ($p = 0.83$).
Conclusions Asthma may be associated with severity of H1N1 influenza among those without any non-asthma comorbid conditions. However, the limited sample size did not allow this study to fully establish a statistically significance. We still recommend asthmatics as a priority group for influenza vaccination and treatment.

PS256

IMPACT OF ASTHMA DISEASE MANAGEMENT PROGRAM ON OVERALL CONTROL AND QUALITY OF LIFE OF ASTHMA PATIENTS

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Background This study was whether implementing an asthma disease management program (SNAP) could improve overall control of the disease and quality of life of asthma patients with moderate to severe asthma.
Method From 2008 to 2010, 404 patients were enrolled into the SNAP program. 271 had baseline ACT score recorded and had clinic visits at least once a year till the time of evaluation These 271 patients' records were reviewed to determine the effectiveness of the program in improving: Overall Asthma Control measured by ACT score and Quality of Life at the last follow-up visit. Descriptive Analysis 70.6% of patients under SNAP program had asthma for more than 10 years at the time of registration. 5.5% had history of near fatal asthma. 20.8% are smokers.
Asthma Control Test (ACT) Score Mean ACT score at enrollment was 15.15 (SD 4.68) versus 20.84 (SD 3.90). Overall there was improvement in ACT score. Patients enrolled in 2008 had greater improvement in ACT score at their last visit than those enrolled in 2009 and 2010 (7.08, 5.66 & 4.69). Mean difference (last and first visit ACT score) between 2008 and 2010 is 2.4 and is statistically significant at p value 0.05 level.
Quality of Life Measures On the last visit, there was a reduction in the proportion of patients who had days symptoms for more than 3 times per week (59.4% vs. 19.9 %,) and nights symptoms for more than 3 times per week (45.8% vs. 12.2 %,) compared to the first visit. But there is no significant change in the number of days with restricted activity on the last visit. At the time of enrollment, 45.0% reported history of hospitalization in the past 12 months while only 3.0% had reported this on the last visit.

PS257

ONSITE NURSE EDUCATION IMPROVES ASTHMA PATIENT SAFETY IN EMERGENCY ROOM

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This study examines the impact of onsite nurse review and education on post-emergency room (ER) outcomes in patients with acute asthma exacerbations.
Methods We report a before versus after study of 30 day ER re-admission and outpatient asthma clinic attendance in adult patients discharged from the ER after successful treatment of acute asthma exacerbations. We compared the results in the year before (2010) versus after (2011) the introduction of an onsite asthma education service in the ER. Before discharge from the ER, an asthma nurse educator taught asthma control medication, inhaler technique, and asthma first aid for acute attacks and give an asthma clinic review date. In 2012 we compared the results in 1,323 patients who received face-to-face versus telephonic versus no education. There were no other changes in asthma management protocols in the ER during these 3 years.
Results Following the intervention, there was significantly increase rates of both 30-day ER re-admission (4.2% Versus 7.3%, $p < 0.01$) and outpatient asthma clinic attendance (35.6% Versus 57.4% $p < 0.01$) in 2010 versus 2011 respectively. In 2012 the ER re-admission rates were 9.1% versus 5.4% versus 2.6% ($p < 0.01$) and the outpatient asthma clinic attendance rates were 38.9% versus 31.7% versus 17.6% $p < 0.05$) in patients who received face-to-face versus telephonic versus no education respectively. There were no significant differences in sex, age and ethnic composition.
Conclusion (1) Onsite nurse education improves patient safety following discharge from the ER. (2) Onsite nurse education was associated with more ER re-visits for poor asthma control and better asthma clinic attendance. (3) The intensity of asthma education was significantly related to safer patient behavior.

PS258

FREQUENCY AND SEASONAL ALTERATION OF ASTHMA EXACERBATIONS RATE IN PULMONARY MEDICINE CLINIC

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Background and Aim of Study Asthma is a chronic inflammatory disorder of the airways that many cells and cellular elements play a role in pathogenesis. Chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. It causes widespread, variable, and often reversible airflow limitation. Aim of our study is to show frequency and seasonal distribution of out-patient Asthma patients who applied to our Pulmonology Clinic.
Method Out-patient records of pulmonary medicine clinic were analyzed and asthma patient records were taken into account. Due to low case numbers in summer time, two summer seasons were included in our study. Asthma cases divided into follow-up and exacerbations groups and both groups' seasonal distribution was analyzed.
Results 3288 patients were applied to our clinic in 13 month period. Total 433 (13.2%) patient were diagnosed as asthma and 189 (43.6%) applied as asthma exacerbations and 244 (56.4%) as asthma follow-up. Asthma total case numbers were 101 (23.3%) in spring (March, April, May), 113 (26.2%) in summer (June, July, August), 105 (24.2%) in fall (September, October, November) and 114 (26.3%) in winter (December, January, February). Seasonal Asthma exacerbations' rate were 49 (11.3%) in spring, 36 (8.3%) in summer, 41 (9.5%) in fall and 63 (14.5%) in winter.
Conclusion 13.2% of patient had asthma diagnosis. Asthma follow-up rate was close to asthma exacerbations. Family practitioners' active participation in asthma treatment and follow-up might be reason for low case number of follow-up group. Asthma acute exacerbations were lowest in summer, highest in winter and moderate in spring/fall. High Asthma exacerbations' rate in winter might be caused by cold weather conditions, increased infectious disease, allergens and air-pollution. Lowering acute exacerbations of asthma can be achieved by collaborative working between patients, respiratory specialist and also family practitioners.

PS259

SERUM EOSINOPHIL CATIONIC PROTEIN LEVELS IN ASTHMA BRONCHIALE PATIENTS

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Objectives Serum eosinophil cationic protein levels in asthma bronchiale patients were compared with healthy controls and the relation between serum eosinophil cationic protein levels, serum total igE levels and serum total eosinophil counts were evaluated.
Patients and Methods Serum eosinophil cationic protein(ECP)levels, serum total igE levels, serum total eosinophil counts of a total of 60 patients with asthma (21 of them with asthma and allergic rhinitis) aged 19 to 52 (39 female, 21 male) and 39 (24 female, 15 male) healthy subjects were compared.
Results Mean serum ECP levels of 60 patients with asthma bronchiale were significantly higher than the control group ($p < 0.05$). The level of serum ECP, serum total igE and serum total eosinophil counts of 60 patients were significantly higher than the control group. Serum ECP levels were high both in control group and asthma bronchiale group with significant eosinophilia.
Conclusion Asthma bronchiale is a chronic inflammatory airway disease. Eosinophils play a key role in the pathogenesis of asthma bronchiale. The degree of inlammation may be associated with proteins which are derived from eosinophils (such as ECP, etc)In the studies conducted with patients with asthma and allergic rhinitis ECP levels in blood and bronchoalveolar lavage were found to be increased. In some studies it has been suggested that it is more convenient to monitor disease activity with serum ECP levels than eosinophil count. In several studies, the increase in serum ECP levels of patients with asthma and allergic rhinitis is correlated with serum eosinophil counts and serum total igE levels. In our study, in accordance with studies in literature, serum ECP, serum total igE levels and serum total eosinophil counts in patients with asthma were significantly higher than the control group.

PS260

RELATIONSHIP BETWEEN MAXIMAL MID EXPIRATORY FLOW AND METHACHOLINE CHALLENGE TEST IN PATIENT WITH ASTHMA

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Background Methacholine challenge test (MCT) is used to assess airway hyper-reactivity in patients with suspicion of asthma. The test is useful when spirometry results are normal but patient's symptoms are suggestive of asthma. A negative MCT rules out asthma diagnosis at the time of the test. A significant number of patients with normal spirometry prove to have a positive MCT, and subsequently asthma. In spirometry, Maximal Mid Expiratory Flow (MMEF) of less than 60% in the presence of normal FEV1/FVC ratio indicates small airways disease which can be seen in asthma. The relationship between reduced MMEF and MCT results is not well studied.
Aim We investigated the relationship between MMEF and the results of MCT in patients with high suspicion of asthma and normal FEV1/FVC ratio. Our hypothesis was that a reduced MMEF could predict a positive MCT result in such patients.
Methods Retrospective analysis was conducted on all MCTs done in our pulmonary function laboratory between June 2010 and May 2013. MMEF is considered abnormal when the value is less than 60% predicted. A positive MCT test is defined as a drop of 20% of baseline FEV1%.
Results Thirty eight MCTs were obtained and analyzed. There were 25 (56%) males. Median age was 32 years (range 16–61). MMEF was abnormal in 9 patients (24%) while MCT was positive in 18 (47%) patients. 14 out of the 29 (48%) patients with normal MMEF had a positive MCT. However, a similar percentage of patients with abnormal MMEF had a positive MCT (4 out of 9 patients, 44%).
Conclusions In patients with clinical suspicious of asthma and normal FEV1/FVC ratio, an abnormal MMEF is not necessarily associated with a positive MCT. Physician should decide on the need to perform a MCT regardless of the value of the MMEF during spirometry.

PS261

PERCEPTION ON THE IMPACT OF ASTHMA RESOURCES NURSES SERVICE AT KKH

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Perception On The Impact Of Asthma Resources Nurses Service At KKHAH Teo[1] N. Mohd,[1] R Lee[1], A Chiang[1], A Tan[1]. N Salleh[1] and FH Chew
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Introduction Asthma is a chronic condition with significant morbidity, mortality and high economic burden. In Singapore, asthma is a very common problem with prevalence as high as 20% among children, and 5% among the adult Left unchecked, the disease could become an emerging problem of epidemic proportions in both children and adults in the near future.
Methods 179 asthmatic child's caregivers who attended high risk asthma clinic at KKH between March to May 2011 who agree to participate in this study were be given a set of questionnaires to be answered.
Results 102 mother is the main caregivers, both parent 64, 5 of fathers, 6 others. 84% of caregivers agree counseling and reinforcement by asthma resource nurses are helpful/The reading material(s) is/are given to them is/are beneficial and adequate. 70% of care givers are comfortable in seeing asthma resource nurse for clinical assessment and evaluation at the asthma clinic. 51% of care givers said that they learn best and would like to learn more about asthma care through talking to asthma resource nurses. 74% of care givers used the Written Asthma Action Plan (WAAP) to manage their child mild asthma attack at home.78% of care givers confident in using the WAAP as a guide to manage their child's condition.
Conclusion Successful asthma management is a cooperative effort between the patients, their family and all health care professional involves. The asthma resource nurse bridges a gap between the patient and the doctors, to provide comprehensive education and maintain the continuity of care.

PS262

INDUCIBLE NOS IS MAJOR SOURCE OF DISTAL AIRWAY NITRIC OXIDE IN STEROID NAIVE ASTHMATICS

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Backgrounds and Aim of Study Nitric oxide (NO) has been reported as an indicator of asthmatic airway inflammation. Furthermore, distal airway NO (Calv) is useful indicator in distal airway inflammation. NO production has been reported in a variety of resident cells and in inflammatory cells. NO synthase (NOS) exists in three forms: nNOS, eNOS and iNOS. NO production in steroid naive (snBA) is thought to be mainly by iNOS-expressing BECs; however, some reports have pointed out the importance of constitutive NOS in animal models. Here, we investigated correlation with NOS mRNA expression and Calv in distal BECs.
Methods Bronchial brushing, BAL and TBLB were performed in BA patients, including snBA and steroid-treated asthma (stBA). BECs were selectively isolated from the distal airway using a sheathed brush. We then examined HE staining and Hansel staining and iNOS expression by immunohistochemistry (IHC). Total RNA was extracted from BECs and BAL cells and iNOS mRNA was measured by qRT-PCR. We then analyzed the correlation of Calv and NOS mRNA expression in BECs.
Results Significant inflammatory-cell infiltrations were noted and expression of iNOS protein in the distal airway mainly in BECs and also macrophages and eosinophils. Quantitative RT-PCR showed significantly higher iNOS mRNA expression in BECs than in BAL cells. There are no increases in expression of nNOS and eNOS but is in iNOS in snBA and iNOS showed a significant correlation with Calv. Among the three of NOS, iNOS mRNA expression is highest in distal BECs.
Conclusion In the distal airway of asthmatics, BECs are the main NO source and iNOS is thought to be the main enzyme.

2-A6: ASTHMA 5

PS263

COMPARATIVE STUDY OF THE EFFECTS OF LOW DOSE BUDESONIDE, HIGH DOSE BUDESONIDE AND MONTELUKAST TO COUGH VARIANT ASTHMA

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Background and Aim of Study Inhaled corticosteroids are considered first line treatment of cough variant asthma (CVA), while anti-leukotriene drugs such as montelukast are also effective as shown by short-term studies. However, their effects have not been compared in CVA.
Methods Newly diagnosed, anti-inflammatory treatment-naive 65 patients (41 females, 50 ± 18 years old) were randomly assigned to receive daily doses of budesonide (BUD) 400 mcg (n = 22), BUD 1200 mcg (22) or montelukast 10 mg (21) for 12 weeks in open-label fashion. Patients were examined for impulse oscillation (IOS) measurements, spirometry, cough visual analogue scale (VAS), capsaicin cough sensitivity, lung volumes, methacholine airway responsiveness and fractional exhaled nitric oxide (FeNO) at baseline and at 12 week. For the IOS, possible measures of small airways dysfunction (reactance at 5 Hz [X5] and low-frequency reactance area [AX]) in addition to resistance of total and central airways were analyzed. After treatment, patients' clinical courses were followed for 1-year.
Results Cough VAS and residual volume improved significantly in all groups, but the degrees of improvement did not differ among the groups. X5 and AX improved and cough sensitivity decreased only in the montelukast group. FeNO fell significantly in the high dose BUD and montelukast groups, the former improved more than the latter. Spirometry, airway responsiveness, and other indices of IOS were unaffected in any group. Coughing tended to relapse more often in the montelukast group during the follow up period.
Conclusions In CVA, the effectiveness of montelukast is comparable with inhaled corticosteroids of varying doses at least for a short-term.

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A SWITCHING LOW DOSE INHALED CORTICOSTEROID TO PRANLUKAST IN MILD PERSISTENT ASTHMA

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Background Treatment guidelines for asthma recommend step-down therapy for well-controlled asthma patients. However, the strategy for step-down therapy has not been well defined. We investigated whether well-controlled patients with mild persistent asthma treated by inhaled corticosteroid (ICS) can accept a step-down therapy with reduction in the dose of ICS or leukotriene receptor antagonist (LTRA), pranlukast (PL).
Method We recruited 40 adult patients with mild persistent asthma that were well controlled for at least 3 months with a low daily dose (200 μg) of fluticasone propionate (FP) or a therapeutically equivalent dose of budesonide (BUD) or ciclesonide (CIC), and randomly assigned for 6 months with either switching to PL (20 patients in PL group) or inhaled FP 100 μg daily or a therapeutically equivalent dose of BUD or CIC (20 patients in ICS group). During study period, patients were monitored FEV1, Peak Expiratory Flow, respiratory resistance and reactance by forced oscillation technique (FOT), and fractional exhaled nitric oxide (FeNO) for every 2 month.
Result During study period, no patients in both treatment groups required hospital admission for an acute exacerbation of asthma and treatment with systemic corticosteroid. The rates of treatment failure were 10% and 35% in the ICS group and the PL group, respectively, and there was no significant difference between both groups. FeNO levels in PL group were significantly increased than ICS group. However, there were no significant differences between both group for the lung function and FOT.
Conclusion Patients with mild persistent asthma that is well controlled with the low dose of ICS can be switched to PL safely. However, 35% of PL group failed to maintain well control for 6 months. Further studies are needed to investigate the therapeutic efficacy of LTRA mono therapy on step-down therapy, using protocols specifically tailored to patients with mild persistent asthma.

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THE MEASUREMENT OF COUGH SENSITIVITY TO METHACHOLINE FOR DISCRIMINATION OF COUGH VARIANT ASTHMA

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Objective The pathophysiology of cough variant asthma (CVA) is poorly understood. We previously identified a feature of CVA as the heightened cough response to bronchoconstriction. In this study, we investigated whether the measurement of cough sensitivity to methacholine (Mch) may help in the diagnosis for cough variant asthma.
Methods The measurements of cough sensitivity to capsaicin (C5), exhaled nitric oxide (ENO), bronchial reversibility to bronchodilator, bronchial responsiveness to Mch (PC20), and cough sensitivity to Mch were performed in patients with chronic non-productive cough (n = 86). Chronic non-productive cough responding to bronchodilator therapy, without wheezes audible on auscultation was diagnosed as CVA. Receiver Operating Curve (ROC) analysis of those measurements for discrimination of CVA from chronic non-productive cough were performed. The measurement of cough sensitivity to Mch was performed as follows. Mch induced bronchoconstriction was detected using partial and full flow-volume curves. We defined a 35% fall in PEF40 (PC35-PEF40) as mild bronchoconstriction. PEF40 was the expiratory flow of partial flow volume curve at 40% above residual volume level. Cough counting was performed during and after inhalation of Mch at PC35-PEF40.
Results The area under the curve for cough sensitivity to Mch was 0.864 and for C5 was 0.619, ENO was 0.593, bronchial reversibility was 0.539, and PC20 was 0.387. Sensitivity and specificity of cough sensitivity to Mch for discrimination of CVA from chronic non-productive cough were 81.4% and 85.2% respectively.
Conclusion The measurement of cough sensitivity to Mch, which is cough counting at mild bronchoconstriction, is useful for discrimination of CVA from chronic non-productive cough.

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DIFFERENCES IN PATIENTS WITH ASTHMA IN THE ELDERLY WITH OR WITHOUT AIRFLOW LIMITATION

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Background and Aim of Study To determine whether asthma in the elderly have distinct clinical characteristics associated with airflow limitation (AFL), we characterized 80 outpatients with asthma in the elderly by clinical history, pulmonary function tests, impulse oscillometry, and blood analysis.
Methods Outpatients aged 65 or older with asthma (n = 80: 40 men and 40 women with a mean ± SD age of 73.11 ± 5.761) were surveyed. AFL was defined as a post-bronchodilator (post-BD) FEV1/FVC < 0.7 in accordance with the Global Initiative for Obstructive Lung Disease. Impulse oscillometry and spirometry were assessed in 53 asthmatics with AFL (75.00 ± 5.704 years, male n = 29) and 27 asthmatics without AFL (69.41 ± 3.775 years, male n = 11) before and after short-acting β2 stimulant treatment. Multiple regression analysis was performed with a forward stepwise approach in variables that were significantly related to AFL in univariate analysis.
Results Mean age in the asthma with AFL was significantly higher than the asthma without AFL. Rate of allergic rhinitis (AR) in asthma with AR was significantly lower than the asthma without AFL. Post-BD FEV1% was related to Age, not to AR. Post-BD FVC, post-BD MMF, post-BD V50, and post-BD V25 were related to AFL, but not to age and AR. Post-BD FEV1 was not related to age, AR, and AFL. All post-BD values of impulse oscillometry were not related to AR and AFL. Post-BD Fres was only related to age.
Conclusion Post-BD FEV1% in elderly asthmatics was related to age, although post-BD FVC and FEV1 were not related to it. All post-BD values of impulse oscillometry in asthmatics were not related to AFL.

PS267

LTRA COULD BE AREDOX FACTOR IN THE AIRWAY INFLAMMATION OF BRONCHIAL ASTHMA

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Obesity is known as a systemic inflammatory disease, and it is also well known as a risk factor of bronchial asthma. A living body is always affected by internal and external stresses. We have Redox system to protect our living body from these oxidative stresses. Inflammation is closely related to oxidative stress. Obesity is one of the major factors of internal oxidative stress. The aim of the present study was to estimate the relationship between obesity and oxidative stress in bronchial asthma. Patients with bronchial asthma were recruited from the out-patient clinic of our department. We estimated the BMI, blood levels of adipokines (leptine, adiponectine), MDA-LDL, and SOD of the patients. Obesity was the risk factor of hospitalization by asthma attack in female patients in the present study. Obesity patients showed significantly higher level in serum leptine, and significantly lower level in serum adiponectine, compared to not-obesity patients. These differences in serum adipokines were more significant in female subjects. Gender differences were observed about oxidative stress in bronchial asthma in the present study. Those who took systeinyl leukotriene receptor antagonist (LTRA) showed higher serum adiponectine level than those without LTRA therapy. So, LTRA may help adiponectine production to relieve airway oxidative stress of bronchial asthma.

PS268

DO YOU THINK QUESTION 5 NEEDS ON ASTHMA CONTROL TEST FOR BRONCHIAL ASTHMA?

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Back Ground Asthma control test (ACT) is used quite frequently as a clinical evaluation of asthma control state.
Aim We confirmed the importance of ACT and examined whether question 5(Q5) is necessary as evaluation criteria of ACT in patients with stable asthma.
Subjects Eighty-two patients with bronchial asthma whose symptom are stable for more than 3 months (average 48 years old, male:40, female:42, Step1:22,Step2:47,Step3:8,Step4:4).
Methods We conducted ACT for subjects and analyzed its points. In addition, we compared with the re-evaluation of 20 points (as total control) excluded Q5.
Results There were 56 patients in 25 points (68%), 13 in 24 points (16%), 9 in 23 points and 4 in 22 points more than well control. The one hand, 73 patients got 20 points (89%) and 8 patients were 19 points (10%) in the re-evaluation except for Q5. The ratio of total control (as 20 points) by severity indicated 100% in Step1, 91.5% in Step2, 75% in Step3 and 25% in Step4.
Consideration We recommended that criteria of ACT excluding Q5 was more effective than one of current ACT as the clinical evaluation, because total control was about 70% in the evaluation of current ACT however it became higher about 90% in the evaluation of ACT excluding Q5. And the evaluation of ACT trends lower and lower according to severity.

PS269

UPREGULATION OF CD11B ON EOSINOPHILS IN ASPIRIN INDUCED ASTHMA

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Background Although a challenge test using non-steroidal anti-inflammatory drugs (NSAIDs) is crucial for diagnosis of aspirin-induced asthma (AIA), it also has drawbacks in terms of possible side effects. Therefore, alternative in-vitro diagnostic methods for AIA are awaited.
Methods Nineteen stable non-AIA patients (9 males and 10 females; mean age, 49.4 years), and 20 AIA patients (9 males and 11 females; mean age, 51.1 years) were enrolled in this study. CD11b and CD16 expressions on the peripheral-blood granulocytes after administration of aspirin and different concentrations of PGE2 in vitro were examined using flowcytometry.
Results Aspirin induced a significant increase in CD11b expression on eosinophils (CD16 negative granulocytes) in 19 AIA patients and one non-AIA patient. Increase in CD11b expression on eosinophils by aspirin administration was suppressed by PGE2 in a dose-dependent manner.
Conclusions The measurement of CD11b expression on peripheral-blood eosinophils showed very high sensitivity(95.0%) and specificity of (94.7%) in diagnosing AIA. Although this method requires laboratory facilities for flowcytometry, it may be very useful in diagnosis of AIA without side effects. In addition, PGE2 may be involved in regulation of CD11b expression on eosinophils by aspirin administration.

PS270

MEASUREMENT OF SERUM FREE IGE IN THE PATIENTS TREATED WITH OMALIZUMAB

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Omalizumab is successfully used as supplementary therapy to patients with poorly controlled atopic asthma. Because the majority of commercially available IgE assays measure both free IgE and omalizumab-bound IgE, the total IgE measurement was not available for the therapeutic monitoring. To aim at the therapeutic monitoring for anti-IgE therapy, we newly established an ELISA for free IgE employing a recombinant human soluble FcεRIα as a capture antigen and a biotinylated polyclonal anti-IgE antibody for detection. The assay was technically robust with a lowest limit of detection of 18.75 ≠g/mL. The spkike-recovery rate in serum was determined between 91.1% and 98.5%. Using newly established an ELISA, we measured the serum free IgE levels in five patients every week after first injection of omalizumab. Omalizumab significantly reduced serum free IgE levels prior to the second omalizumab injection in all patients. We also measured the serum free IgE levels in 8 patients treated with omalizumab over 12 months. It is believed that benefit of omalizumab treatment in severe asthma needs to keep serum free IgE concentrations below 50 ≠g/ml. In 3 of 8 patients with long-term use of omalizumab, the serum free IgE concentrations were higher than 50 ≠g/ml. The free IgE ELISA allows us to easily quantify free IgE and thus to monitor patients treated with Omalizumab. Our data suggest that the reevaluation of injection doses would be required in long-term use of omalizumab.

PS271

IL-33 AND REGULATED AND NORMAL T CELL EXPRESSED AND SECRETED (RANTES) IN BAL FLUID IN ASTHMA PATIENTS WITHOUT CIGARETTE SMOKING

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Background Inflammatory cytokines and chemokines have been reported to play important roles in the pathogenesis of bronchial asthma. However, no criteria for the classification of 'smoker' and 'atopic' in bronchial asthma have been defined. In this study, we compared the levels of several cytokines found in the bronchoalveolar lavage (BAL) fluid of patients classified as having bronchial asthma.
Methods Cell subpopulations in BAL fluid were counted. BAL fluid levels of in IL-4, -5, -13, -17, and -33 and regulated and normal T cell expressed and secreted (RANTES) were measured using a bead suspension array in 36 asthma patients (13 males, 23 females; mean age, 39.53 years) who had never smoked, 18 asthma patients (11 males, 7 females; mean age, 30.67 years) who were ex or current smokers (Brinkman index (BI): 1–399), and 10 asthma patients (9 males, 1 female; mean age, 50.2 years) who were current heavy smokers (BI: above 400). Relationships were assessed by Spearman's rank correlation analysis.
Results The number of lymphocytes in BAL cell subpopulations of never smokers were significantly higher than those of heavy smokers. The number of neutrophils was significantly higher in heavy smokers than in never smokers. Levels of IL-33 and RANTES were significantly higher in never smokers than in heavy smokers. In addition, the levels of IL-33 and RANTES in never smokers were significantly higher in atopic asthma patients than in non-atopic asthma patients. A good correlation was noted between RANTES and lymphocytes or IL-33 in atopic asthma patients who were never smokers.
Conclusions Differences in the cell types of BAL fluid, as well as in the levels of IL-33 and RANTES in asthma patients with or without smoking, might reflect pathogenesis.

2-A7: ASTHMA 6

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ETHNIC SENSITIVITY ASSESSMENT OF FLUTICASONE FUROATE (FF)/VILANTEROL (VI) IN ASTHMA PATIENTS IN JAPAN AND KOREA: A PRE-SPECIFIED SUBGROUP ANALYSIS

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Background and Aim of Study FF/VI is a combination inhaled corticosteroid/long-acting $beta_2$ agonist in development as a once-daily asthma therapy. This analysis evaluated ethnic sensitivity of FF/VI or FF alone in asthma patients in Japan and Korea.
Methods A pooled analysis of randomised, double-blind, multicentre phase IIb/IIIa trials. Efficacy data from three studies were compared between patients from Japan (n = 148) and 'Not-Japan' countries (n = 3066). Change from baseline in trough FEV_1 after 12 weeks with FF/VI 100/25 mcg, FF 100 mcg or placebo was analysed from two studies using an ANCOVA model, with terms for baseline FEV_1, region, gender, age, treatment group, study and region by treatment interaction. FF/VI 200/25 mcg and FF 200 mcg data were from one study. Safety data from six studies were compared between patients from Japan/Korea (n = 194) and Not-Japan/Korea (n = 4037). Pharmacokinetic and pharmacodynamic data were collected.
Results Versus placebo, improvements (mean change [95% CI]) in trough FEV_1 were reported in the Overall, Japan and Not-Japan populations, respectively, for FF/VI 100/25 mcg (181 mL [111,252], 323 mL [104,542], 168 mL [95,241]) and FF 100 mcg (105 mL [34,175], 216 mL [–3,436], 93 mL [20,166]). Treatment differences for Japan versus Not-Japan: FF/VI 100/25 mcg (155 mL [–71,382]); FF 100 mcg (124 mL [–103,351]). Changes from baseline were similar in patients from Japan and Overall for FF/VI 200/25 mcg and FF 200 mcg. In all treatment groups, including placebo, a greater proportion of patients from Japan/Korea versus Not-Japan/Korea reported on-treatment adverse events. FF $AUC_{(0–24)}$ and VI C_{max} were higher in patients from Japan versus Not-Japan, however no clinically relevant effects on cortisol concentrations or heart rate were observed.
Conclusion The efficacy/safety profile of FF/VI (100/25 mcg, 200/25 mcg) in asthma patients from Japan/Korea is consistent with the Not-Japan/Korea and Overall populations, results which suggest these patients do not require different clinical doses.
Funding GlaxoSmithKline (HZA106827 [NCT01165138], HZA106829 [NCT01134042], HZA106837 [NCT01086384], B2C109575 [NCT00600171], FFA108685 [NCT00603278], FFA109687 [NCT00603382]).

PS273

GLOBAL GENE EXPRESSION PROFILES DURING ALLERGIC AIRWAY SENSITIZATION TO HOUSE DUST MITE ALLERGEN IN MICE

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Background Allergic sensitization is important step in the pathogenesis of asthma. However, little is known about which molecules are critical regulators for establishing allergic sensitization through the airway. Thus we investigated the global gene expression analysis to identify candidate genes and signaling pathways involved in the house dust mite extract (HDM) -induced allergic airway sensitization in mice.
Methods We sensitized and challenged mice with HDM or saline as control through the airway on day1, 8, 15. On day18, HDM-sensitized and challenged mice got asthma-like responses, including eosinophilic airway inflammation and airway hyperresponsiveness. On day 0 (the day before first sensitization), day7 (the day before second sensitization) and day14 (the day before challenge), we extracted total RNA from lung tissues. Then we performed mRNA microarray analysis. Data analysis was performed using GeneSpring and Ingenuity Pathways Analysis.
Results Repeated HDM instillation into airway induced stepwise up-regulation of myeloid differentiation-2 (MD-2), the lipopolysaccharide-binding component of the Toll-like receptor 4 signaling complex.
Conclusions Our data suggest that innate immune-related gene including MD-2 might regulate to establish allergic airway sensitization to HDM in mice.

PS274

EXOSOMAL MICRORNAS IN THE SERUM ARE POTENTIAL AS A REAL-TIME BIOMARKER FOR ALLERGIC INFLAMMATION IN THE AIRWAY OF MICE

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Background MicroRNAs (miRNAs) have been reported as useful therapeutic and diagnostic targets for patients with asthma. Exosomal miRNAs in serum are stable so that this might be useful as biomarkers. However, little is known regarding which exosomal miRNAs in the serum are suitable for the real-time monitoring of allergic inflammation in the airway. We, therefore, investigated the miRNA microarray analysis to identify candidate exosomal miRNAs in the serum involved in the allergic inflammation in the airway of mice.
Methods We sensitized and challenged mice with house dust mite extract (HDM) or saline as control on day1, 8 and 15. On day 18, we collected lung tissues and serum, and extracted total RNA from lung tissues and exosomes in the serum. Then we performed miRNA microarray analysis using these extracted RNA. Data analysis was performed using GeneSpring software. Gene network analysis was performed using Ingenuity Pathways Analysis.
Results We identified same HDM-inducible miRNAs both in the lung and exosomes in the serum.
Conclusions Our data suggest that exosomal miRNAs in the serum we identified might be new diagnostic biomarker or therapeutic targets for allergic inflammation in the airway.

PS275

SELECTIVE SECRETION OF EXOSOMAL MICRORNAS IN A MICE MODEL OF BRONCHIAL ASTHMA

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Exosomes are cellular secretory vesicles containing microRNAs (miRNAs). Secreted exosomes are able to transfer miRNAs into the recipient cells, and consequently transferred microRNA potentially modulate the function of the cells. We hypothesized that airway secreted exosome derived miRNA profile in allergic airway inflammation might differ from that of normal condition. We studied exosomal miRNA profile of the mice with house dust mite (HDM)-induced allergic airway inflammation. The exosomes were obtained from bronchial alveolar lavage fluid (BALF) from the mice 2 days after the last allergen exposure. The number of purified exosomes was increased 8.9 times in the HDM-exposed mice compared to the sham mice. The exosomal miRNAs in the BALF were analyzed by a miRNA array (1966 microRNAs probes). The profiles of exosomal miRNAs in the HDM exposed mice were significantly different from that of the sham mice. Interestingly, over 90% of the increased exosomal miRNAs after HDM exposure (2-fold or more, $p < 0.05$), decreased inversely in the lung tissues with allergic inflammation. In contrast, over 80% of the decreased exosomal miRNAs after HDM exposure (0.5-fold or less, $p < 0.05$), increased inversely in the lung tissues. Our observations suggest a possibility that exosomal miRNAs are selectively secreted to the airway fluid in allergic inflammatory condition. The regulation of cellular transcriptome by selective secretion of exosomal miRNAs might be involved in the pathogenesis of allergic inflammation in the airway.

PS276

URIC ACID, A DANGER SIGNAL, ACTIVATES HUMAN EOSINOPHILS

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Rationale Uric acid (UA) is an important endogenous danger signal released from injured cells by inflammation and infection. Generation of UA is also implicated in the effects of an authentic Th2 adjuvant, aluminum hydroxide. Because eosinophils specifically accumulate to the sites of Th2-type inflammation, we hypothesized that UA acts as an activator for eosinophils.
Methods Eosinophils isolated from peripheral blood of normal individuals were incubated in the presence or absence of monosodium urate (MSU), an uric acid crystal, and then release of ATP and cytokines were evaluated.
Results Eosinophils exposed to MSU crystals rapidly (i.e., within 1 min of exposure) released ATP into the extracellular milieu. Eosinophils incubated with MSU crystals, but not those incubated with uric acid solution, produced IL-6 and IL-8/CXCL8. Other cytokines and chemokines were also produced by eosinophils incubated with MSU crystals.
Conclusions UA stimulated eosinophils to release ATP and product cytokine(s). Thus, human eosinophils may respond to particulate damage-associated endogenous danger signals. These responses by eosinophils to tissue damage may explain the self-perpetuating nature of chronic inflammation in certain human diseases, such as asthma.

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CHEMOKINE EXPRESSIONS OF DISTAL BRONCHIAL EPITHELIAL CELLS BY CDNA MICROARRAY ANALYSIS IN STEROID NAIVE BRONCHIAL ASTHMA

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Background and Aim of Study Distal airway inflammation thought to one of reason of difficult to treatment of asthma. In addition, distal airway inflammation is not easy to detect by spirometry or computed tomography (CT). Even if distal airway disease is mild-symptomatic, distal airway tissue of high-level eNO cases shows infiltration of abundant inflammatory cells and also high levels of iNOS mRNA expression in bronchial epithelial cells (BECs). A previous report showed invasion of inflammatory cells, including eosinophils, in the outer smooth muscle layer. These inflammatory cells are thought to be mediated by migration by chemokines that produced by BECs. Various chemokines are expressed in BECs in asthma; however, it is not still clear what kinds of chemokines are produced in distal BECs in steroid-naive bronchial asthma (snBA).
Methods Bronchial brushing was performed in stable asthmatics (3 snBA and 4 steroid-treated asthma (stBA). BECs were selectively isolated from the distal airway. Freshly isolated distal BECs and total RNA was extracted and processed for Microarray analysis. Microarray analysis was performed using GeneSpring GX12 software and included cluster analysis, gene ontology (GO) analysis, and pathway analysis. Chemokine expression was validated by qRT-PCR.
Results We extracted 1109 genes which showed a fluctuation of expression of > 1.5 fold, with a significant difference between snBA and stBA. Expression of 417 genes increased in snBA while that of 692 genes increased in stBA. Ten GO terms were extracted with a significant difference in increased genes in snBA. qRT-PCR confirmed higher expression of the chemokines CCL15, CCL17 and CCL26 in snBA than in stBA.
Conclusion Increasing chemokines production was found in the distal airway of asthmatics, even in mild-symptomatic patients but have significant airway inflammation, suggesting that the control of distal airway inflammation is important.

PS278

REQUIREMENT FOR THE RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS IN ALLERGIC AIRWAY INFLAMMATION

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Background and Aim of Study The receptor for advanced glycation end-products (RAGE) is a multi-ligand receptor which belongs to the immunoglobulin superfamily. RAGE expression is increased in patients with chronic obstructive pulmonary disease (Am J Respir Crit Care Med. 2010;181:917) and asthma (Respir Med 2011;105:519), however, the role of RAGE in allergic airway disease is not well defined.
Methods RAGE-deficient ($RAGE^{-/-}$) mice and wild-type ($RAGE^{+/+}$) mice were sensitized to ovalbumin (OVA) by intraperitoneal injection and subsequently challenged with OVA via the airways. Airway inflammation, cytokine levels in bronchoalveolar lavage (BAL) fluid were measured.
Results $RAGE^{-/-}$ mice showed significantly lower numbers of eosinophils in the BAL fluid compared to $RAGE^{+/+}$ mice following sensitization and challenge. The levels of IL-5 and IL-13 in BAL fluid of $RAGE^{-/-}$ mice were lower, as were the numbers of periodic acid-Schiff positive cells in the lung.
Conclusions These data suggest that RAGE contributes to the development of allergen-induced inflammation and Th2 cytokine production in the airways.

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EFFECTS OF PIRFENIDONE ON INCREASED COUGH REFLEX SENSITIVITY IN GUINEA PIGS

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Background and Aim of Study Pirfenidone, an antifibrotic drug with anti-inflammatory and antioxidant effects, delays fibrosis in idiopathic pulmonary fibrosis (IPF). Patients with IPF have a greater cough reflex sensitivity to inhaled capsaicin than healthy people, and cough is an independent predictor of IPF disease progression; however, the effects of pirfenidone on cough reflex sensitivity are unknown.
Methods After challenge with an aerosolized antigen in actively sensitized guinea pigs, pirfenidone was administered intraperitoneally, and the cough reflex sensitivity was measured at 48 h after the challenge. Bronchoalveolar lavage (BAL) was performed, and the tracheal tissue was collected.
Results Pirfenidone suppressed the capsaicin-induced increase in cough reflex sensitivity in a dose-dependent manner. Additionally, increased levels of prostaglandin E2, substance P, and leukotriene B4, but not histamine, in the BAL fluid were dose dependently suppressed by pirfenidone. The decrease in neutral endopeptidase activity in the tracheal tissue was also alleviated by pirfenidone treatment. The total number of cells and components in the BAL fluid was not influenced.
Conclusion These results suggest that pirfenidone ameliorates isolated cough based on increased cough reflex sensitivity associated with allergic airway diseases, and potentially relieve chronic cough in IPF patients who often have increased cough reflex sensitivity. Prospective studies on cough-relieving effects of pirfenidone in patients with IPF are therefore warranted.

PS280

INTERLEUKIN-23 MAY CONTRIBUTE TO DIFFERENCE IN SEVERITY OF EOSINOPHILIC AIRWAY INFLAMMATION BETWEEN SEXES IN A MURINE MODEL OF ASTHMA

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Background and Aim of Study It is well known that women suffer from severe asthma more frequently than men. Interleukin (IL)-23-IL-17-producing CD4+T cell (Th17 cell) axis may play an important role in the development of chronic inflammatory diseases including asthma. The aim of this study is to investigate whether differences in asthma severity between sexes are associated with the production of IL-23/IL-17 in an experimental model of allergic asthma.
Methods Eosinophil counts and cytokine profiles in bronchoalveolar lavage (BAL) fluids were assessed in ovalbumin (OVA)-sensitized and challenged male and female IL-23-deficient mice and wild-type C57BL/6 mice.
Results Aerosolized OVA challenge caused marked eosinophilia in BAL fluids. The numbers of eosinophils in BAL fluids were significantly higher in male IL-23-deficient mice than in male WT mice. On the other hand, there was no significant difference in the numbers of eosinophils in BAL fluids between female IL-23-deficient mice and female WT mice. The levels of IL-17 in BAL fluids tended to be lower in male IL-23-deficient mice than in male WT mice while there was no significant difference in the levels of IL-17 between female IL-23-deficent mice and female WT mice.
Conclusion The difference in severity of eosinophilic airway inflammation between sexes may be associated with the different production of IL-23.

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ABSTRACT WITHDRAWN

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EXPERIENCES OF PULMONARY COMPLICATIONS IN TWO NONAGENERIANS WITH FEMORAL NECK FRACTURES, BOTH WITH AND WITHOUT OPERATION

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We experienced two cases of femoral neck fracture in extremely elderly patients who developed pulmonary complications, right-side pleuritis in one and bilateral aspiration pneumonia in the other. The first case was a 94-year old woman. Her case of left femoral neck fracture was complicated with right-side recurrent pleuritis. We performed several pleural punctures and administered antibiotics. The pleuritis was partly due to parapneumonic effusion. Surgery for the fracture was subsequently performed. Pleural effusion did not recur, and the patient was discharged. The second case was a 92-year old man whose right femoral fracture was complicated with aspiration pneumonia in the bilateral lungs. The family did not wish to do the operation because of the patient's extreme age. We performed IVH and the administration of antibiotics of TAZ/PIPC or PIPC conservatively. The patient improved gradually, and oral feeding became possible. The rehabilitation of his legs gradually increased his ADL according to the spontaneous healing of the femoral neck fracture. Since a supine position was required after the femoral fracture, protection against decubitus and skin care was also needed. In any case, when treating the very elderly for femoral fractures in the early stages, pulmonary complications (pneumonia, etc.) might be prevented as reported also by several other references.

PS283

EFFICACY AND SAFETY OF MOXIFLOXACIN IN PATIENTS WITH NURSING AND HEALTHCARE-ASSOCIATED PNEUMONIA

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Background Nursing and healthcare-associated pneumonia (NHCAP) is common in elderly patients and is also associated with aspiration and drug resistance to antibiotics. Moxifloxacin (MFLX) is a respiratory quinolone effective to anaerobes. Additionally, it is unnecessary to reduce the amount of MFLX even in patients with renal dysfunction. Therefore, we assessed the efficacy and safety of MFLX in patients with NHCAP.
Patients and Methods NHCAP patients with mild and moderate severity by A-DROP system of JRS community-acquired pneumonia guideline visited our hospitals from September 2010 to March 2012. Clinical symptoms, chest X-rays and/or CT, peripheral white and red blood cell and platelet counts, serum CRP, AST, ALT, BUN, creatinine were evaluated. Clinical efficacy of MFLX was categorized into effective, ineffective and undeterminable. Patients aged over 65 years old were considered aged patients. All side effects were also evaluated during MFLX treatment. Collectable sputum samples were also bacteriologically evaluated.
Results Forty patients were evaluated, and average age was 74.1 yeas old, male/female were 19/20, 92.5%(37/40) of them had one or more comorbidities. Median duration of administration was 7 days (3–15 days). The efficacy in all patients was 87.5% (35/40). The efficacies in each age group were 87.9% (aged over 65 years old), 87.5% (aged under 64 years old), and in each pneumonia severity group by the A-DROP system were 91.2% (mild), 85.7% (moderate). Diarrhea was observed in one patient (2.5%) after starting MFLX administration. Sputum samples were investigable in 20 patients, and Gram-positive cocci in 15 samples, Gram-negative rods in 16 samples and Candida in one sample were detected. In these samples, 9 samples showed S. aureus (1), S. pneumoniae (2), alpha-Streptococcus (1), K. pneumoniae (1), H. influenzae (1), M. catarrhalis (2), P. aeruginosa (1).
Conclusion MFLX is effective and safe in patients with NHCAP.

PS284

SERUM IGA ANTIBODIES AGAINST GLYCOPEPTIDOLIPID CORE ANTIGEN IN PATIENTS WITH PULMONARY DISEASE DUE TO NONTUBERCULOUS MYCOBACTERIA OTHER THAN MYCOBACTERIUM AVIUM-COMPLEX

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Background and Aim of Study Enzyme immunoassay kits for the detection of serum IgA antibodies specific for glycopeptidolipid (GPL) core antigen are useful for rapid and accurate serodiagnosis of *Mycobacterium avium*-complex pulmonary disease (MAC-PD), but false-positive results are possible in patients with PD due to other nontuberculous mycobacteria (NTM) such as *M. fortuitum*, *M. chelonae*, *M. abscessus*, and *M. scrofulaceum*, because these organisms also possess GPL on the surface of their cell wall. However, there are few such case reports.
In this study, we investigated serum IgA antibodies against GPL core antigen in patients with PD due to NTM other than MAC.
Methods We examined the date of patients with PD due to NTM enrolled in a multicenter prospective study between December 2011 and June 2012.
Results Total 42 patients were enrolled, 36 with MAC, 4 with *M. abscessus*, 1 with *M. fortuitum*, and 1 with *M. xenopi*. As to the result of antibody, 75% of patients with MAC-PD were positive, all 4 with *M. abscessus* were positive, and all patients with other NTM were negative. There were no significant differences in clinical characteristics between patients with MAC-PD and *M. abscessus* PD. In patients with MAC-PD, there was a positive correlation between the total numbers of involved pulmonary segments and antibody levels ($r = 0.401$, $p < 0.05$). Patients with *M. abscessus* PD had an average of 9.5 involved pulmonary segment numbers (range, 7–12).
Conclusion These results suggest that patients with *M. abscessus* PD often test positive for serum IgA antibodies against GPL core antigen; and one reason may be that these patients have extensive lesions.

PS285

CLINICAL SIGNIFICANCE OF ASPERGILLUS ISOLATION FROM RESPIRATORY SAMPLES IN PATIENTS NON-TUBERCULOUS MYCOBACTERIOSIS

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Background & Aim Recent reports suggest a rising incidence of non-tuberculous mycobacteriosis (NTM) complicated with pulmonary aspergillosis, especially chronic necrotizing pulmonary aspergillosis (CNPA). This disorder is a chronic pulmonary aspergillosis that is treated with antifungal therapy in Japan. The early differential diagnosis may be difficult because both NTM and CNPA have similar symptoms and common chest computed tomography (CT) findings. In addition, a simple colonization must be also ruled out when aspergillus is isolated from respiratory samples. Interaction between NTM and antifungal drugs has been also reported. The aim of this study was to evaluate the clinical significance of aspergillus isolation from respiratory samples in patients with NTM.
Methods This study comprised 31 NTM patients in whom aspergillus was isolated from respiratory samples. The patients were admitted in our institution from January 2006 through September 2012.
Results The diagnosis of NTM complicated with CNPA was done in 9 patients (29.0%) and in all of them antifungal drugs were prescribed in addition to NTM treatment. On the other hand, NTM with aspergillus colonization was diagnosed in 22 patients (71.0%) and all of them received no antifungal drugs. Among patients with NTM and CNPA, 5 (55.6%) had cavitary lesions on chest CT, Aspergillus fumigatus was isolated in 4 (44.4%), 4 (44.4%) were positive for anti-aspergillus antibody, and all patients received the antifungal drug itraconazole.
Conclusion These results suggest that the clinical significance of aspergillus isolation from respiratory samples in patients with NTM should be defined based on the fungal pathogenicity, the host immunological status, results of laboratory examination (serum, bacterium and imaging) and the clinical response to NTM treatment and antifungal therapy.

PS286

THORACOSCOPIC SURGERY UNDER LOCAL ANESTHESIA FOR ACUTE EMPYEMA

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Aims Thoracoscopic surgery permits adequate evacuation and drainage for acute empyema. We have tried to manage the empyema by thoracoscopic surgery under local anesthesia.
Methods From April 2000, 150 patients with acute empyema underwent thoracoscopic surgery under local anesthesia. The operation was performed in lateral position, with the involved side upward. Eight or 12 mm port was located between 5th and 8th intercostal spaces. Pleural effusion was aspirated and fiberscope was introduced through the port. Fibrin net was evacuated. After lavage, drains were positioned under thoracoscopic view.
Results The average age was 74 years old (range 45 to 95). The mean operating time was 45 min (range 20 to 98). Postoperative fever subsided within 48 hours in almost all cases. The pathological development can be devided into two stages. Stage 1 is exudative ($n = 52$) and Stage 2 is fibrinoprulent ($n = 98$). The conversion rate to open thoracotomy under general anesthesia was 1.3% (two cases in Stage 2) due to the recurrence of empyema. These patients recovered after the thoracotomy with decortication. The direct complication rate was 0 %. Mortality rate is also 0%.
Conclusions Thoracoscopic surgery under local anesthesia appeared to be safe, effective and minimally invasive method.

PS287

THE IMPORTANCE OF HOST RESISTANCE FOR THE ONSET OF PNEUMONIA AMONG CEREBROVASCULAR DISORDER PATIENT IN RECOVERY STAGE

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Background and Aim of Study Post stroke pneumonia is one of the most common serious adverse conditions among cerevrovascular disorder patients. And dysphagia is an important risk factor of aspiration pneumonia. Although the onset of aspiration pneumonia is caused by disruption of balance between invasion (oral flora, aspiration) and host resistance, many studies were focused on the invasion such as dysphagia. We aimed to determine the risk factor on the host resistance for pneumonia among cerebrovascular disorder patients in four rehabilitation hospitals.
Methods Subjects were 160 cerebrovascular disorder patients who newly admitted to 4 rehabilitation hospitals. These subjects were divided into two groups based on the onset of pneumonia in the hospitals. We investigated patients' status on admission on 17 items and examined the risk factors of pneumonia by using univariate analysis and multivariate logistic regression analysis adjusted for dysphagia.
Results The incidence rate of pneumonia was 8.1% (13/160 parsons). In multiple logistic regression analysis, the onset of pneumonia was associated with conditions as follows: activity level (odds ratio [OR], 4.8; 95% confidence interval [CI], 1.3–18.4; $p < 0.05$); nutrition method (OR, 4.7; CI, 1.2–18.7; $p < 0.05$); albumin level (OR, 0.09; CI, 0.02–0.47; $p < 0.01$); medical history of cardiac disease (OR, 4.3; CI, 1.2–14.8; $p < 0.05$); respiratory disease (OR, 4.5; CI, 1.3–15.7; $p < 0.05$); and cerebrovascular disorder (OR, 3.7; CI, 1.1–12.4; $p < 0.05$).
Conclusion Our study revealed importance of the host resistance for the onset of pneumonia; and found followings as risk factor of pneumonia: recumbency, malnutrition, tube feeding, and multiple medical conditions. This result suggested that intervention to improve activity level and nutrition status can be a prevention of post stroke pneumonia.

PS288

COMPARISON OF THE CLINICAL FEATURES BETWEEN SURVIVORS AND NON-SURVIVORS IN ADMITTED NURSING AND HEALTHCARE-ASSOCIATED PNEUMONIA

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Background and Aim of Study Nursing and healthcare-associated pneumonia (NHCAP) is a new concept of the treatment strategy for pneumonia in Japan. Although several studies were reported, the efficacy or the prognostic factors are still unknown. To reveal the clinical differences between the survival and the non-survival patients, we retrospectively examined the admitted NHCAP patients.
Methods The patients who diagnosed to develop NHCAP at the admission to Tsurumi Hospital from June 2011 to August 2012 were included. We divided the patients into survivor group and non-survivor group by 30-day-mortality, and compared the clinical manifestations and the treatments. Pneumonia was diagnosed by existing of new abnormal shadow in the chest X ray or having fever or positive inflammation parameters.
Results The numbers of patients in survivor and non-survivor groups were 29 and 13, respectively. There were no significant differences in age, severity, Charlson Comorbidity Index and administrated antibiotics. Non-survivor group had significantly higher degree in performance status (survivor vs non-survivor: 3.1 ± 1.2 and 3.8 ± 0.4) and significantly lower serum albumin level (3.0 ± 0.6 and 2.6 ± 0.6, respectively).
Conclusions NHCAP patients suffer the pneumonia also with some comorbidities. This study indicated that the prognosis of NHCAP might not depend on the treatments or the severity of the pneumonia, but on the physical activities and the nutritional status of the patients.

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SALVAGE THERAPY WITH OPEN WINDOW THORACOSTOMY AND LOCAL ANTI-MICROBIAL ADMINISTRATION FOR *ASPERGILLUS* EMPYEMA

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A 76-year-old female was diagnosed as systemic sclerosis and collagen vascular diseases associated interstitial pneumonia and administration of prednisolone (10 mg/day) and mizoribine (150 mg/day) was initiated since 2009. Cavitary mass lesion was recognized in the right lower lobe of lung in August 2011, and it became larger in its size. She was undergone bronchoscopy for further examination. The culture of bronchial washing fluid of the cavitary lesion resulted in positive for *Mycobacterium avium*, *M. intracellulare*, *Aspergillus fumigatus*, and *A. terreus*. At that time, the culture result of *Aspergillus spp.* was considered as colonization, she was diagnosed with pulmonary non-tuberculosis mycobacteriosis, and administered clarithromycin 800 mg/day, rifampicin 450 mg/day and ethambutol 750 mg/day. In February 2012, she developed the right hydropneumothorax. The microbial examination revealed Gaffky number 8 on right pleural effusion and *M. avium* was cultured. The right pneumothorax and empyema was refractory to the drainage therapy, the patient received right lower lobectomy. Five months after surgery, the infiltration of right middle lobe gradually deteriorated and developed the fistula. The dead space of right thorax and pleural effusion were also increased. *A. fumigatus* was isolated from right pleural effusion and the patient was diagnosed with *Aspergillus* empyema. Intravenous micafungin (MCFG) was started. However, the disease state was unresponsive to conservative medical management, we performed the open window thoracostomy and the debridement of the focus in the parietal pleura. Additionally, local antifungal treatment with daily dressing with amphotericin B immersed gauze was started in combination with systemic MCFG administration. Antifungal treatments were continued over 3 months and the patient gradually improved. Although *Aspergillus* empyema is a rare and life-threatening infectious disease, the standard therapeutic strategy does not exist. We report an *Aspergillus* empyema case successfully treated with open window thoracostomy and systemic and local anti-microbial administrationand review the literatures.

PS290

A CASE OF DISSEMINATED *MYCOBACTERIUM AVIUM* COMPLEX (MAC) INFECTION IN A RELAPSING POLYCHONDRITIS PATIENT

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Background Relapsing polychondritis (RP) is a rare immunemediated disease which is associated with inflammation in cartilaginous tissue throughout the body. The main stay of treatment for PR is immunosuppressive agents including corticosteroids and anti-tumor necrosis factor-α (anti-TNF-α), and anti-inflammatory agents. Little is known about illness caused by nontuberculous mycobacteria (NTM) in the patients with immusosuppressive agents. We here report intractable MAC infection in the patient with RP.
Case Report A 69-year-old male with a pre-diagnosed RP was admitted to our hospital due to fever and sputum production. In the last few years, the patient had been treated with a biologic agent (adalimumab) and immunosuppressant in combination with oral or intravenous corticosteroids. Chest CT showed granular shadow and multiple nodules in both lung with mediastinum lymphadenopathy. *M. intracellurale* was isolated two times from sputum specimens and he was diagnosed pulmonary MAC. We started clarithromycin (CAM) 800 mg/day, rifampicin (RFP) 450 mg/day, and ethambutol (EB) 750 mg/day. Status of the patient was not recovered in spite of this treatment. Paravertebral and subcutaneous abscess were developed with fever and increased size of mediastinum lymphadenopathy. Since *M. intracellurale* was detected by biopsy of each abscess, disseminated MAC infection was confirmed. Antibody to HTLV-1, HIV and IFN-γ were negative. Although we discontinued biologic agent and decreased prednisolone to 5 mg/day slowly with extensive administration of anti-NTM drugs, mediastinum lymph nodes were enlarged with abscess formation. We considered it as paradoxical worsening phenomenon which sometimes seen in patients with tuberculosis. We increased prednisolone up to 10 mg/day again. After the increase of steroid, his symptoms gradually improved and the size of lymph nodes and abscesses began to reduce. CAM, RFP and EB have been currently continued and so far no exacerbation of MAC is detected. A literature review of MAC-infected cases related with anti TNF-α therapy is also present in this case report.

PS291

CLINICAL CHARACTERISTICS OF COMMUNITY-AQUIRED SPORADIC WITH LEGIONELLA PNEUMOPHILLA

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Aim of Study Legionella pneumophila has been increasingly recognized as a cause of community-acquired pneumonia and may progress rapidly without appropriate therapy. So, it is important to understand the clinical features of them. In this regard, we assessed those of sporadic community-acquired Legionella pneumonia requiring hospitalization in our hospital.
Materials and Methods We reviewed the patients who were admitted to our hospital, from 2009 to 2012 due to Legionella pneumonia. We confirmed the diagnosis of Legionella pneumonia by positive urinary antigen test for Legionella spp.
Results A total of nine cases were admitted to our hospital with laboratory-confirmed Legionella pneumonia. The median age was 73 years (range 57–87), and 8 of them were males. All patients were positive urinary antigen test for Legionella spp., three patients (33.3%) had positive culture of Legionella pneumophila from sputum. Seven patients had at least one underlying diseases (4 hypertension, 2 diabetes, 1 renal cell cancer, 1 interstitial lung pneumonia and 1 scleroderma). The following symptoms and findings were seen (9 fever elevation, 7 diarrhea, 6 productive cough). There were hepatic disorder in 6 cases, renal disorder in 6 cases, hyponatremia in 5 cases, rhabdomyolysis in 4 cases and disseminated intravascular coagulation in 3 cases. One patient showed dysarthria, dysmetria and ataxic gait, which were similar to cerebral infarction. Five cases had respiratory failure. All but one patients were treated with pazfloxacin and the other one in combination with pazfloxacin and steroid therapy. According to the pneumonia severity index, one patient was low risk, 6 patients were medium risk and 2 patients were high risk. All patients improved and none of them required mechanical ventilation.
Conclusion Clinical manifestations are unreliable in diagnosing Legionella pneumonia. We must keep it in mind that Legionella pneumophila is one of the important pathogens in community-acquired pneumonia.

PS292

PREVENTION OF A NOSOCOMIAL INFECTION CAUSED BY INFLUENZA VIRUS A USING PROPHYLACTIC ADMINISTRATION OF OSELTAMIVIR: WITH REVIEW OF LITERATURES

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Background and Aim of Study The aim of this study was to describe the effect of oseltamivir in controlling a nosocomial influenza viral infection.
Methods Intervention was carried out in the ward of the University of the Ryukyus hospital. Symptomatic staff members were sent home for 1 week, and the infected inpatients were isolated. In addition, in an episode of influenza infection among the staff members and inpatients, oseltamivir (75 mg once a day for 7 days) was administered to all staff members as well as inpatients who had close contact with the influenza patients.
Results In the hospital ward, 8 staff members (nurses and doctors) and 10 hospitalized patients were definitively diagnosed with influenza A viral infection based on results of the rapid diagnostic test. Although a relatively large number of the staff member s and inpatients had an influenza virus infection, it was possible that the use of oseltamivir efficiently prevented a nosocomial outbreak. It was very difficult to diagnose infection based on clinical symptoms. There are many reports regarding influenza prophylaxis. Although, there are few reports concerning prophylaxis of nosocomial infection before the outbreak of pandemic A H1N1, there are many articles concerning prophylactic use of neuraminidase inhibitors (NIs) in nosocomial settings after the outbreak of pandemic A H1N1. In hospital settings, all reports concluded that the prophylactic uses of NIs are effective and safe to control influenza virus nosocomial infection.
Conclusion It was possible to end outbreak immediately by using oseltamivir prophylaxis. With review of literatures, it was considered that prophylaxis with anti-influenza drugs will be recommended in hospital settings.

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CLINICAL AND RADIOLOGICAL CHARACTERISTICS OF HUMAN METAPNEUMOVIRUS PNEUMONIA IN AN OUTBREAK AT A LONG-TERM CARE FACILITY

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Background and Aim of Study Human metapneumovirus (hMPV) was discovered in 2001 as a member of the Paramyxoviridae family and accumulating data shows that hMPV is one of the most common causative agents in human respiratory tract infection. Although a lot of studies have revealed the clinical characteristics of hMPV infection in children, there are few reports focusing on that in adults. An outbreak of hMPV infection occurred at a long-term care facility for mentally handicapped patients in Okinawa, located in a subtropical region of Japan. We evaluated the clinical and radiological findings in patients with hMPV infection.
Methods RNA was extracted from nasopharyngeal swabs using a DNA/RNA elution kit and analyzed with a multiplex PCR kit (Seeplex RV15 OneStep ACE Detection, Seegene Inc, Seoul). We retrospectively evaluated the medical and nursing records of all patients in the facility during the outbreak period. The chest X-rays and CT scans were analyzed by three physicians specialized in pulmonary diseases.
Results The outbreak occurred from March 28 to April 30 in 2012 and 63 patients had symptoms such as fever, running nose, sore throat and cough. hMPV-RNA was detected in 11 out of 14 patients. Out of 63 symptomatic patients in total, 24 (38%) had pneumonia on the chest X-ray. Bilateral shadows spread radially from the bilateral hili with bronchial wall thickening was observed in most patients with pneumonia. CT scans were performed in 5 patients and segmental distributions of parenchymal abnormalities were commonly observed. Bacterial co-infection was detected in 6 patients and *Streptococcus pneumoniae* was isolated from 4 patients. Compared with patients without pneumonia, patients with pneumonia were older and had more abnormalities in the laboratory examination.
Conclusion hMPV caused pneumonia at a high rate and a bilateral bronchopneumonia pattern was a characteristic finding.

PS294

OUT-PATIENT UPPER RESPIRATORY TRACT INFECTIONS RATE IN PULMONARY MEDICINE CLINIC

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Background and Aim of Study Respiratory system was constantly attacked by multiple infectious agents. These attacks lead to infections of nose, paranasal sinuses, ear, pharynx and nasopharynx which are called upper respiratory tract infections (URTI). If coughing is prominent symptom, some of the patients with URTI apply to Pulmonary Medicine outpatient clinic. The aim of our study is to express out-patient URTI rate in our Pulmonary Medicine clinic.
Method Out-patient records of pulmonary medicine clinic were analyzed and URTI patient records were taken into account. Due to low case numbers in summer time, two summer seasons were included in our study.
Results 3288 patients were admitted to our clinic in 13 month period. Total 539 (16.4%) patient were diagnosed as URTI. URTI case numbers were 112 (20.8%) in spring (March, April, May), 102 (18.9%) in summer (June, July, August), 114 (21.2%) in fall (September, October, November) and 211 (39.1%) in winter (December, January, February).
Discussion 16.4% of the patients who admitted to our department were diagnosed with upper respiratory tract infections, and treatment was given. Because of the coughing which is the major symptom of respiratory diseases, the patients with URTI apply to Pulmonary Medicine outpatient clinic. Some of the patients with URTI who have not only coughing but also sore throat, postnasal drip and nasal congestion apply to Pulmonary Medicine clinic instead of ENT clinic. Reason of this might be patient's fear of the lower respiratory tract infections and pneumonia risk.

PS295

SAFETY AND TOLERABILITY OF TEDIZOLID PHOSPHATE, A NOVEL OXAZOLIDINONE, VERSUS LINEZOLID IN TWO PHASE III STUDIES IN SKIN/SKIN STRUCTURE INFECTIONS

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Background Tedizolid phosphate (TZP) is a novel antibiotic under clinical development in HAP/VAP (phase III). Two successfully completed, randomised, double-blind, multi-national phase III trials demonstrated the efficacy of TZP in the treatment of acute bacterial skin and skin structure infections; both studies showed TZP to be non-inferior to linezolid (LZD).[1,2] Here we compare the safety of TZP and LZD using pooled data from these trials.
Methods Patients were randomised [ESTABLISH-1 study (E1): N = 667; ESTABLISH-2 study (E2): N = 666] to receive either TZP (200 mg QD, 6 days then placebo for 4 days) or LZD (600 mg BID for 10 days) orally in E1 or intravenously with possible oral switch in E2, at the same dosage. Safety assessments included physical examinations, laboratory evaluations, ECGs, and recording of adverse events (AEs).
Results Rates of treatment-emergent AEs (TEAEs) overall were similar between TZP and LZD groups [E1+E2: 42.8% TZP vs 43.2% LZD]. However, incidence of gastrointestinal TEAEs was lower among patients treated with TZP than LZD [E1+E2: 16.0% TZP vs 23.0% LZD]. Drug-related TEAEs were also lower with TZP than LZD [E1+E2: 22.4% TZP vs 27.9% LZD]. Rates of TEAEs leading to discontinuation of study drug were similar with TZP and LZD (0.5% and 0.9%, respectively). There were no differences in physical exam findings or ECG changes. TZP had less impact on platelet counts (any measurement post-baseline through last dose of active drug) than LZD [E1+E2: below lower limit of normal (LLN): 6.4% TZP vs 12.6% LZD, P = 0.0002; substantially abnormal (<75% of LLN): 2.1% TZP vs 4.5% LZD, P = 0.0175].
Conclusions Both TZP and LZD were generally well tolerated. However, patients receiving TZP treatment had fewer gastrointestinal TEAEs, fewer drug-related TEAEs, and better haematological parameters.

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PS296

RECURRENCE OF CHRONIC PULMONARY ASPERGILLOSIS AFTER DISCONTINUATION OF ANTIFUNGAL AZOLES

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Object To assess risk factors for recurrence of chronic pulmonary aspergillosis (CPA) after discontinuation of antifungal azoles.
Method We retrospectively investigated medical records of CPA patients who stopped taking antifungal azoles after improvement of the CPA between January 2005 and June 2012. Clinical characteristics, radiological findings, blood tests and treatment regimens were checked. Recurrence of CPA was defined as the restart of antifungal drugs with worsening radiological findings.
Results Thirty patients aged 35–81 were elicited, including 22 male (73%) and 23 smokers (77%). Preceding lung diseases consisted of 21 tuberculosis sequelae (70%), 1 non-tuberculous mycobacteriosis (3%), 8 emphysema (27%), and 1 bronchiectasis (3%). Microbiological test for respiratory specimens revealed positive for Aspergillus in 14 cases (47%) and serum anti-Aspergillus antibody revealed positive in 26 cases (87%). Fungus balls were radiologically detected in 5 cases (17%). As for treatment, itraconazole was prescribed in 28 cases (93%), and voriconazole in 9 cases (30%). CPA recurred in 14 cases (47%) after discontinuation of azoles. Median progression free duration was 235 days (47–865 days). There were no differences in clinical characteristics and blood tests between recurrence group and non-recurrence group. In radiological findings, cases in the recurrence group more frequently exhibited radiological abnormalities in multiple lobes than cases in the non-recurrence group (7 cases vs. 2 cases; p = 0.03). Anti-fungal treatment duration was significantly longer in the recurrence group (963 ± 439 days vs. 622 ± 56 days; p = 0.03).
Conclusion CPA recurred in about half cases after discontinuation of antifungal treatment. Cases with longer treatment to improve and with multiple lobe involvement were high risk of CPA recurrence.

PS297

AUTOPHAGY IS A DEFENSE MECHANISM IN THE INFECTION OF LUNG EPITHELIAL CELLS FOR STREPTOCOCCUS PNEUMONIA

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Background and Aim of Study The Gram-positive pathogen Streptococcus pneumonia(Spn) has been intensely studied for almost over a hundred years, more and more studies found that autophagy is a protective mechanism for human lung epithelial cells in the infection of Spn. This study was designed to investigate the expression of Microtubule-associated protein light chain 3(LC3) in human alveolar epithelial cells A549 and the effect of Streptococcus pneumoniae and 3-Methyladenine (3 MA) on it, lay the foundation for studying on the role of autophagosome in the process of Streptococcus pneumoniae infection.
Methods Human pulmonary epithelial cells cultured in vitro and stimulated with Streptococcus pneumonia. Extract the Ribonucleic acid (RNA) of A549 cells on 12 hours and detect LC3 mRNA expression by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). The necrosis cells of control group, 3-MA group, Spn group and Spn added with 3-MA group were detected by the necrosis kit after 12 hours by Non-Radioactive cytotoxicity assay respectively.
Results The expression of LC3 mRNA stimulated of 3 MA deteced by RT-PCR was different. The necrosis test showed the blank group and 3-MA group was not significantly different, Spn group and Spn added with 3-MA group significantly different. The expression of LC3 mRNA in alveolar epithelial cells stimulated with Streptococcus pneumoniae was significantly different. The necrosis number of alveolar epithelial cells which added 3 MA was increased.
Conclusion Our results indicate that autophagy signaling pathway prevents apoptosis in type II alveolar epithelial cells infected with Streptococcus pneumoniae and may represent a molecular target for promoting cell survival during infection by respiratory pathogens.

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PS298

A STAPHYLOCOCCUS AUREUS PORE-FORMING TOXIN SUBVERTS THE ACTIVITY OF ADAM10 TO CAUSE LETHAL INFECTION IN MICE

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Staphylococcus aureus is a major cause of human disease, responsible for half a million infections and approximately 20,000 deaths per year in the United States alone. This pathogen secretes α-hemolysin, a pore-forming cytotoxin that contributes to the pathogenesis of pneumonia. α-hemolysin injures epithelial cells in vitro by interacting with its receptor, the zinc-dependent metalloprotease ADAM10. We show here that mice harboring a conditional disruption of the Adam10 gene in lung epithelium are resistant to lethal pneumonia. Investigation of the molecular mechanism of toxin-receptor function revealed that α-hemolysin upregulates ADAM10 metalloprotease activity in alveolar epithelial cells, resulting in cleavage of the adherens junction protein E-cadherin. Cleavage is associated with disruption of epithelial barrier function, contributing to the pathogenesis of lethal acute lung injury. A metalloprotease inhibitor of ADAM10 prevents E-cadherin cleavage in response to Hla; similarly, toxin-dependent E-cadherin proteolysis and barrier disruption is attenuated in ADAM10-knockout mice. Together, these data attest to the function of ADAM10 as the cellular receptor for α-hemolysin. The observation that α-hemolysin can usurp the metalloprotease activity of its receptor reveals a previously unknown mechanism of pore-forming cytotoxin action in which pathologic insults are not solely the result of irreversible membrane injury and defines ADAM10 inhibition as a strategy to attenuate α-hemolysin-induced disease.

PS299

INFLUENZA EPIDEMICS DURING 2007 AND 2013 IN OKINAWA, SUBTROPICAL REGION IN JAPAN: SURVEILLANCE OF RAPID ANTIGEN RESULTS

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Background and Aim of Study Seasonality in influenza is well known. In Japan, winter is the epidemic season. To the contrary, the epidemics of influenza occur during the summer in tropical and subtropical areas including South East Asia. This study evaluated the epidemics of influenza incidence in Okinawa, a subtropical region in Japan during 2007 and 2013, using surveillance of rapid antigen tests results.
Methods Weekly incidence and results of influenza rapid antigen test (RAT) performed in four acute care hospitals in the Naha region of the Okinawa Island during January 2007 and 2013 were anonymously collected for surveillance of regional influenza prevalence.
Results During January 2007 and May 2013, 150,709 patients were tested with RATs in the Naha region of Okinawa. 33,988 cases (22.6%) were influenza A virus antigen positive and 6,362 cases (4.2%) were influenza B virus antigen positive. Intense epidemics of influenza A were observed in February-April 2007, January-February 2009, August 2009-January 2010 (the pandemic of 2009), January 2011, January, July-August 2012, and January 2013. Two epidemic peaks were noted during the influenza pandemic of 2009. The epidemic curve during the pandemic was different from others. No epidemic occurred during 2010 summer. The epidemics of influenza from spring to early summer were mainly due to influenza B. It was noted that influenza cases were reported in every week during study period. Lower mean ambient temperature was associated with higher incidence of conventional influenza, while no significant association of ambient temperature and influenza incidence was during the pandemic of 2009.
Conclusion The epidemics of influenza in Okinawa occurred in summer as well as in winter. Influenza B was often responsible for the epidemics during spring and summer. Influenza epidemic patterns in Okinawa were apparently different from mainland Japan, which is in temperate zone.

2-B3: BRONCHOSCOPY AND INTERVENTIONAL TECHNIQUES

PS300

ROLE OF FOB IN THE DIAGNOSIS OF BRONCHIAL CARCINOMA: BANGLADESH PERSPECTIVE

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Background Bronchial carcinoma currently ranks as the leading cause of cancer related deaths in men and women. At the time they are diagnosed, the majority of lung cancers have progressed to an advanced state. So early diagnosis is essential. Fibre optic bronchoscopy (FOB) exerts its role in this regard.
Materials and Methods This observational study was carried out in the NIDCH, Mohakhali, Dhaka, Bangladesh from January to December, 2012. In this period, total 1190 Patients underwent FOB after fulfilling inclusion and exclusion criteria. Biopsy, brush and bronchoalveolar lavage (BAL) were obtained from suspected cases to confirm bronchial carcinoma.
Results 1190 patients were included in this study with a male- female ratio 9:1. More than 76% patients aged 40 years and above. Mitotic lesion was detected in 243 cases (20%). Inflammatory lesion was detected in 70% cases and remaining patients had normal or some other rare findings. Histopathology of bronchial biopsy from the mitotic lesion of 188 cases revealed that 68 patients (36%) had squamous cell carcinoma and 24 patients (13%) had adenocarcinoma. Histopathology of bronchial brushing revealed that 37 patients (12%) had squamous cell carcinoma and 76 patients (25%) had adenocarcinoma.
Conclusion Bronchoscopy is the most useful investigation in bronchial carcinoma. It can provide histological confirmation, the extent of the disease, evidence of inoperability and endobronchial site of the tumour. But newer technique like endobronchial ultrasound (EBUS), transbronchial needle aspiration (TBNA), simultaneous autofluorescence endoscopy (SAFE) should be introduced to increase further diagnostic yield, which already we have started in Bangladesh.

PS301

ENDOBRONCHIAL ULTRASOUND: AN INNOVATION IN BRONCHOSCOPY IN BANGLADESH

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Technical development in last two decades has made it possible for pulmonologists to do endobronchial ultrasound (EBUS). With EBUS miniprobe, the multilayered structure of the tracheobronchial wall can be analyzed better than any other imaging modality. Instead of fluoroscopic guided biopsy, EBUS can be used to biopsy peripheral lesions. EBUS-transbronchial needle aspiration has proved valuable for sub-carinal hilar and mediastinal lymph nodes. In National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka we have introduced EBUS for the first time in Bangladesh. So far, we have done EBUS in 107 patients and our result is as follows: Adenocarcinoma 32 (30%), Squamous cell carcinoma 27 (25%), Small cell carcinoma 9 (8%), Tuberculosis 22 (21%), Lymphoma 2 (2%), inconclusive, 15 (14%). This is very much conclusive in comparison with conventional modalities of diagnostic procedure which we used to do previously (e.g. conventional bropnchoscopy, CT-guided FNAC, etc.). Studies have shown that EBUS is cost-effective as it reduces the need for more morbid and costly invasive procedure like mediastinoscopy or thoracotomy. Prospective studies are needed in Bangladesh to see how EBUS will help in populations having lymphadenopathy in Chest X-ray, where other procedure does not give conclusive diagnosis.

PS302

AIRWAY STENTING: A NEW STEP IN BANGLADESH

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Background Self-expanding metal stents have been used successfully to overcome large airway obstruction due to malignant pulmonary disease. The technique has been modified to place stents under direct vision using the fibreoptic bronchoscope. The effect of this procedure on lung function and patient well being was investigated in three patients in NIDCH, Dhaka, Bangladesh. Stent insertion was uncomplicated.
Methods Three patients with malignant tracheobronchial tumours were treated for symptoms of life threatening airways obstruction or collapse of a lung by the insertion of an expandable metal stent(s) under local anaesthetic using a fibreoptic bronchoscope. All had inoperable cancer and histopathological diagnosis was conclusive. All patients had the stents inserted at one sitting and one patient needed the debulking of the tumour. Measurements were performed in all the patients before and after stenting and included objective measures (pulmonary function tests, arterial blood gas tensions) and non-objective measures (patient well being, performance status).
Results Overall, 100% of patients showed symptomatic improvement. Patients in whom measurements were performed all the patients showed improvement in forced expiratory volume in one second (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR) and arterial oxygen tension (PaO2). There were no perioperative complications.
Conclusions In suitable patients with either extraluminal or intraluminal tumour, or both, the insertion of expandable metal stents using a fibreoptic bronchoscope and local anaesthetic is a valuable addition to other palliative therapies in the treatment of lung cancer.

PS303

COMPARISON OF SPRAYED AND NEBULIZED TOPICAL ANESTHETIC PATIENT UNDERGOING FIBER OPTIC BRONCHOSCOPY IN ADAM MALIK GENERAL HOSPITAL

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Background Topical anesthetics can affect the procedures for implementing fiber-optic bronchoscopy (FOB). Some way can be done under local anesthesia. This study compare spray and nebul topical anesthetic in patients undergoing FOB.
Methods This study was conducted at Adam Malik Hospital involving 64 patients, 55 (85.9%) men, aged between 22 to 75 years will be done bronchoscopy. Randomly, each sample will be spray with 10% lignocaine 5–7 sprayer (n = 32) or nebulized 5 mL of 2% lidocaine (n = 32). In addition, each patient will receive 2% lignocaine through the bronchoscope into the airway during procedure under direction operator. All patients received diazepam 5 mg intramuscularly for premedication 3 hours before procedure. The amount of coughing during procedure are recorded and after procedure patients were asked to indicate the sense of discomfort in Visual Analoque Scale.
Results The procedure was performed during bronchoscopy are 100% washing and 25% brushing in spray group, and 100% washing and 31.3% brushing in nebuls group. Lignocaine dose used in both groups there is a significant difference (p = 0.002) where the average lignocaine on spray group and nebulized group are 204.38 mg and 170.94 mg respectively with 41.05 mg SD. Number of cough in the two groups was not significant (p = 0.469) where the average cough in spray group 1 (0–10) times and nebulized group 2 (0–9) times. Average VAS score in spray group 1.60 cm and 1.65 cm in nebulized group. VAS score in the two groups did not different significantly (p = 0288). Statistical result on the number of coughs and VAS score in both groups showed no differences in discomfort with p value 0.410 and 0.378.
Conclusion The effect of spray and nebulized topical anesthetic are equally to reduce patient discomfort undergoing FOB.
Keyword FOB, spray, nebuls, VAS.

PS304

A FOREIGN BODY OF THE HAIR CRAB'S SHELL IN THE BRONCHUS RETRIEVED THROUGH THE TRACHEOSTOMY: A CASE REPORT

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A foreign body of the hair crab's shell in the airway is very rare. Management of this type of foreign body is difficult and even thoracotomy might be considered. We experienced a case of a foreign body of the hair crab's shell in the bronchus retrieved through the tracheostomy. The patient was a 64-year-old man who aspirated a piece of hair crab shell accidentally when sucking the leg meat. Mild cough and throat discomfort developed immediately. He presented to our hospital the next day complaining of dyspnea in the supine position that had continued overnight. Physical examination showed inspiratory stridor of the left lung. Although the chest X-ray was normal, the chest CT scan revealed a foreign body of the hair crab's shell in the left main bronchus, which was confirmed by flexible bronchoscopy. Initially we tried to grasp the shell with alligator forceps but failed due to its slippery surface. It was only moved slightly centrally with a retrieval net and basket forceps. Therefore he underwent tracheostomy under general anesthesia to facilitate the following procedure. Since the spines on the shell had penetrated the bronchial mucosa, it was impossible to retrieve the shell using a rigid bronchoscope and forceps. Finally it was removed through the tracheostomy by nasal forceps and the rigid endoscope for endoscopic sinus surgery.

PS305

HIGH-FLOW THERAPY DURING THE BRONCHOSCOPY IN PATIENTS WITH SEVERE RESPIRATORY FAILURE

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Background High-flow therapy (HFT) attracts rising attention as a new method to supply high flow oxygen using nasal cannula. HFT can also generate the positive pressure on the respiratory tract. Purpose: To examine the safety and efficacy of HFT during the bronchoscopy without intubation for severe respiratory failure patients.
Method Three patients with severe hypoxemia underwent bronchoscopy without intubation using HFT. HFT was set as flow of 35 L/min and FiO_2 of 60–100%. During the procedure, SpO_2 was monitored continuously. Arterial-blood-gas analyses were also done at the time when the patients used reservoir mask before the bronchoscopy, and at the time of NHF before and after the bronchoscopy.
Results All patients did not show the decrease of SpO_2, during the bronchoscopy, and showed no desaturations before and after the procedure.
Conclusion HFT was safe and effective for the bronchoscopy in patients with severe respiratory failure.

PS306

INCREASED DIAGNOSIS RATES USING ULTRATHIN BRONCHOSCOPY AND THIN BRONCHOSCOPY WITH THE EBUS-GUIDE SHEATH METHOD WITH VIRTUAL BRONCHOSCOPIC NAVIGATION ASSISTANCE

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Background At our institution, we generally conduct an ultrathin (UT) (diameter 2.8 mm) bronchoscopy examination followed by a thin (diameter 4.0 mm) bronchoscopy examination using the EBUS-GS method, both with the assistance of virtual bronchoscopic navigation (VBN).
Methods From May 1, 2011, to December 31, 2012, we examined 53 cases with an abnormal lung shadow less than 30 mm in diameter with UT bronchoscopy using VBN, followed by thin bronchoscopy with the EBUS-GS method and VBN.
Results With assistance from VBN, we diagnosed 33 cases (62.3%) using UT bronchoscopy and 33 cases (62.3%) by thin bronchoscopy with EBUS-GS. Cases with a positive diagnosis were increased to 37 (69.8%) by the use of both. When limited to cancer cases, 32 (72.7%) were found positive using UT bronchoscopy and 32 (72.7%) were positive using thin bronchoscopy with EBUS-GS. The diagnosis rate was elevated to 81.8% (n = 36) by use of both methods.
Conclusion With the assistance of VBN, the diagnosis rates of UT bronchoscopy and thin bronchoscopy with EBUS-GS were not largely different. However, when both were utilized, the rate increased by 9.1% for cancer and 7.5% for all cases.

PS307

USEFULNESS AND SAFETY OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION IN OLDER PATIENTS

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Background and Aim Usefulness and safety of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) have been established recently, but no study has evaluated whether or not aging increases the risk of the procedure. In the present study, we aimed to assess the usefulness and safety of EBUS-TBNA in older patients.
Methods The medical records and database of 109 patients who received EBUS-TBNA between 2008 and 2011 at Nagoya University Hospital, Nagoya, Japan were reviewed retrospectively. All patients underwent bronchoscopy under light sedation with midazolam. A total of 34 patients were aged 70 years or older (the older group) and 75 were aged 69 years or younger (the younger group). We analyzed patients' characteristics, changes of clinical parameters, usable doses of midazolam and lidocaine, procedure duration, geographic data of biopsied lymph nodes, diagnostic yield, and complications in both groups.
Results There were more commodities in the older group. Four patients (11.8%) in the older group had poor performance status (2–3). Systolic blood pressure at baseline was significantly higher in the older group. There were no statistical differences between the two groups in some clinical parameters (minimum oxygen saturation [SpO2], reduction in SpO2, maximum oxygen supplementation, elevation of systolic blood pressure, increase in heart rate) during the procedure. Diagnostic performance in older patients was similar to that found in younger patients. There was no difference in the frequency of complications between both groups.
Conclusion Safety and usefulness of EBUS-TBNA in older patients were comparable with those in younger patients.

PS308

THE ROLE OF MEDICAL THORACOSCOPY IN COMPLICATED PARAPNEUMONIC EFFUSIONS: ITS UTILITY AT THE BEDSIDE

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Complicated parapneumonic effusions are common. Yet, their optimal management continues to be a matter of debate. Medical thoracoscopy has been playing an increasing role in the management of complicated pleural infections but its utility remained controversial. Here, we report two cases of complicated parapneumonic effusions, in which medical thoracoscopy may have found its niche. The first patient was a 32 year old male admitted to cardiology with the diagnosis of tricuspid valve infective endocarditis with tricuspid regurgitation. This was complicated by septic emboli to the lungs, spleen, right iliacus and right obturator externus muscle. On day 30 of admission, he developed a large right complicated parapneumonic pleural effusion for which initial chest tube drainage was unsuccessful. After a multidisciplinary consult with the cardiothoracic surgeon, the patient was referred to the pulmonologist for a trial of intrapleural fibrinolysis first, as his operative risk was deemed significant. He underwent medical thoracoscopy as well as intrapleural fibrinolysis. A repeat chest radiograph (CXR) on day 5 of fibrinolysis showed dramatic improvement. The second patient was a 49 year old male, premorbidly wheelchair bound, with multiple comorbidities who was admitted with a left complicated parapneumonic effusion. Two consecutive chest tubes inserted yielded poor drainage. Decision was made to proceed with medical thoracoscopy as he was deemed a high risk surgical candidate. Multiple locules and dense adhesions were noted during the procedure. These were broken down to achieve drainage and a new chest drain was inserted. A repeat CXR one month later demonstrated complete resolution of the left pleural effusion. Hence, before the jury is out with regards to the optimal management of complicated parapneumonic effusions, a multidisciplinary approach would be appropriate and we strongly believe that medical thoracoscopy has a role in the carefully selected patient.

PS309

CT GUIDE TRANSTHORACIC BIOPSY USING 18 GAUGE COAXIAL CORE NEEDLE: SOMDECH PHRA DEBARATANA MEDICAL CENTER RAMATHIBODI HOSPITAL SDMC EXPERIENCE

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Background Transthoracic needle biopsy is one of diagnostic procedure of peripheral lung lesion and pleural lesion. However the performance and complication of procedure is varied depend on lesion characteristic and operator skill.
Materials and Methods Retrospective study of patients with peripheral lung lesions underwent CT guide transthoracic biopsy. Biopsy procedure was performed using 18 gauge co-axial needle cutting biopsy under spiral scan technique with 1.0 mm collimation in department of Radiology SDMC medical center in 2012.
Results Total 46 patients who were eligible for biopsy was performed by single experienced intervention radiologist. Female were 63.6% of cases. Mean age of patient was 64.4 years. Most common chest radiographic finding was intra-pulmonary mass lesion. The locations of lung lesions were RUL (22.7%), RML (22.7%), RLL (15.9%), LUL (22.7%), and LLL (13.6%). Two cases were extra-pulmonary pleural lesions and one having multiple pulmonary nodules. The results of biopsy were adenocarcinoma (47.7%) of all biopsy procedures which most of those having lesion size more than 3 cm diameter. The remaining diagnostic results were tuberculosis (9.0%), squamous cell carcinoma (4.5%), small cell carcinoma (2.2%), poorly differentiated carcinoma (2.2%), mesothelioma (2.2%), chronic fungal infection (2.2%) and silicotic nodule (2.2%). Other non diagnostic pathological finding was chronic interstitial pneumonitis with fibrosis (13.6%). Inadequate samples were noted in 2 cases having less than 2 cm size lesion. Pneumothorax was commonly observed procedure related complication was 68% of all biopsies and 93% having mild degree of pleural air observed from imaging and did not require drainage or chest tube thoracostomy. Among patients developed pneumothorax 50 % having lesion less than 3 cm diameter.
Conclusion Co-axial needle thoracic biopsy provides acceptable diagnostic performance for peripheral lesion which mostly are malignancy. In addition, minimal pneumothorax is commonly observed after procedure.

2-C1: RESPIRATORY STRUCTURE AND FUNCTION

PS310

OUTCOME OF THE FOUR WEEK PULMONARY REHABILITATION PROGRAM AT THE UNIVERSITY OF PERPETUAL HELP DALTA MEDICAL CENTER

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Pulmonary Rehabilitation is an essential component in the management of obstructive lung disease. The recommended minimum length of a program is six weeks. However, the program in our institution has been shortened to four weeks due to logistic and practical purposes. This study aims to determine if the program provided benefit to its participants with regard to functional capacity, exercise tolerance and quality of life (QOL). Data from 19 participants, 6 with chronic obstructive lung disease and 13 with bronchial asthma were analyzed. The FEV1, 6 minute walk test and chronic respiratory questionnaire were used to measure the participants' functional capacity, exercise tolerance and QOL. These parameters were measured before starting and upon the completion of the program. Participants with COPD had an average age of 59.67 years, 5 were male and 1 female. Upon completion of the 4 week program, half had an improvement on functional capacity, two thirds had improved exercise tolerance, while five out of six felt improvement of QOL. Participants with bronchial asthma had an average age of 58.24 years, 6 were male and 7 were female. Less than half (46%) had improved exercise capacity, three-fourths were noted to have increased exercise tolerance while eight out of five (62%) showed improvement of QOL after the 4 week program. The 4 week pulmonary rehabilitation program of our institution showed modest improvement in the functional capacity, exercise tolerance and QOL of the participants. It is still to be determined if the shortened duration of the program provides significant improvement as more data are needed.

PS311

EXPIRATORY MUSCLE AND UPPER AIRWAY MUSCLE ACTIVITY DURING REVERSE SNIFF

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Background Expiratory muscle activity during reverse sniff, a maneuver akin to "blowing your nose", increases with stepwise increments in reverse sniff nasal expiratory pressure (RSNEP), and this maneuver is useful for assessment of expiratory muscle strength (ERJ P3519, 2012). In patients with neuromuscular diseases, RSNEP may be influenced not only by expiratory but also upper airway muscle activity. In fact, upper airway muscle significantly contributed to sniff nasal inspiratory pressure, a reliable maneuver for measurement of inspiratory muscle strength (ERJ P913, 2008). How do expiratory and upper airway muscles behave during reverse sniff at sitting and supine positions?
Methods In 7 healthy subjects, age 25.4 ± 4.4 years, we inserted fine wire electrodes into genioglossus (GG) and transversus abdominis (TA) muscles using high-resolution ultrasonography. RSNEP was measured through a catheter that occluded one nostril, while contralateral nostril remained open. Subjects performed short, sharp, maximum and variable intensity of reverse sniff, beginning from FRC at sitting and supine positions. GG and TA EMG activities were expressed as percent of maximum EMG ($\%EMG_{max}$).
Results Mean RSNEP at sitting and supine positions were 74.7 ± 25.5 and 76.0 ± 30.2 cmH_2O, respectively. In all subjects, both GG and TA EMG activities increased with stepwise increments in RSNEP at sitting and supine positions. There were significant linear relationships between RSNEP and EMG activity of each muscle (GG: sitting $r = 0.66–0.89$, supine $r = 0.71–0.94$, TA: sitting $r = 0.77–0.92$, supine $r = 0.66–0.96$). $\%EMG_{max}$/RSNEP (slope) of GG at supine was significantly higher than that at sitting, while in TA there was no significant difference of slope between two positions.
Conclusion We conclude that during reverse sniff, 1) both GG and TA contribute for producing RSNEP, and 2) GG activity is more influenced by posture than TA activity.
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PS312

A CASE WITH ISOLATED RIGHT HEMIDIAPHRAGMATIC RUPTURE

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Diaphragmatic rupture due to blunt thoracic trauma is a rare entity. There is no spesific symtom in these patients. We here want to present a case with diaphragmatic rupture that is seen rare after a blunt thoracic trauma. 50 year old male patient had a history of falling from a 4 meters of height three days ago. After the trauma, no surgical pathology had been found and was given analgesic treatment. He was admitted to our clinic because of no relieving of pain, in addition increasing of pain. The physical examination of the patient revealed no abnormal findings except pain in his right lumbal region on palpation. The plain roentgenogram of the patient was reported normal. As suspecting a diaphragmatic injury computed tomography was performed. Computed tomography revealed isolated right posterolateral diaphragmatic rupture. Surgery was advised to the patient. Suspecting diaphragmatic injury is the mainstay in diagnosis of diaphragmatic rupture. Progressive herniation can occur if the rupture is diagnosed late. If not treated on time, strangulation of the abdominal organs can ocur that leads to a lifetreating status. In order to prevent traumatic patients from such complications, diaphragmatic rupture should be kept in mind in trauma patients.

PS313

A RETROSPECTIVE ANALYSIS OF SIX CASES WITH PNEUMOMEDIASTINUM

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Pneumomediastinum is defined as the presence of free air in the mediastinum. Trauma plays an important role in the etiology but it may occur spontaneously. The most common syptoms are; swelling due to subcuthaneous emphysema, chest pain, dispne and hoarseness. Mostly this pathology recovers spontaneously and it rarely requires surgical intervention. Herein we aim to present 6 pneumomediastinum cases that we followed in our clinic between 2004 and 2012. The mean age of patients was 21.5 (20–24 years). The most common complaints of patients; neck pain, swelling at the neck and upper parts of the body and dispnea. None of the patients described trauma history. One patients had a history of swelling of the neck and arms a few times. Four of six patients were investigated with endoscopy and FOB and no pathology has been found. Four of patients regressed spontaneously. One patient who presented with pneumothorax and pneumomediastinum after a status epilepticus attack, was treated with chest tube. One of our patients was severly disturbed due to subcuthaneous emphysema. We placed intra venous catheters subcuthaneously to infra and supra clavicular regions, in order to purge free air. The mean hospitalization time was seven days (5–10 days). Primary spontaneous pneumomediastinum is a rare pathology. Most of the patients regress spontaneously at the first week with out the need of surgical intervention but a close follow-up is important. We think additional endoscopic screening tests will not provide a significant benefit for diagnosis and follow-up of these patients.

PS314

REEXPANSION PULMONARY EDEMA AFTER LEFT RECURRENT PNEUMOTHORAX

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Reexpansion pulmonary edema is a rare complication that occurs after reexpanding the collapsed lung by the factors such as pneumothorax, pleural effusion and atelectasis. More than 72 hours collapsed lung and rapid reexpanding are the most important risk factors. We aimed to present a case that observed in our clinic. A 20-year-old male patient presented to our clinic with left-sided chest pain 3 days after the onset. In his medical history he was treated two times for spontaneous pneumothorax last year. In his physical examination, breath sounds diminished on the left side. Chest X-ray revealed that his left upper lobe partly and lower lobe totally collapsed. Left tube thoracostomy was performed than clamped. While safety reexpansion was being performed, the patient complained from dyspnea. Oxygen saturation level was %80–85. pO2 pressure was measured as 68.8 mmHg in blood gas. Control chest X-ray revealed acute pulmonary edema on the left lung. The patient lay on the right side. The patient treated with diuretics, oxygen and fluid restriction. The symptoms began to decline after 6 hours. At 8. hour, pO2 pressure level was measured as 87.9 mmHg in the blood gas. Edema significantly regressed at 24th hour chest x-ray. VATS was performed at 3rd day of the tube thoracostomy. The patient was discharged postoperative 14th day and no complication occured. Reexpansion pulmonary edema is a rare complication with high mortality if not correctly evaluate. If the lung collapses for a long time, RPE should be considered and we should concentrate on possible findings.

PS315

A NEUROFIBROMATOSIS CASE ACCOMPAYING WITH MASSIVE CHEST WALL INVOLVEMENT

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Neurofibromatosis (von Recklinghausen disease) is a genetically-inherited disorder in which the nerve tissue grows tumors (neurofibromas). Desease is characterized with neurofibromas, cafe au lait spots and lisch nodules. We aim to present a neurofibromatosis case with massive chest wall involvement.21 year old -male patient, admitted with chest wall deformity, skin lessions, the complaint of swelling and pain in the back. The disease started in childhood with the appearance of axillary skin hyperpigmented lesion. A swelling appeared on his back in 2002 and it started to increase in size. The lesion was resected in 2004 and pathological diagnosis was neurofibroma. Physical examination: asymmetric deformity on the right side of the chest wall; Big cafe-u lait spots; Multiple spots the average diameter of 3 cm at other parts of the body. When we evaluated the Thorax CT we have seen right side of the chest wall was involved by the neurofibromas and the concomitant ribs were massively deformed. Multiple lisch nodules were detected in ophtalmic examination. No pathological findings detected on brain MRI and no significant restriction was found in pulmonary function test. The patient is in follow-upThe patient described here is a very typical case of neurofibromatosis. Multiple systematic symptoms may ocur on theese patients. As in our case, a detailed investigation is required for NF patients, because of the risk for generalized involvement of other organs. And because of malignant potential, these patients must be followed up closely.

PS316

DERMATOFIBROSARCOMA WITH BILATERAL MULTIPLE PULMONARY METASTASIS: CASE REPORT

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Dermatofibrosarcoma protuberans (DFSP) is a rare, slow groving soft tissue tumor that originated in the dermis. Pulmonary metastasis can be seen especially in fibrosarcomatous variant of DFSP. Wide surgical resection is recommended for the treatment but local recurrence rate is high. We aimed to present our dermatofibrosarcoma with bilateral multiple pulmonary metastasis case which is rarely seen. A 23-year old male patient was consulted to our clinic for bilateral pulmonary multiple nodules. In his medical history: When he was 8; a tumor was resected from his right suprascapular region and it was reported as fibrohistiocytic tumor. At the age of 22; a tumor occured on the same region and then resected again. His last histopathological result was reported as The fibrosarcomatous variant of dermatofibrosarcoma protuberans (FS-DFSP) The patient underwent to bilateral thoracotomy at different seances.12 nodules from right lung and 21 nodules from left lung were resected. All of them were reported as DFSP metastasis. The patient was discharged postoperative 7th day and no complication occured. Although DFSP is a locally agressive and low grade tumor; fibrosarcomatous variant of DFSP has high local recurrence and distant metastasis rate. Distant metastasis occurs with local recurrence. That's why cases with recurrence and fibrosarcomatous variant, should be examined more carefully for pulmonary metastasis.

PS317

EFFECTS OF POSTURAL CHANGE ON RESPIRATORY SYSTEM IMPEDANCE IN HEALTHY SUBJECTS

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Head-up postures (30–60 deg) are commonly used for respiratory care and rehabilitation to relax abdominal muscles, partly for the easy breathing in immobile patients. However, whether the ventilatory impedance is decreased during the postures are not well known. In this study, respiratory system resistance (Rrs) and reactance (Xrs) are evaluated during 4 postures from supine to upright using forced oscillation technique (FOT) in 13 healthy subjects (Age: 23.4 ± 3.5, Male = 13). Following tidal quiet breathing that included 5 stable respiratory cycles, R5, R20 (Rrs at 5 and 20 Hz), and X5 (Xrs at 5 Hz) were assessed using a commercialized FOT apparatus (MostGraph-01, Chest MI, Inc, Tokyo, Japan), in which multi-frequency pulse waves (hanning) at the interval of 0.25 sec were used to oscillate the lung. Vital capacity (VC) and inspiratory capacity (IC) were assessed using a conventional spirometry (HI-801, Chest MI, Inc, Tokyo, Japan). FOT and spirometry were performed at 4 postures, including supine (0 deg), head-up (30 deg, 60 deg), upright (90 deg) positions, in random orders. The more increased degree of head-up, the more decreased R5 and R20 (ANOVA: $p < 0.001$) and increased X5 ($p < 0.05$). R5 and R20 at 90 deg were significantly lower than those of the other 3 positions ($p < 0.01$). Although IC linearly decreased from the upright to the supine postures (ANOVA: $p < 0.001$), the changes of R5, R20, and X5 did not seem linear. We speculated that the changes in Rrs during the head-up reflect not only the lung volume but also other mechanisms such as the upper airway collapse by gravity.

PS318

USEFULNESS OF CARDIOPULMONARY EXERCISE TESTING IN EVALUATING UNEXPLAINED DYSPNEA

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Aim To evaluate the usefulness of Cardio Pulmonary Exercise Testing in evaluating patients with unexplained dyspnea.
Methods Retrospective analysis of patients undergoing CPETwith stationary cycle ergometer for unexplained dyspnea during January 2010-December 2011 at the Singapore General Hospital. Results reported by three consultants independently and consensus reached. The outcomes of the patients and significant investigations, over the next 2 year period were reviewed.
Results Out of 62 subjects who underwent CPET,32 patients with maximal exercise test were analysed. Of those 32 subjects, mean work rate was 119.22(35–210), mean Vo2 max was 22.5 ml/kg/min (9.5–37.8). 6 subjects (18%) had normal exercise tests. None had health care visits related to dyspnea over 2 years.19 subjects (59%) had cardiac limitation or deconditioning with mean Vo2 max 20.9 ml/kg/min (11.36–28.88), mean anaerobic threshold 28.58% (17–48), and mean O2/HR of 8.74(5–13).5 subjects had no cardiac evaluation.13 subjects had cardiac evaluation with two abnormal findings (one ischaemia and one heart failure). Seven subjects (22%) had deconditioning with mean Vo2 max 25.9 ml/kg/min (9.55–32), mean and Anaerobic threshold 34.5% (27–46). One subject had normal cardiac evaluation. None had health care visits related to their dyspnea over the 2 years. In our study, among those with maximal exercise testing, 2 subjects with normal study group had cardiac evaluation, 1 with cardiac limitation group had CT thorax revealing TB and 1 in the deconditioning group had coronary angiogram. The remaining 87% (28/32) either had targeted investigations pertaining to the limitation or did not undergo any investigation with 2 year stability.
Conclusion CPET is a useful tool to channel out subsequent evaluation for dyspnea in a focused manner thereby limiting the amount of investigations that have to be undergone otherwise in the outpatient setting.

2-C2: PULMONARY CIRCULATION

PS319

THE RESEARCH ON INFRARED THERMAL IMAGING DETECTING DVT PATIENTS: EFFECTIVENESS AND ACCURACY

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Purpose We intended to determine the clinical effectiveness and accuracy of infrared thermal imaging (IRTI), a novel technique for noninvasive imaging detection of vessel function, in diagnosing lower limb DVT in humans.
Methods 64 DVT patients and 64 non-DVT volunteers who had been definitely diagnosed by Doppler vascular compression ultrasonography (CUPS) or angiography enrolled in this research. We utilized IRTI sensor to detect the lower limbs of the 64 DVT patients. IRTI pictures captured were studied by qualitative pseudocolor analysis and quantitative temperature analysis in terms of mean area temperature average (Tav) and mean linear temperature (Tla) in the region of interest (ROA) as shown in IRTI. The differences in Tav and Tla between the DVT and non-DVT sides in IRTI of each patient as well as TDTav and TDTla between DVT patients and non-DVT volunteers were compared.
Results Qualitative pseudo-color of IRTI analysis revealed that the bilateral infrared presentation and distribution characteristics (PDC) were visibly asymmetry and that there were abnormally high temperature districts at the DVT side, which was assumed as positive. Out of the 64 definite DVT patients, 62 were positive in IRTI (96.88%). Of the IRTI positive cases, 53 (82.81%) had infrared PDC at coincident DVT situs and 9 case (14.52%) did at coincident DVT sides compared with the results of CPUS or angiography. There were highly statistically significant differences both between DVT side and non-DVT side in DVT group ($p < 0.01$) and between DVT group and non-DVT group ($p < 0.01$).
Conclusion IRTI can be used in detecting and screening DVT effectively and accurately.
Key Words Infrared thermal imaging (IRTI), deep venous thrombosis (DVT), detect, screen.
This work was supported by Key Laboratory of Respiratory Disease Foundation for Young Scientists of China, Key Laboratory Foundation of Jilin University and Higher Education Foundation of Guangzhou (Grant No. 2012C220).

PS320

FIVE CASES WITH OUT-OF-PROPORTION GROUP 3 PULMONARY HYPERTENSION WITH FAVORABLE HEMODYNAMIC RESPONSE TO VASODILATORS

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Background A certain subset of group 3 pulmonary hypertension (PH) patients are known to exhibit advanced, or out-of-proportion, PH. For this population, vasodilator treatment is not generally recommended because of the lack of evidence and possible deterioration of ventilation/perfusion mismatch.
Objective To investigate the efficacy and safety of vasodilator treatment in patients with out-of-proportion group 3 PH. Subjects Since 2010, we have treated 5 consecutive patients with progressive dyspnea due to such PH, using sildenafil alone (n = 3), sildenafil plus beraprost (n = 1) or sildenafil plus bosentan (n = 1). The underlying pulmonary diseases were early-onset chronic obstructive pulmonary disease (n = 1), rheumatoid arthritis-associated interstitial pneumonia (n = 1), cystic lung disease (n = 1) and combined pulmonary fibrosis and emphysema (n = 2).
Results Before treatment, all patients presented with progressive dyspnea, and demonstrated increased mean pulmonary arterial pressure (MPAP) (44 ± 7 mmHg) and pulmonary vascular resistance (PVR) (907 ± 177 dyn*s*cm^{-5}). Vasodilator treatment was well-tolerated and, at the follow-up assessment 3–4 months later, all patients noted less dyspnea and significant reduction in MPAP (34 ± 5 mmHg, –22 ± 14%) and in PVR (546 ± 191 dyn*s*cm^{-5}, –41 ± 11%). Pulmonary oxygenation was deteriorated in 1 patient, but was improved or not significantly changed in the remaining 4 patients.
Conclusions All five patients with progressive group 3 out-of-proportion PH responded favorably to vasodilators. Vasodilator therapy, particularly using sildenafil, may represent a promising option in this population when introduced in the early phase of disease.

PS321

QUANTITATIVE MEASUREMENT OF CROSS-SECTIONAL AREA OF SMALL PULMONARY VESSELS USING HIGH-RESOLUTION CT IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Background It is generally recognized that there is narrowing and diminution of the small vessels on pulmonary angiography in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Previous studies have shown that these vascular alterations could be assessed by the cross-sectional area of small pulmonary vessels (CSA) on high-resolution CT (HRCT) in patients with COPD. However, it is unknown whether there is a correlation between CSA and hemodynamics in patients with CTEPH.
Aims We retrospectively evaluated the relationship between the CSA on HRCT and hemodynamics measured by right heart catheterization (RHC).
Materials and Methods 53 patients (61 ± 12 yrs, 14 male) with proven CTEPH underwent non-enhanced 64-slice HRCT and RHC. The HRCT images with 0.5 mm section thickness and 10 mm spacing were selected from all of the CT images in each patient. Using a semiautomatic image-processing program (Image J), CSA less than 5 mm^2 and 5–10 mm^2, and total lung area were measured, and the percentage of the total CSA less than 5 mm^2 and 5–10 mm^2 for the lung area (%CSA$_{<5}$ and %CSA$_{5–10}$, respectively) were calculated. The correlations of %CSA with hemodynamics measured by RHC were evaluated.
Results Mean pulmonary arterial pressure (mPAP) and pulmonary vascular resistance (PVR) from RHC were 41 ± 10 mmHg and 8.3 ± 3.2 Wood Units, respectively. %CSA$_{<5}$ and %CSA$_{5–10}$ were 1.085 ± 0.170% and 0.443 ± 0.088%, respectively. The correlation coefficients of %CSA$_{<5}$ with mPAP and PVR were –0.46 (P < 0.001) and –0.60 (P < 0.001), respectively. The correlation coefficients of %CSA$_{5–10}$ with mPAP and PVR were –0.24 (P = 0.09) and –0.37 (P = 0.006), respectively.
Conclusions This study suggests that %CSA$_{<5}$ measured on HRCT is inversely correlated with PVR and can be used to evaluate hemodynamics in CTEPH subjects.

PS322

PULMONARY HYPERTENSION IN HEMODIALYSIS END STAGE RENAL DISEASE PATIENTS

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Background and Aim Study Cardiovascular events are the most common causes of increased morbidity and mortality in hemodialysis (HD). Recent studies abroad have reported a high incidence of pulmonary hypertension (PH) in ESRD patients with HD. The aim of this study was to evaluate the proportion and to evaluate possible predisposing factors of this phenomena in Cipto Mangunkusumo National Center General Hospital.
Methods In this Cross Sectional study, PH was screened by Doppler echocardiography in 100 patients one hour following dialysis and done by one independent operator without knowing clinical background of patients. History taking, physical examination, and secondary data from medical records including laboratory data were included.
Results Pulmonary hypertension was detected in 27 patients (27%). Of those with PH, brachial AV shunt was seen in 21 patients (77.8%) with diabetic nephrophaty as the common etiology of this group was seen in 10 patients (37%), and mean PAP was 36 ± 20.6 mmHg. Cardiac output > 5 l/min was seen in 13 patients (48.1%) with EF > 50% seen in 18 patients (66.7%). The determinant factors in this study was left ventricular diastolic dysfunction (p: 0.001; OR: 11.629; CI95%: 2.571 to 50.627).
Conclusion This study demonstrates the determinant factors regarding PH in HD patients was left ventricular diastolic dysfunction. The role of AV shunt and shunt location, anemia, high cardiac output, hypertension, ureum and creatinin level, albumin level, duration of HD, and dislipidemia as the etiology of PH in patients with ESRD did not hold in this study.
Keywords Pulmonary hypertension, ESRD, hemodialysis, Left ventricle diastolic dysfunction.

PS323

ASSOCIATION BETWEEN THE USE OF CALCIUM CHANNEL BLOCKER AND PULMONARY HYPERTENSION IN END STAGE RENAL DISEASE PATIENTS WITH HEMODIALYSIS

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Background and Aim of Study Pulmonary hypertension (PH) has been reported in hemodialysis (HD) patients. However data regarding its incidence and mechanism are scarce. Published journal abroad had been identify the risk and protective factors in this syndrome. This study evaluated the use of Calcium Channel Blocker (CCB) as a protective factor on Pulmonary Hypertension at End Stage Renal Disease (ESRD) patients with hemodialysis.
Methods A Cross Sectional study conducted on hundreds HD patients in RSCM who consumed CCB for at least a year with oral single dose, PH was screened by Doppler echocardiography one hour following dialysis. It was done by one independent operator without knowing clinical background of the patients. Bivariate analysis was done using chi square and multivariate analysis with logistic regression.
Results Out of 100 HD patients, PH was detected in 27 patients (27%). Of those with PH, brachial AV shunt was seen in 21 patients (29.2%) with diabetic nephrophaty as the common etiology of this group was seen in 10 patients (37%), and mean PAP was 36 ± 20.6 mmHg. Cardiac output > 5 l/min was seen in 13 patients (28.8%) with EF > 50% seen in 18 patients (20.7%). After adjusted with variable left ventricular diastolic dysfunction, ejection fraction, and diabetes melitus as confounders, the used of CCB is associated with lower risk of PH (p: 0.017; OR 0.258; 95% CI 0.085 to 0.783).
Conclusion This study demonstrates that the use of CCB is associated with lower risk of PH in ESRD patients with hemodialysis.
Keywords Pulmonary hypertension, ESRD, hemodialysis, the use of CCB.

PS324

A CLINICAL ANALYSIS OF 23 DEATHS CASE WITH PULMONARY THROMBOEMBOLISM

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Objective To investigate Acute pulmonary thromboembolism related factors of death and provide some reference so as to reduce pulmonary thromboembolism mortality.
Methods Conducted a retrospective study of deaths clinical date with acute pulmonary thromboembolism in the period from January 2003 to January 2012 at the General Hospital of Ningxia medical University.
Results There were 43 cases dead in 842 PTE patients hospitalized during 9 years, only 23 cases caused by PTE. The PTE inpatient mortality was 2.73%. There were 10 patients (43.5%) who were less than 60 years old, and 13 patients (56.5%). more than 60 years. Twelve patients died of PTE itself, ten subjects died of recurrent pulmonary embolism (43.5%), major bleeding caused one person to death (4.3%). It is a total of sixteen patients (69.6%) from PTE Onset to death time less than 14 days, and seven patients (30.4%). more than 14 days. There were eight patients complicated with heart disease in the 23 people, eight patients with VTE history, seven patients with the history of operation, three patients with chronic pulmonary disease, five patients with hospital acquired pneumonia. 21 patients underwent echocardiography, Seventeen subjects showed right ventricular enlargement (80.95%). Seven patients received thrombolytic therapy, while another fourteen patients received anticoagulant therapy, there were two people only received general supportive care.
Conclusion The patients who were above 60 years of age and complicating with cardiopulmonary disease at increased risk of death. Recurrent pulmonary embolism is the main reason of death in patients with PTE. Acute pulmonary embolism was at high risk of death within 14 days.

PS325

COMPARISON OF THE DIAGNOSTIC UTILITY OF MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY IN ASSESSMENT OF PULMONARY ARTERIAL HYPERTENSION

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Background and Aim of Study To evaluate the reliability on phase contrast(PC) MR imaging and CT in prediction of pulmonary hypertension (PH) in patients with suspected PH.
Subjects and Methods The study protocol was approved by the institutional review board. The subjects were forty-seven patients who had or suspected of having PH (30 male and 17 female; mean age, 69.8, 24 with interstitial pneumonia, 14 with heart failure and 9 of other diseases, including chronic pulmonary arterial thromboembolism and so on). Right heart catheterization (RHC), cardiac magnetic resonance (MR) imaging, and chest CT were performed. Mean velocity, minimum area, and maximum area of mean pulmonary artery (MPA) were measured on phase-contrast MRI (PC-MRI). On CT images MPA diameter was obtained. We also measured the volume of fibrosis and normal lung using computer-aided system. These parameters were correlated with mean pulmonary arterial pressure (mPAP) measured by RHC using Pearson's correlation analysis. The area under the receiver operating characteristic (ROC) curve were constructed to assess the predictive value of these parameters in the identification of PH.
Results Nineteen patients had PH at rest (mPAP more than 25 mmHg by RHC). CT measurement of MPA diameter ($r = 0.509$, $p < 0.01$), PC-MRI measurements of Minimum area ($r = 0.588$, $p < 0.01$) and Maximum area ($r = 0.547$, $p < 0.01$) and Mean velocity ($r = -0.426$ $p < 0.01$) of MPA had a significant correlation with mPAP. No significant correlation was seen between fibrosis volume and mPAP. In ROC analysis, the area under the curve of Minimum area was 0.797(95%CI: 0.650–0.944) for Minimum area, 0.710(95%CI: 0.553–0.868) for Mean velocity on MRI, and 0.775(95%CI: 0.626–0.923) for CT diameter of MPA.
Conclusion MRI will be useful option for diagnosis PH. CTMPA is a simple measure in the patient for suspicious PH.

PS326

A CASE OF SPONTANEOUSLY REMITTED PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH HERBAL MEDICINE

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Background and Aim of Study Pulmonary arterial hypertension (PAH) associated with drugs is a well-recognized subgroup. At the 2008 WHO meeting in Dana Point, updates were made to reflect the strength of these associations as definite (aminorex, et al.), possible (cocaine, et al.), likely (amphetamine, et al.) and unlikely (oral contraceptives, estrogen). Other than these candidates may cause drugs-associated PAH.
Methods A 38-year-old woman took the herbal medicine "bofutsushosan" for two weeks then stopped taking it due to general malaise and exertional dyspnea. The cause of exertional dyspnea was seeked to find.
Results After discontinuation of bofutsushosan, dyspnea continued for three months and echocardiography revealed tricuspid regurgitation pressure gradient of 40 mmHg, suspecting the existence of PH. A chest roentgenogram showed prominent hilar pulmonary artery with CTR of 51.5%. 6MWD was 486 m with lowest oxygen saturation of 89%. The perfusion scans were normal and contrast CT scans did not show pulmonary embolism. Right heart catheterization revealed elevated PAP of 64/21 with mPAP of 41, pulmonary capillary wedge pressure of 9, and a CI of 4.67, resulting in calculated PVR of 326. She was treated with oxygen and diet therapies. Her dyspnea on exertion gradually disappeared after discharge, and 8 months later she did not need oxygen. Her BNP was normalized and a chest roentgenogram revealed an improved cardiac enlargement. She was admitted to our hospital for revaluation 18 months after first catheterization. Right heart catheterization revealed normal PAP of 26/8 (15) mmHg, CI of 3.70 and PVR of 102.
Conclusion This is the first report of spontaneously remitted PAH induced by herbal medicine. This report may provide clinicians the important information that early suspicion and recognition of pulmonary hypertension are needed for the patients with exertional dyspnea, who took herbal medicine, to avoid further deterioration.

PS327

UNEVENNESS OF PERFUSION IN THE REGIONAL AND TEMPORAL LUNG DETERMINES CHANGES IN MEAN PULMONARY ARTERIAL PRESSURE

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Pulmonary arterial hypertension (PAH) has become an important topic for basic and clinical research in recent years. Morphologic research has shown that specific PAH-lesions are located in the small arteries of the lobule and correlate with hemodynamic measurements. However, it still remains to be shown how pathological changes of the small arteries in the lobule develop into PAH. Based on both the fractal properties of the pulmonary arterial tree and asynchronous phasic contractions of the lobular arterial muscles under the evenness of pulmonary capillary pressure (PCP) in the lung, we have constructed an integrated model of pulmonary circulation that demonstrates a mathematical relationship between mean pulmonary arterial pressure (MPAP) and cardiac output (CO). Using the relationship between MPAP and CO, we have been able to explain the pathogenesis of pulmonary hypertension (PH) in terms of statistical changes between regional and temporal perfusion in the lung. In order to clinically detect the early stages of PH, we have suggested that it is important to establish pulmonary functional imaging of regional and temporal perfusion.

PS328

A DNA MICROSATELLITE ASSOCIATION STUDY AND ASSOCIATION OF TIMP3 GENE POLYMORPHISM IN JAPANESE PATIENTS WITH HIGH ALTITUDE PULMONARY EDEMA

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Background and Aim of Study High altitude pulmonary edema (HAPE) is a non-cardiogenic life-threatening pulmonary edema that characterized by exaggerated hypoxic pulmonary hypertension. The pathogenesis remains to be conclusively elucidated and genetic polymorphisms are highly proposed to be associated with HAPE. The aim of this study is attempt to identify the candidate human genes those might associate with the development of HAPE.
Methods The case group included 53 Japanese HAPE susceptible subjects who had developed HAPE during climbing mountains higher than 2,500 m. The control group enrolled 67 Japanese HAPE resistant subjects who were elite alpinist and did not develop HAPE during their histories. A case-control association study was performed using 400 polymorphic microsatellite markers by PCR and sequenced by Gene Scan software.
Results Nine markers showed statistically significant associations with the susceptibility to HAPE, and three markers showed significant associations with the resistance to HAPE. We also evaluated the association of HAPE with six single nucleotide polymorphisms (SNPs) in inhibitor of metalloproteinase 3 (*TIMP3*) gene that included a resistance microsatellite marker (D22S280). One of six SNPs in *TIMP3* gene (*rs130293*) was significantly associated with the HAPE susceptibility ($P < 0.0005$).
Conclusion This is the first genomewide association study in HAPE. It revealed several candidate genes in associations with HAPE. Our findings also elucidated that the polymorphism of *TIMP3* gene was significantly associated with the susceptibility to HAPE. This study provides the first evidence that the development of HAPE may be determined by the interaction of multiply genes and TIMP3 may influence the risk for HAPE.

2-C3: CLINICAL ALLERGY & IMMUNOLOGY

PS329

DRUG RASH WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) SYNDROME WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) TRIGGERED BY ANTI-TUBERCULOSIS (ANTI-TB) DRUGS

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We report here a case of a previously healthy 16-year old girl was treated with anti-TB drug combination (Isoniazid, Rifampicin, Pyrazinamide, Ethambutol) for TB adenitis and noted resolution. However, 40 days after drug intake, flu-like symptoms, pruritic erythematous maculopapular rashes, and eventually dyspnea developed. Vital signs were stable but patient was febrile at 40C. She had multiple erythematous to hyperpigmented macules and confluent patches over the face, trunk and extremities; dryness and slight scaling on the lips, but no conjunctivitis. She had anicteric sclera, supple neck, multiple cervical lymphadenopathies and bibasal crackles. There was eosinophilia and transaminitis. Peripheral blood smear showed leukocytosis without atypical lymphocytosis. Antinuclear antibody (ANA) was negative. Arterial blood gasses revealed uncompensated respiratory alkalosis with moderate hypoxemia. PaO2/FIO2 ratios were less than 200 consistent with ARDS.
Discussion Our patient was diagnosed as a definite case (final score 7) of DRESS syndrome based on the postulated scoring system by Kardaun et al. Clinical features were typical – fever more than 38.5C, lymphadenopathy, eosinophila more than 1,500/uL, skin rash more than 50% suggesting DRESS, biopsy suggesting DRESS, and visceral involvement (lungs and liver). Significant improvement of skin lesions was noted after intravenous hydrocortisone, antimicrobials, and antihistamines were given. However, fever persisted, desaturations and hypotension ensued. Diffuse bilateral lung infiltrates progressed. Patient died. To our knowledge, because of its rarity (incidence of 1 in 1,000 and 1 in 10,000 exposures), this represents the first reported case of DRESS syndrome due to anti-TB drugs in the Philippines. Overall mortality in DRESS syndrome is 10%.
Conclusion General awareness and pharmacovigilance are important due to the severity and life-threatening potential of this type of drug reaction. We proposed an algorithm in the diagnosis and management of DRESS.

PS330

TIOTROPIUM DECREASES THE RISK OF EXACERBATIONS IN PATIENTS WITH SYMPTOMATIC ASTHMA REGARDLESS OF BASELINE CHARACTERISTICS

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Background and Aim of Study The addition of tiotropium provides bronchodilation and reduces exacerbations in patients with severe asthma (Kerstjens et al. NEJM 2012;367:1198–207). Subgroup analyses were performed to determine whether this positive effect was limited to definable subgroups of patients.
Methods Eligible patients had a ≥5-year history of asthma, and had experienced ≥1 exacerbation in the previous year. Time to first severe exacerbation from the pooled data after 48 weeks was a primary end point. Secondary end points included time to first episode of asthma worsening. Subgroup analyses of time to first severe exacerbation were performed in groups defined by baseline characteristics, including age, allergic status, smoking status and reversibility.
Results 912 patients were randomised: 456 received 5 μg tiotropium via the Respimat® Soft Mist™ Inhaler and 456 received placebo once daily for 48 weeks. In the total study group, the time to first severe exacerbation was increased by the addition of tiotropium (risk reduction 21%; hazard ratio 0.79; $p = 0.03$). The time to first episode of asthma worsening was increased in the tiotropium group compared with placebo (risk reduction 31%; hazard ratio 0.69; $p < 0.001$). Subgroup analyses showed that neither the time to first severe exacerbation nor the time to first episode of asthma worsening was dependent on baseline characteristics (no significant interactions).
Conclusions The increase in time to first severe exacerbation and first episode of asthma worsening found with the addition of tiotropium was not limited to specific subgroups of patients, including some characteristics that are usually found in patients with chronic obstructive pulmonary disease, such as former smoking, non-allergic status or minimal reversibility. Tiotropium seems effective across a broad spectrum of patients with severe persistent asthma who remain symptomatic and experience exacerbations despite the combination use of moderate- to high-dose inhaled corticosteroids plus long-acting beta agonists.

PS331

ELEVATED TRYPTASE LEVEL IN BRONCHOALVEOLAR LAVAGE FLUID FROM PATIENTS WITH CHRONIC EOSINOPHILIC PNEUMONIA

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Background Chronic eosinophilic pneumonia (CEP) generally responds to steroid therapy. However, relapse frequently occurs and prolonged steroid therapy is needed in such cases. Mast cells play an important role in allergic diseases and interstitial lung diseases. Tryptase released from activated mast cells is associated with intractable pathogenesis. Little is known of the clinical significance on measurement of mast cell tryptase in bronchoalveolar lavage fluid (BALF) from patients with eosinophilic pneumonia.
Methods The BALF from 16 patients with eosinophilic pneumonia [CEP 8 patients, Acute eosinophilic pneumonia (AEP) 4 patients, Drug-induced eosiophilic pneumonia (Drug) 4 patients] was analyzed by B12 a monoclonal antibody-based tryptase immunofluoroassay, which can detect both monomer (inactive from) and tetramer (active form) of both α and β tryptases. The relationship between clinical characteristics and tryptase in BALF was analyzed retrospectively.
Results Tryptase in BALF could be detected in 7 patients (CEP 6, AEP 1; the tryptase-positive group), but not in 9 patients (CEP 2, AEP 3, Drug 4). The concentrations of tryptase in the tryptase-positive group were 2.45 ± 0.46 ng/ml in CEP ($n = 6$, Mean ± SD) and 1.0 ng/ml in AEP ($n = 1$). The tryptase concentration was significantly higher in CEP than in AEP and Drug ($p < 0.05$). Recurrence of eosinophilic pneumonia was seen in 7 patients with CEP, but not AEP and Drug. Six patients with CEP had asthma history. Of them, one patient had allergic bronchopulmonary aspergillosis and another one had chronic eosinophilic sinusitis.
Conclusion Tryptase in BALF can be detected in patients with CEP. The tryptase-positive patients with CEP tended to relapse and have complication of asthma. Mast cell tryptase may be associated with intractable pathogenesis in CEP. This work was supported in part by grant No. 22590844 from the Japanese Ministry of Education, Science and Culture.

PS332

DECREASES IN REGULATORY T CELLS AND INCREASES IN ACTIVATED B CELLS FRACTIONS IN PATIENTS WITH ACTIVE EOSINOPHILIC GRANULOMATOSIS AND POLYANGIITIS

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Introduction Eosinophilic granulomatosis with polyangiitis (EGPA; also known as Churg-Strauss syndrome), a rare disease characterized by the presence of allergic granulomatosis and necrotizing vasculitis, is often effectively treated with corticosteroids. However, relapse rates are high and, for unknown reasons, some EGPA patients suffer frequent relapses after entry into initial remission. Regulatory T (Treg) cells and B cells are implicated in the development and progression of EGPA. We explored the influence of Treg cells and a co-stimulatory factor present on B cells on the development and course of EGPA.
Methods We studied 45 EGPA patients (19 of whom experienced frequent relapses and 26 of whom seldom relapsed) and 67 (control) patients with general asthma. We determined the counts or percentages of whole-blood cells exhibiting the following characteristics: $FOXP3^+$ cells among $CD4^+$ Treg cells; $CTLA\text{-}4^+$ cells among $CD4^+/CD25^+$ Treg cells; and $CD27^+$, $CD80^+$, $CD86^+$, or $CD95^+$ cells among $CD19^+$ B cells. We also measured serum IgG concentrations.
Results Compared with patients with asthma or seldom-relapsing EGPA, frequently relapsing EGPA patients with active disease exhibited decreased counts of Treg cells and increased percentages of B cells that scored as $CD80^+$, $CD27^+$, or $CD95^+$. Patients with frequently relapsing EGPA had increased percentages of $CD27^+$ and $CD95^+$ B cells, and fewer $CD19^+$ B cells, than did patients in the other two groups. Lower $CD19^+$ B cell counts were associated with reduced Treg cell counts and a lower serum IgG concentration.
Conclusion In patients with frequently relapsing EGPA, decreases in Treg cell numbers and increased percentages of activated B cells may induce apoptosis of B cells.

PS333

CLINICAL FEATURES OF ADULT PATIENTS WITH PNEUMOCYSTIS PNEUMONIA DURING THE TREATMENT FOR RHEUMATOID ARTHRITIS IN OUR HOSPITALS

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Aim of Study We indicated clinical features of Pneumocystis Pneumonia (PCP) that developed during the treatment for Rheumatoid Arthritis (RA) in our hospital.
Materials and Methods We reviewed retrospectively the patients who were admitted to our hospital, from 2002 to 2013 due to PCP. We confirmed the diagnosis of PCP by detection of Pneumocystis jirovecii by Grocott stain in respiratory specimens, detection of Pneumocystis jirovecii by PCR in respiratory specimens and pneumonia caused by other pathogens was excluded.
Results A total of 10 cases were admitted to our hospital with laboratory-confirmed PCP during the treatment for RA. Our patients consisted of 4 males and 6 females with a median age of 74.1 years (range; 61 to 81 years). All patients were receiving corticosteroid therapy or immunosuppressant therapy. There were no patients receiving Trimethoprim-Sulfamethoxazole (TMP-SMX) for PCP prophylaxis. Nine patients was elevated plasma β-D glucan level on admission, but one patient was normal range. Three patients died with respiratory failure. There were no significant differences between survivors and non-survivors at the time of admission to our hospitals. Non-survivors showed rapid progression, and their periods from the admission to the death were in the range of 6 to 15 days.
Conclusions RA patients treated with corticosteroid or immunosuppressant should receive TMP-SMX for PCP prophylaxis. We should always keep in mind the development of PCP during the treatment for Rheumatoid Arthritis in our hospitals.

PS334

EFFECTS OF RAPAMYCIN ON PULMONARY VASCULAR REMODELING OF ALLERGIC VASCULITIS IN MURINE MODEL

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Background We reported allergic granulomatous vasculitis with eosinophil infiltration in an asthma model of C57BL/6 sensitized with ovalbumin <OVA>. TGF-β is thought to play an important role in fibroblasts proliferation and is critical to vascular remodeling in vasculitis. Rapamycin inhibits vascular endothelial cells proliferation and canalization.
Objectives To elucidate the role of in vascular remodeling of allergic granulomatous vasculitis, we examined the effects of Rapamycin on the vasculitis of the murine model.
Methods C57BL/6 mice <6–8 weeks> were sensitized with ovalbumin OVA and alum. The positive controls <n = 5> were exposed to aerosolized OVA daily for 7 days. The other group of mice <Rapamycin treated mice <n = 5>> were administered with Rapamycin <0.5 mg/kg intraperitoneal administration> in parallel with daily exposure to aerosolized OVA for 7 days. On 7th day, bronchoalveolar lavage <BAL> was performed and the lungs were excised for pathological analysis. Cytokines in BALF were measured.
Results While there was no significant difference of total cell number in BAL fluids between the control and the Rapamycin treated group, the ratio of eosinophils reduced significantly in the Rapamycin treated group. <mean: control group 83.2% vs Rapamycin group 70.3%> The concentrations of TGF-β in BAL fluids reduced significantly in the Rapamycin treated group. The pathological scores reduced significantly in the Rapamycin treated group compared to the control group. Intra luminal infiltration and proliferation of MIB1 positive myofibroblasts and α-SMA positive cells in pulmonary arteries were reduced dramatically in the Rapamycin treated group compared to the control group.
Conclusion Rapamycin suppressed pulmonary vascular remodeling in a murine model of allergic vasculitis with eosinophil infiltration.

PS335

IDENTIFICATION OF A MECHANISM FOR LUNG INFLAMMATION CAUSED BY *MYCOPLASMA PNEUMONIAE* USING A NOVEL MOUSE MODEL

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Background Human *Mycoplasma pneumoniae* (MP) pneumonia is characterized by alveolar infiltration withneutrophils and lymphocytes and lymphocyte/plasma cell infiltrates in the peri-bronchovascular area(PBVA). No mouse model has been able to mimic the pathological features seen in humanMP pneumonia, such as plasma cell-rich lymphocytic infiltration in PBVA.
Material and Methods To figure out the mechanism for inflammation by MP infection using a novel mouse model that mimics human MP pneumonia, mice were pre-immunized intraperitoneally with Th2 stimulating adjuvant, alum, alone or MP extracts withan alum, followed by intratracheal challenge with MP extracts.
Results The toll-like receptor-2, which is the major receptor for mycoplasma cell wall lipoproteins, was strongly up-regulated in alveolar macrophages in a latter group after the pre-immunization but prior to the intratracheal challenge.
Conclusion Acceleration of innate immunity by antecedent antigenic stimulation can bean important positive-feedback mechanism via alveolar macrophages in lung inflammation during MP pneumonia.

2-D1: COPD 6

PS336

EVALUATION OF RESPIRATORY REACTANCE AFTER INHALATION OF INDACATEROL IN COPD PATIENTS

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Background and Aim of Study Bronchodilators such as beta2-agonists and anticholinergics are central to symptom management in COPD. Indacaterol is a novel, once-daily, inhaled long-acting beta2-agonist currently in development for the treatment of COPD. The improvement in forced expiratory volume in 1 second was seen as early as 5 min after inhalation of indacaterol. But the immediate effet of indacaterol on bronchodilation of patients with COPD is not fully understood. The forced oscillation technique (FOT) can determine respiratory system impedance, which consists of respiratory resistance (Rrs) and reactance (Xrs), and is measured over a wide range of frequencies during tidal breathing. We examined the immediate effect of indacaterol on COPD patients using FOT.
Methods Mild to severe untreated COPD patients (n = 16) were recruited at Yamagata university Hospital (Yamagata, Japan). Rrs and Xrs were determined at 5 min prior to inhalation of indacaterol and at 2, 5, 10, 20, 40 and 60 min after inhalation using Mostgraph-01 (Chest MI, Inc, Tokyo, Japan).
Results The value of Xrs at 5 Hz (Xrs5) and the difference between the maximal and minimal values of Xrs5 significantly increased at 2, 5, 40 and 60 min after inhalation compared with those of pre inhalation. The values of resonance frequency and area low Xrs significantly decreased at 2, 5, 40 and 60 min after inhalation compared with those of pre inhalation.
Conclusion The Inhalation of indacaterol improved Xrs for two phases (2–5 min and 40–60 min after inhalation) in untreated COPD patients.

PS337

LONG-TERM EFFECT OF HOME-VISITING NURSING ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)- 3-YEAR FOLLOW-UP SURVEY OF VISITING NURSING PROGRAMS –

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Background and Aim of Study Chronic obstructive pulmonary disease (COPD) is characterised by progressive airflow obstruction, worsening exercise performance and health deterioration. This study aimed to evaluate the long-term effectiveness of visiting nursing programs for COPD patients on following factors: improving lung function, exercise tolerance, health related quality of life (HRQL) of patient, and activities of daily living (ADL).
Methods 126 persons with respiratory diseases were received visiting nursing program between 2004 and 2012. Among these, we obtained data on 3-year follow-up date from 22 persons with COPD. We included interventions involving an outreach nurse visiting patients in their homes, providing support, education, and monitoring health. We analyzed long-term changes on following: Body Mass Index (BMI); lung function (VC, %VC, FEV1.0, FEV1.0%, %FEV1.0); 6 minutes walking distance (6MWD); HRQL (CRQ; Chronic Respiratory Disease Questionnaire, SF-36; MOS 36-Item Short-Form Health Survey); and the Nagasaki University Respiratory ADL questionnaire (NRADL). Wilcoxon signed-rank test was applied for statistical analysis.
Results There were no significant differences in BMI, lung function, 6MWD, CRQ, and SF-36 (RP, BP, GH, VT, SF, MH) when compared with initial and final stages. On the other hand following three factors showed significant differences; SF-36 (PF) (MD 7.15,95%CI [3.69 to 10.60], $p < 0.01$), SF-36 (RE) (MD –5.04, 95%CI [–9.99 to –0.09], $p = 0.04$), and NRADL (MD 0.54, 95%CI [2.23 to 15.13], $p = 0.01$).
Conclusion This study showed long-term effect of visiting nursing on physical function and CRQ with COPD patients, although COPD is characterized by progressive airflow obstruction, worsening exercise performance and health deterioration. This study showed the usefulness of visiting nursing on COPD with these results. This study showed the needs of evidence with large randomized clinical trial, and longer period of the research.

PS338

PREDICTORS OF PHASE III SLOPE OF NITROGEN SINGLE-BREATH WASHOUT IN COPD

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Background and Aim of Study The nitrogen (N2) single-breath washout (SBW) test is a measure of ventilation distribution inhomogeneity and also a small airway function that offers complementary information to spirometry; however, the relevance to the forced oscillation technique (FOT) and pulmonary emphysema in COPD is not fully understood. We hypothesized that pulmonary functions, forced oscillatory parameters, and emphysema extent would contribute independently to the results of the SBW test. In this cross-sectional study we assessed the relationship between the phase III slope (delta N2) derived from N2 SBW and these parameters.
Methods Spirometry, lung volumes, N2 SBW, and the broadband frequency FOT using MostGraph-01 were performed in 56 patients with stable COPD. We used respiratory system resistance at 5 Hz, resonant frequency, and the difference between inspiratory and expiratory respiratory system reactance at 5 Hz as the expiratory flow limitation (EFL) index. Emphysema extent was measured by high-resolution computed tomography and scored.
Results The median (range) value of FEV1 was 52.6 (17.8–108.0) % predicted; forced vital capacity, 81.4 (34.9–144.0) % predicted; delta N2, 4.36 (1.68–13.71) %N2/L; respiratory resistance at 5 Hz, 4.02 (1.83–7.64) cmH_2O/L/s; resonant frequency, 10.87 (4.46–27.07) Hz; EFL index, 0.63 (–0.47–5.25) cmH_2O/L/s; and emphysema score, 10 (0–23). In multiple regression analyses, the delta N2 was independently predicted by forced vital capacity, resonant frequency, and emphysema score ($R2 = 0.57$, $p < 0.0001$).
Conclusion The degree of ventilation inhomogeneity derived from N2 SBW is independently predicted by spirometry, lung mechanics, and the degree of emphysema.

PS339

INDICATOR OF ARTERIOSCLEROSIS IN PATIENTS WITH COPD

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Background Cardiovascular events are an important part of the comorbidities and complications in COPD patients. Analyzing the data of the ratio of serum Eicosapentaenoic Acid to Arachidonic Acid: EPA/AA and Ankle Brachial Pressure Index: ABI, which were useful as an indicator of arteriosclerosis, we examined the correlation between them in this study.
Methods A total of 149 subjects, male 84, female 65, were enrolled into the study after informed consents were obtained until January 2013 from May 2007 in Erimo town clinic in Hokkaido. We divided potential subjects into three groups: Group 1a had a history of COPD and sever exposure to tobacco smoke; Brinkman Index more than 800, Group 1b had a history of COPD and the other exposure history, Brinkman Index less than 800, and Group 2 had a history of other diseases without COPD, such as diabetes, hypertension, and hyperlipidemia.
Results G1a was 38 subjects, male 28, female 10, G1b was 35 subjects, male 19, female 16, and G2 was 76 subjects, male 37, female 39, respectively. ABI in G1a: G1b: G2 0.81 ± 0.48: 0.83 ± 0.24, 0.91 ± 0.21, EPA/AA in G1a: G1b: G2 0.41 ± 0.13: 0.42 ± 0.11: 0.47 ± 0.16. G1a demonstrated significant decline in ABI and EPA/AA, when compared with G2. However there was no significant difference in the data between G1b and G2.
Conclusion In COPD patients with severe exposure to smoke, significant decline in ABI and EPA/AA was observed. The results indicate that these patients have an increased risk of smoke-related cardiovascular diseases such as acute myocardial infarction and stroke.

PS340

REGIONAL AND SEASONAL CHARACTERISTICS OF COPD EXACERBATIONS AT ONE UNIVERSITY HOSPITAL IN INCHEON

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Exacerbations are a prominent feature of the natural history of Chronic obstructive pulmonary disease(COPD). Quality of life is known associated with exacerbation. Patients with severe respiroatory distress, mortality is poor. This data and statistical analysis is still unknown to us in Korea. There is the Namdong Industrial Complex in Incheon. In April, Asian dust comes from china and Mongolia. Incheon is located near by this area. So Patients in Incheon may affect this season. We studied characterictics about seasonal and regional distribution of COPD exacerbations. Patients who met the current consensus of COPD definition were enrolled from January 2001 to December 2011 in Gachon University Gil Medical Center in Inchon, Korea. Retrospectively, we analyzed the clinical characteristics, pulmonary function test, cause of exacerbation, regional and seanal distribution. COPD has been divided mild (12.5%), moderate (40%), severe (34.3%) and very severe (13.2%) by the Global Initiative for Chronic Obstructive Lung Disease(GOLD). Male were 82.9%. Mean age was 73.1 years. Cause of exacerbation is pneumonia (55%), upper airway infection (17%), pneumothorax (4%), heart failure (1.5%) and lung cancer(1.3%). There is no regional distribution of COPD exacerbation in Incheon. COPD exacerbation have two peak in April(10.3%) and December(10.8%). 2.7% patients of exacerbation have experienced two or more per year. In conclusion, COPD exacerbation have two peak in April and December. There is no regional distribution of COPD exacerbation in Incheon. Pneumonia is main cause of COPD exacerbation.

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RELATION BETWEEN SERUM LDH AND EXERCISE CAPACITY IN COPD PATIENTS

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Introduction Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease caused by smoking in which pathogenesis remains unclear. Although chronic inflammatory response from COPD affects lungs with significant systemic consequences, there has been few studies about the correlation between clinically useful inflammatory biomarker and exercise capacity. This study was designed to find the relationship amongst pulmonary function test, inflammatory biomarkers such as lactate dehydrogenase (LDH) and blood urea nitrogen (BUN), and patients' exercise capacity.
Subjects and Method From March 2009 to December 2010, 33 patients with COPD recorded daily number of steps for 4 weeks with the pedometer. The patients who recorded daily number of steps for more than 2 weeks were enrolled and data from 3 patients were excluded due to inadequate recordings. Obtained data were analyzed dividing dates into 1) 14-day average, 2) weekdays, and 3) weekends and the correlation of the number of steps with serum LDH & BUN level were evaluated.
Results There was no correlation between exercise capacity of patients with COPD and serum LDH, BUN levels. Correlation was not found between serum LDH level and the average number of steps for 14 days ($p = 0.640$), the average number of steps on weekdays ($p = 0.393$), and the average number of steps on weekends ($p = 0.107$). There was also no correlation between serum BUN level and the average number of steps for 14 days ($p = 0.057$), the average number of steps on weekdays ($p = 0.060$), and the average number of steps on weekends ($p = 0.097$). No correlation was found between the exercise capacity measured by the pedometer and FEV1 either.
Conclusion There was no correlation amongst preexisting pulmonary function test markers, inflammatory biomarkers such as LDH & BUN and exercise capacity in COPD patients.

PS342

THE RELATIONSHIPS BETWEEN TRACHEAL INDEX AND LUNG VOLUME PARAMETERS IN MILD-TO-MODERATE COPD

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Background The morphological change related to chronic obstructive pulmonary disease (COPD) occurs from mild stage of COPD. Although overinflated lung in COPD is known to be related to morphological tracheal deformity, relationship between morphological change of trachea and lung volume parameters in mild-to-moderate stage of COPD has yet not been determined. Thus, our aim was to investigate the association of tracheal index (TI) with lung function parameters including those related to lung volume in COPD patients with mild-to-moderate airflow limitation.
Materials and Methods A retrospective study was conducted with 193 mild-to-moderate airflow limitation patients and 193 subjects with normal lung function as control group. Two independent observers measured TI at three different anatomic levels on chest radiographs and CT.
Results Compared with the control group, TI was significantly reduced, and saber-sheath trachea was more frequently observed in COPD patients with mild-to-moderate airflow limitation at all three different trachea levels. TI had apparent inverse correlations with total lung capacity, functional residual capacity, and residual volume, which were particularly notable in TI measured at the upper margin of the aortic arch on chest CT. Even after adjustments of covariates, this association persisted.
Conclusions TI is reduced even in mild-to-moderate COPD patients, and TI measured on chest CT shows significant inverse relationships with all lung volume parameters, suggesting that tracheal morphology might change from early stages of COPD.

PS343

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH COPD EXACERBATION IN SOUTH KOREA

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Background Exacerbations of chronic obstructive pulmonary disease (COPD) have been associated with decline in health status. A study was performed to investigate the demographic and clinical characteristics of patients with COPD exacerbations in South Korea.
Methods A South Korean multicenter, observational study was performed, with a retrospective and prospective phase for 1 year each, in patients with COPD diagnosed by 2010 global initiatives for chronic obstructive lung disease (GOLD) criteria. We investigated demographic characteristics, all COPD exacerbations defined as events that require treatments with systemic corticosteroid and/or antibiotics (moderate) or hospitalization (severe), lung function via spirometric values, comorbidities and COPD assessment test (CAT) score.
Results Among the 790 patients who completed the study, there were 401 patients (51%) with exacerbations of COPD for two years. The mean age, smoking history, and phenotype distributions were similar between exacerbators and non-exacerbators. However, body mass index (BMI) ($p = 0.0164$) and post bronchodilator forced volume in one second (FEV1) ($p < 0.0001$) were lower in exacerbators than in non-exacerbators. The mean CAT score ($p < 0.0001$) was higher in exacerbators (18.2(±8.1)) than in non-exacerbators (14.4(±7.6)). Likewise, the number of comorbidities ($p = 0.002$) was higher in exacerbators (327 cases) than in non-exacerbators (281 cases). The history of COPD ($p = 0.0061$) of exacerbators was longer than non-exacerbators.
Conclusions This study found that a higher number of comorbidities and a higher mean CAT score are significantly associated with a higher rate of COPD exacerbations in South Korean COPD patients. Interestingly, this study showed that the BMI of exacerbators was lower than that of non-exacerbators.

2-D2: COPD 7

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ADDITIVE ANTI-INFLAMMATORY EFFECT OF ROFLUMILAST WITH LONG ACTING BETA-AGONIST (LABA) IN THE TREATMENT OF MODERATE TO SEVERE COPD: A META-ANALYSIS

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Background Airflow obstruction in COPD is caused by chronic inflammation and permanent structural changes in the smaller airways and lung parenchyma. Current studies on anti-inflammatory treatments for COPD have focused on targeted inhibition of phosphodiesterase 4, the major enzyme of cAMP in inflammatory cells. Roflumilast, a targeted inhibitor of phosphodiesterase 4, reduces inflammatory products such as leukotriene B and TNF-a in inflammatory cells.
Methods The patients considered were those >40 years old with a diagnosis of moderate to severe COPD (confirmed by a post-bronchodilator [FEV1]/FVC ratio <0.70 and post-bronchodilator FEV1 <50% of predicted value). All patients were current or former smokers with a minimum smoking history of at least 20 pack years, and have history of chronic productive cough. The intervention being tested is Roflumilast in combination with LABA, and the search strategy focused on RCTs in which an experimental group included Roflumilast with LABA vs. LABA with placebo. The primary efficacy endpoints observed were change in pre-bronchodilator FEV1 from baseline to each post randomisation visit. Secondary endpoints included postbronchodilator FEV1, pre- and post-bronchodilator FVC and transitional dyspnea index. Statistical analyses were performed using the RevMan computer software.
Results Three thousand nine hundred and five patients were included in the three trials that reported change in mean prebronchodilator FEV1 from baseline to each post randomisation visit. LABA with Roflumilast was noted to have significant difference when compared with LABA and placebo in improving prebronchodilator FEV1 ($p < 0000.1$). Secondary outcomes tested also showed significant difference in comparing LABA with Roflumilast vs. LABA with placebo ($p < 0000.1$).
Conclusion Roflumilast improves lung function in patients with moderate-to-severe COPD who are already being treated with LABA. The use of oral, once daily anti-inflammatory agent instead of inhaled corticosteroids as concomitant therapy to LABA has advantages, such as increased compliance and no demonstrable increase risk of pneumonia.

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CHANGES OF CATHEPSIN B AND CYSTATIN C LEVELS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Plasma levels of inflammatory protein, cathepsin B and its naturally inhibitory protein cystatin C were examined in chronic obstructive pulmonary disease (COPD) patients during and two weeks as well as 8 weeks after acute exacerbation (AE). The changes of of plasma levels of these proteins were evaluated to speculate whether they are well correlated with the inflammatory statuses of COPD exacerbation. 46 COPD patients, including 44 male and 2 female, were included in this study. Plasma were collected in three different times, i.e., during, and 2 weeks as well as 8 weeks after AE. 18 healthy subjects, including 10 male and 8 female, were studied as control. Enzyme-linked immunosorbent assay(ELISA) wad use to measured the plasma levels of the study proteins. The plasma levels of cathepsin B were significantly higher in COPD patients at 2 weeks and 8 weeks after AE when compared with those of healthy subjects. In COPD patients, the plasma levels of cathepsin B were significantly higher at 2 weeks after AE than those at the time of AE. The plasma level of cystatin C showed significantly higher than the plasma levels of healthy subjects at time of AE, also 2 weeks and 8 weeks after AE. However, there was no significant difference between the time of AE and 2 or 8 weeks after AE. In conclusions, the persistently significant higher plasma levels of cystatin C in COPD patients not only on AE but also at 2 and 8 weeks after AE than those in healthy subjects might represent a chronic inflammatory status in COPD. Moreover, plasma level of cathepsin B significantly increased at 2 weeks after AE and which returned to be non-significant at 8 weeks after AE in COPD patients.

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THE ACCEPTABILITY OF TAI CHI IN CAUCASIAN PEOPLE WITH COPD

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Aim Tai Chi is an ancient Chinese martial art which involves a series of slow and controlled movements. It is practised increasingly in the West as a mean of exercise. The aim of this study was to determine the acceptability of Tai Chi by Caucasian people with COPD who had completed a 12-week Tai Chi training program.
Methods Participants with COPD who finished a twice weekly, 12-week short-form Sun-style Tai Chi training program, completed a survey of eight questions. Each question was answered by putting a stroke on a 10 cm visual analogue scale, with a higher score indicating a better experience. The number of supervised training sessions attended during the 12-week period and the number of unsupervised home practised days were also reported.
Results Twenty-three participants, all Caucasians with no previous experience of Tai Chi, completed the survey (mean (SD) age 74 (8) years, mean FEV_1% 59 (17)% predicted). Participants attended 21 (2) supervised training sessions out of a possible 24 sessions and practised 4 (1) days per week for unsupervised home training. Results for four of the eight survey questions: 1. 'How enjoyable was the Tai Chi program?' (mean (SD) score 8.9 cm (1)); 2. 'How helpful was the Tai Chi program in improving physical fitness (7.9 cm (2)), balance (7.9 cm (2)) and shortness of breath?' (7.0 cm (2)); 3. 'How hard was it to remember the Tai Chi movements?' (5.3 cm (3)) 4.'Would you continue Tai Chi training as your regular exercise regimen?' (8.4 cm (2)).
Conclusion Participants reported that short-form Sun-style Tai Chi was a highly enjoyable exercise which improved their physical fitness, balance and shortness of breath. Participants were also very adherent to the supervised and unsupervised training sessions. Importantly, participants indicated that they would continue Tai Chi as their regular exercise regimen.

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EFFICACY AND TOLERABILITY OF BUDESONIDE/FORMOTEROL ADDED TO IPRATROPIUM PLUS THEOPHYLLINE IN SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background and Study Aim Ipratropium bromide (IB) and sustained-release theophylline (T-SR) are widely used in Chinese COPD patients. Recent insights into the molecular action of theophylline suggest a low dose may enhance the anti-inflammatory effects of steroids. This trial assessed the efficacy and tolerability of the ICS/LABA combination, budesonide/formoterol (BUD/FORM), as an add-on to IB plus T-SR in Chinese patients with severe COPD (NCT01415518).
Methods This parallel-group, open-label trial randomised patients (forced expiratory volume in 1s [FEV_1] </–50% predicted) to BUD/FORM (160/4.5 μg two inhalations BID) + IB (20 μg two inhalations four times daily) + T-SR (0.1 g orally, BID) or IB+T-SR for 12 weeks. The primary endpoint was change in pre-dose FEV_1 from baseline (visit 3) to treatment period (mean of visits 4, 6 and 8).
Results Patients ($n = 584$; mean age 64.1 ± 8.8 years; 73% GOLD grade III disease) were randomised to BUD/FORM + IB+T-SR ($n = 292$; full analysis set [FAS], $n = 290$) or IB+T-SR ($n = 292$; FAS, $n = 292$). There were no differences in baseline characteristics between groups. The improvement in pre-dose FEV1 from baseline was significantly greater with BUD/FORM + IB+T-SR than with IB+T-SR alone, with an increase of 6.9% (95% CL: 4.3, 9.6%; $p < 0.001$). There was a 43% reduction in exacerbation rate (rate ratio 0.565, $p = 0.0425$) and a 6.3 point improvement in SGRQ-C (–11.3 vs –4.6, $p < 0.0001$) with the addition of BUD/FORM. Few patients experienced adverse events (AEs) related to treatment (1.0% BUD/FORM + IB+T-SR; 0% IB+T-SR), or discontinued due to AEs (1.0% BUD/FORM + IB+T-SR; 2.1% IB+T-SR).
Conclusions The addition of BUD/FORM to IB+T-SR was well tolerated and associated with clinically significant benefits in lung function, exacerbation rate and health-related quality of life in Chinese patients with severe COPD. This study demonstrates the benefit of BUD/FORM used in combination with a widely used local regimen.
Funding AstraZeneca.

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USING A NOVEL SCORING SYSTEM TO EVALUATE THE EFFECTIVENESS OF SELF-CARE EDUCATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background Mastering effective breathing and sputum clearance techniques are essential for patients with COPD. Moreover, enhancing patients' self-management skills could contribute to reduce hospital readmissions. In order to facilitate the bedside education, the physiotherapy department of North District Hospital had developed a patient education package in 2010. To evaluate the effectiveness of this learning process, an assessment chart known as "Breathing Control and Bronchial Hygiene" (BCBH) score was devised and patients' performance was used to correlate with hospital readmissions.
Methods All COPD patients referred for Respiratory Collaborative Care Team's service received an assessment and daily bedside coaching with educational aids. Review was made before patients' discharge. The chart evaluates the management of exacerbation (6 points), techniques of breathing control (8 points) and sputum clearance (4 points) giving a total score of 18.
Results From November 2010 to November 2012, 468 patients were assessed. Majority (78%) were elderly (aged 70 or above). Mean total scores increased from 5.7 at baseline to 9.1 at discharge. Baseline mean scores were lower for the elderly (5.4) than those age < 70 (6.6). At discharge, scores improved to 8.4 for the elderly and 11.7 for those age < 70. Hospital readmission rates within 28 days were 25.3% and 17.6% respectively.
Conclusion This study shows that BCBH scoring could be used as an objective measure of patient's learning. Patients aged below 70 had higher scores and lower hospital readmission rates. Educating elderly patients is challenging. Although visual aids are incorporated in patient booklets, a certain level of literacy is necessary. Engaging care-givers in the patient education may help to reinforce the techniques learnt. Although further studies are needed to determine the minimal clinically important improvement for the BCBH score, results of the younger group suggest that a score of 12 would be necessary to demonstrate competency.

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CAN CAT SCORE BE APPLIED IN OUR OLD CHINESE COPD PATIENTS?

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Background and Aim of Study Chronic obstructive pulmonary disease is a major burden to many healthcare systems worldwide, including Hong Kong. In 2008, the hospitalized COPD inpatients reached 30,935 and it is the fifth leading cause of death in Hong Kong. How to monitor and assess this large patient group is a hot debate in the medical field for years and there is a rather simple tool came up lately, the COPD Assessment Test, CAT score. This questionnaire aims at reflecting the health status of the patients and thus hoping to have a role in assisting patients and physicians in quantifying the impact of COPD on the patient's health status. According to the CAT Development Steering Group, the experts believe that a difference or change of 2 or more units suggests a clinically significant difference in health status. The aim of our study is to see the meaning and application of these 2 units of change in our elderly Chinese COPD patients.
Methods All COPD patients coming up for medical consultation are requested to do the CAT questionnaire. As the literacy among our patients is rather low, we unify the protocol that our rehabilitation nurse will read the 8 questions to them and get their scores. All these patients will be asked again by the same nurse after their medical consultations, i.e., about 30 minutes later, without their prior awareness.
Results We have interviewed 50 consecutive patients, 24 patients, 48% had changes of their scores with more than or equal to 2 units. Further analysis found that this significant change is correlated to older age, lower education level and frequent hospitalizations in the past 1 year.
Conclusion CAT score may not be that applicable in our group of old Chinese COPD patients with low education level.

PS350

THE RELATIONSHIP BETWEEN COPD ASSESSMENT TEST (CAT) SCORE AND AIRFLOW LIMITATION IN JAPANESE PATIENTS AGED OVER 40 WITH SMOKING HISTORY

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Background and Aim of Study Epidemiological studies estimate COPD patients in Japan exceed 5.3 million yet over 90% of them are undiagnosed, therefore there is an urgent need to find these undiagnosed patients and treat them earlier. The COPD Assessment Test (CAT) was developed as a simple patient-completed tool for assessing and monitoring the impact of COPD on health status. It is easy to implement in routine use within Primary Care, we hypothesized that the CAT may have utility for case-finding patients who need to have spirometry to diagnose with COPD in Primary Care.
Methods Two multi-center, non-interventional, prospective studies (Study 1 and 2) were conducted in 15 and 17 centers across Japan. Subjects in both studies were aged 40 years or older with smoking history. Subjects in Study 1 had not been diagnosed with COPD but had experienced repeated respiratory tract infections, and subjects in Study 2 routinely visited for their cardiovascular diseases. Subjects completed the CAT prior to lung function testing by hand-held spirometry (Hai-checker). We investigated the relationship between CAT score and the airflow limitation.
Results CAT score were available from a total 3,062 subjects (2,067 in Study 1 and 995 in Study 2); 88.8% were male and age was 61.5 ± 11.6 years (mean ± SD). Airflow limitation was found in 400 (19.4%) subjects in Study 1, and 269 (27.0%) in Study 2. CAT score in subjects with airflow limitation was higher than subjects without airflow limitation in both studies: 8.3 (95% Confidence Interval [CI] 7.5–9.2) vs 6.4 (95%CI 6.0–6.8) in Study 1, 8.6 (95% CI 7.9–9.2) vs 7.4 (95% CI 7.1–7.6) in Study 2.
Conclusion This suggests that the CAT has the potential to identify subjects who need spirometry to diagnose with COPD, particularly in those with a history of frequent exacerbations or comorbidity of cardiovascular disease.

PS351

THE EFFICACY OF COMBINATION WITH INDACATEROL AND TIOTROPIUM COMPARED WITH TIOTROPIUM ALONE IN THE PATIENTS WITH VERY SEVERE COPD

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Background and Aim of Study Combination with long-acting muscarinic antagonist (LAMA) and long-acting β2-agonist (LABA) demonstrate superior bronchodilation compared with LAMA or LABA monotherapy in patients with COPD. Indacaterol, once-daily, inhaled ultra-LABA, has been shown to be effective with moderate to severe COPD. However the efficacy of combination with LAMA and indacaterol is unclear in patients with very severe COPD. The aim of this study was to estimate the efficacy of combination with two once-daily inhaled bronchodilator, indacaterol and tiotropium, in patients with very severe COPD.
Methods S ix Japanese patients with very severe COPD according to Global Initiative for Chronic Obstructive Lung Disease criteria were enrolled. The patients who had been already administered with tiotropium (Handihaler®) 18 μg once daily received indacaterol 150 μg in addition once daily concurrently. The efficacy outcomes were evaluated in spirometry data and health status assessed by COPD assessment test (CAT) at baseline with tiotropium alone and at week 8, 12, and 16 with tiotropium and indacaterol.
Results FEV1 at week 8 with tiotropium plus indacaterol was increased in comparison with tiotropium alone in four of six patients. Although one patient dropped out at week 8 because of no improvement, the others kept increasing FEV1 at week 12 and 16. However, there were no statistically significant differences in inspiratory capacity and CAT scores. The combination therapy showed in subjective symptoms remarkable improvement in two patients, no significant differences in three, and getting worse in one.
Conclusion The combination therapy of indacaterol and tiotropium increased FEV1 in some parts of patients with very severe COPD. Although it seemed that there was no correlation between the degree of improvement in FEV1 and CAT score, some patients felt remarkable efficacy in subjective symptoms with this combination.

2-D3: COPD 8

PS352

PREVALENCE OF ASTHMA, COPD, AND COPD WITH VARIABLE AIRFLOW OBSTRUCTION IN A GENERAL JAPANESE POPULATION: THE HISAYAMA STUDY

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Background Recent studies have discriminated a disease phenotype of COPD with variable airflow obstruction (COPD-VAO), corresponded with "overlap syndrome" proposed by several investigators. The prevalence of this phenotype in a general population is, however, unknown in Japan. The age and occupational distributions of the town of Hisayama have been almost identical of those of Japan from the 1960s to the present. During an observational study for the town residents, we estimated the prevalence of asthma, COPD, and COPD-VAO.
Methods All registered residents aged above 40 (n = 2178, approx. 45% of the total population in those age residents) were solicited to participate in a town-wide health check-up including spirometry. Only subjects who had a FEV1/FVC of less than 0.7 were recommended to have further evaluations in the departments of pulmonary medicine in Kyushu University Hospital or National Fukuoka-Higashi Hospital. Their medical records, including bronchodilator responsiveness, were carefully reviewed by two pulmonologists in a blinded fashion. Subjects were classified into asthma, COPD, COPD-VAO, or others. On the estimation that subjects without further evaluation would have similar prevalence, the prevalence of each disease was calculated.
Results In 464 subjects with FEV1/FVC of less than 0.7, 183 subjects had further evaluations and medical records of 176 subjects were processed for the assessments. Prevalence of asthma, COPD, and COPD-VAO, corresponded to 1.9%, 8.1%, and 0.8%, respectively.
Conclusion We could estimate the prevalence of asthma, COPD, and COPD-VAO in a general Japanese population aged above 40.

PS353

PREDICTORS OF PULMONARY FUNCTION MAINTAINING IN PATIENTS WITH COPD AFTER ADDED MEDICAL THERAPY

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Background and Aim of Study Forced expiratory volume in 1 second (FEV_1) in chronic obstructive pulmonary disease (COPD) is known to annually decrease more obviously than normal subjects. However, airflow limitation of COPD is partly reversible, and several drugs for COPD are newly developing. The aim of this study is to evaluate the change of pulmonary function of COPD after added medical treatments and to identify predictors of the change of pulmonary function.
Methods We studied 37 patients who visit Kumamoto University Hospital or General Hospital in Kumamoto City with FEV_1/FVC less than 0.7, diagnosed with COPD and treated with medication by respiratory physicians more than 1 year. Their clinical backgrounds, pulmonary function tests, lung imaging studies at first visits, treatments, and the latest pulmonary function tests were collected retrospectively from their medical records. The significant predictors of change of FEV_1 from first to latest pulmonary function tests were evaluated using multiple regression analysis.
Results FEV_1 at first visit were 1283 ± 538 ml (56 ± 22% predicted) and that was 68 ± 216 ml increased at latest visit (45 ± 123 ml/year). The significant predictors of favorable courses of FEV_1 were 1) less smoking history, 2) higher reversibility by inhalation of short acting inhaled β_2 agonist (SABA) at first visit, and 3) use of long acting inhaled β_2 agonist (LABA).
Conclusion We confirmed that the COPD patients having higher reversibility by inhalation of SABA with less smoking history maintain their pulmonary function by medical therapy.

PS354

THE COSMOS-J (COPD SYMPTOM BASED MANAGEMENT AND OPTIMIZE TREATMENT STRATEGY IN JAPAN) STUDY PROTOCOL

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Background and Objective The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011 proposed a COPD assessment framework focussed on symptoms and on exacerbation risk. This study will be conducted in Japanese subjects with moderate-to-severe COPD and with an mMRC score of 1 or greater. It will assess whether the GOLD 2011 strategy is effective in medical practice in a real world setting in Japan. The purpose of this study is to assess the control of COPD using a symptom and exacerbation risk treatment strategy based on GOLD 2011. This abstract summarizes the methodology of the study, in advance of the publication of the results.
Methods This study is a 24-week, multicentre, randomised, double-blind, double-dummy, parallel group trial. 400 patients will be recruited and randomised to receive treatment with either salmeterol/fluticasone propionate (SFC) 50/250 mcg twice daily or tiotropium bromide 18 mcg once daily. COPD management of patients will be assessed at 4-weekly intervals and if patients remain with high levels of symptomatic impact on their daily health life, as measured by the CAT score, or experience an exacerbation, they have the option, after discussion between doctor and patient, to step up to treatment with both medications, i.e. SFC and tiotropium (TRIPLE therapy). The primary endpoint is the number of patients who are able to remain on the randomised therapy. Patients still not well controlled on TRIPLE have the option to add further treatments. The possibility of step-down from TRIPLE based on lack of response is also incorporated. The results of this study will help physicians to understand when TRIPLE therapy is more effective for management of symptoms and exacerbations in patients with moderate to severe COPD. This study will also clarify what proportion and what type of patients can be managed on single therapy and which on TRIPLE therapy.

PS355

LIFE STYLE AND PARTICIPATION RESTRICTIONS IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background The pulmonary rehabilitation for chronic obstructive pulmonary disease (COPD) patients is intended to improve the lung functions, exercise functions, and activities of daily living (ADL). When we produce the pulmonary rehabilitation program, it is necessary to know their life style in detail. However, there are few reports about the lifestyle of them.
Methods Thirty-nine severe COPD patients (66.1 ± 6.9 years old) were participated in this study, and divided them into two groups (Group A and Group B). Group A consisted of 23 patients (Severe COPD; Stage III), and Group B consisted of 16 patients (Very Severe COPD; Stage IV). We investigated their lung functions, nourishment states, exercise functions, ADL level and life style. We performed informed consent to all the members when investigating it.
Results Lung functions and exercise functions of B group were significantly lower than those of A group. The ADL level in both groups was lower, especially in B group. They had few daily roles at home and seldom participated in community activities. And many of them had various anxieties about their daily activities and social participation such as "going out", "trip".
Conclusion To improve the QOL of sever COPD patients, it is necessary to improve not only basic ADL but also other daily and social activities.

PS356

IMPACT OF AIRFLOW LIMITATION ON PERIOPERATIVE STATES OF THORACIC SURGERY

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Background and Aim of Study Airflow limitation may be common among patients who need thoracic surgery and may influence perioperative status and postoperative outcomes. The objectives of our study were to investigate the prevalence of airflow limitation among patients who had thoracic surgery in our hospital and to analyze its impact on postoperative complications and outcomes after surgery.
Methods We retrospectively reviewed clinical records of patients who underwent thoracic surgery in Juntendo University Hospital from 1996 to 2013. The patients who lacked data of pulmonary function before surgery were excluded. Patients were classified into two group, Group A who had airflow limitation (FEV1/FVC < 70%) before surgery and Group B without airflow limitation, and analyzed the prevalence of comorbidities, frequency of postoperative complications.
Results Of 4676 patients who underwent thoracic surgery, 3667 cases who has preoperative pulmonary function data were analyzed. The mean age was 61.2 ± 13.8 years old, 59.6% was male, and 51.5% was current or ex-smoker. Comorbidies that were more prevalent in Group A included hypertension, diabetes mellitus, cardiovascular diseases, COPD, bronchial asthma, neurological diseases and collagen vascular diseases ($P < 0.01$) while no significant difference in prevalence was noted in hyperlipidemia and interstitial lung diseases. Postoperative complications including respiratory failure requiring oxygen supplementation, atelectasis, delirium, re-operation, arrhythmia, and prolonged air leakage were significantly prevalent in Group A ($P < 0.01$) The period of postoperative hospital stay showed no significant difference between Group A and B.
Conclusion Patients with airflow limitation had more comorbidity and postoperative complications after thoracic surgery than those without airflow limitation.

PS357

CIRCULATING NEUTROPHILS AND $FEV_{0.5}/FIV_{0.5}$ IN SEVER COPD

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Background Inflammatory cells and mediators may lead to destructive changes in airways and lung hyperinflation in sever chronic obstructive pulmonary disease (COPD).
Aims To tested the hypothesis that neutrophils in venous blood have a relationship with the ratio of forced expiratory to forced inspiratory volumes for the first 0.5 second ($FEV_{0.5}/FIV_{0.5}$) as a measure of hyperinflation in sever COPD.
Methods Five male outpatients with COPD (83 ± 4 age, forced expiratory volume in 1 second (FEV_1) 39.1 ± 7 % predicted), all ex-smokers and undergoing long-term oxygen therapy, were included. Measurements were obtained more than four times for the ratio of circulating neutrophil count to peripheral white blood cell count (neutrophil %), FEV_1, FEV_1%predicted, C-reactive protein (CRP) and $FEV_{0.5}/FIV_{0.5}$ from July 1, 2011, to July 31, 2012.
Results Neutrophil%(69.9 ± 10.8 %) was significantly correlated with $FEV_{0.5}/FIV_{0.5}$ (0.79 ± 1.23) ($rs = -0.56579$, $p < 0.01$), FEV_1(0.67 ± 0.11 L)($rs = 0.572239$, $p < 0.05$), and FEV_1% predicted (41.15 ± 8.06 %)($rs = 0.540248$, $p < 0.05$). CRP(0.36 ± 0.44 mg/dl) was not significantly correlated with $FEV_{0.5}/FIV_{0.5}$.
Conclusion This report suggests that circulating chronically increasing Neutrophil% might be able to progress the lung hyperinflation in sever COPD.

PS358

COPD ASSESSMENT TEST (CAT) SCORES REFLECT EXERCISE INTOLERANCE, DESATURATION ON EXERTION AND SMALL AIRWAY OBSTRUCTION IN COPD PATIENTS

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Background The Global Initiative for Obstructive Lung Disease (GOLD) 2011 update document on COPD bases on levels of dyspnea including CAT, exacerbation history and %FEV1.0, while the previous GOLD categorized disease severity according to %FEV1.0 only.
Objectives To assess the usefulness of CAT scores by using GOLD 2011 classification.
Methods We studied patients with COPD in our hospital between August 2008 and July 2011. They were classified to 4 groups in accordance with the GOLD2011. We compared CAT scores with clinical indicators of six minute walk test (6MWT) and pulmonary function test (PFT) between group A (mild, low CAT scores) versus B (mild, high CAT scores), C (severe, low CAT scores) versus D (severe, high CAT scores) and A+C (low CAT groups) versus B+D (high CAT groups). Clinical indicators of 6MWT included six minute walk distance (6MD) and desaturation area (DA), and PFT included $\%DL_{CO}$, maximal mid-expiratory flow (MMF) and δN2.
Results The 60 COPD patients were examined. They were 72.9 ± 7.5 years old and 86.7% were male. 19(32%) were classified as GOLD 2011 group A, 6(10%) group B, 15(25%) group C, 20(33%) group D. 6MD and $\%DL_{CO}$ in Group D was significantly lower than in group C. 6MD, $\%DL_{CO}$ and MMF in Group B+D was significantly lower than in group A+C. DA and δN2 of Group D and B+D was higher than that of group C and A+C, respectively. There were no differences in all clinical indicators between group A and B.
Conclusion Our results suggested that exercise intolerance, desaturation on exertion and small airway obstruction might correlate with high CAT scores in COPD patients with low pulmonary function.

PS359

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN OUTPATIENTS WITH CARDIOVASCULAR DISEASES IN JAPAN

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Background and Aim of Study Although cardiovascular disease and chronic obstructive pulmonary disease (COPD) share common risk factors and COPD patients frequently have comorbid cardiovascular diseases, the prevalence of COPD in outpatients with cardiovascular diseases in Japan is unknown.
Methods In a multi-center, non-interventional, prospective study conducted at 17 centers across Japan, we investigated the prevalence of airflow limitation compatible with COPD (defined as FEV1/FEV6 < 0.73 by hand-held spirometry, Hai-checker) in outpatients routinely visiting for their cardiovascular diseases and who were aged 40 years or older with a smoking history. Each subject completed the COPD Assessment Test (CAT) prior to hand-held spirometer testing.
Results A total of 1,001 subjects participated and the spirometry data of 995 subjects were available. 95.5% of subjects were male and age was 66.6 ± 10.0 (mean ± SD) years old. The prevalence of airflow limitation compatible with COPD was 27.0% (n = 269), and 87.7% of these subjects (n = 236) have not been diagnosed as COPD before. In subjects with CAT score >10, the prevalence of airflow limitation was 36.5%, and higher than in subjects with score < 10, it was 23.4%; sensitivity was 0.37 and specificity was 0.76.
Conclusion The prevalence of airflow limitation in this study indicates that a quarter of outpatients with cardiovascular diseases have COPD, although almost all of them are undiagnosed. This suggests that it is important to look routinely for COPD in cardiovascular disease outpatients. Use of the CAT in cardiology clinics in patients over 40 years old with smoking history may be a simple way for assessing patients who need to have spirometry to diagnose COPD.

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PS360

EFFICACY OF INDACATEROL ADD-ON THERAPY IN PATIENTS WITH STABLE COPD TREATED WITH TIOTROPIUM

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Aim The study evaluated the clinical benefit of once daily long-acting β2 agonist indacaterol add-on therapy in the stable COPD patients with muscarinic antagonist tiotropium treatment.
Methods Japanese 18 patients(17 male/1 female, mean age72 ± 7.2, severity stageII 8/stageIII 10) with COPD, treated with tiotropium 18 μg more than 3 months and had some COPD symptoms, were added indacaterol 150 μg once daily. Respiratory function, IOS, CAT, 6MWD and the questionnaire of usability Breeze Heller were assessed before and after 8 weeks add-on therapy.
Results Three question of CAT (Activity, breathlessness, Confidence), 6MWD, IC,% V25 has improved significantly on 8 weeks after add-on therapy. The other three question of CAT (Chest tightness, sleep, energy), FEV1, FVC, IOS (R5, R20, R5-R20, X5, AX, Fres) was no significant difference, but some subjects showed a significant improvement. The questionnaire survey of usability Breeze Heller showed that it is easy to use.
Conclusion This result suggest that respiratory function, air trapping, symptoms, QOL, physical activity and exercise tolerance are improved by combining different mechanisms bronchodilators with LAMA blocking the M3 receptor and LABA to stimulate the β 2 receptor.

PS361

MINI NUTRITIONAL ASSESSMENT SHORT FORM (MNA-SF) CAN PREDICT EXACERBATION IN COPD INDEPENDENTLY OF COPD ASSESSMENT TEST (CAT)

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Background The CAT is an eight-item questionnaire designed to assess and quantify the impact of COPD symptoms on health status and is widely used in many countries. The nutritional impairment is an important systemic manifestation associated with poor prognosis and deteriorated quality of life. However, a relationship between nutritional status and the CAT scores is unknown.
Aim To determine the relationship between the CAT score and nutritional status assessed by MNA-SF and compare the ability of CAT to predict exacerbation with that of MNA-SF.
Methods Pulmonary function, modified MRC scale (mMRC) and body mass index (BMI) were evaluated in 60 stable patients with COPD (mean age:72 yr, mean $\%FEV_1$:61.4%). The CAT and MNA-SF were also completed. After initial assessment, exacerbations were recorded prospectively for one year.
Results The mean CAT score was 14.4 ± 7.5 (low impact:37%, medium impact:38%, high impact:20%, very high impact:5%). The mean MNA-SF score was 11.4 ± 2.4 (well nourished:51%, at risk:37%, malnourished:12%). The CAT scores were significantly correlated with mMRC and $\%FEV_1$, but not correlated with BMI and MNA-SF scores. The MNA-SF score was correlated with exacerbation frequency, whereas the CAT score was not associated with exacerbations frequency.
Conclusion The CAT appears to assess health status of COPD independently of nutritional status. MNA-SF as well as CAT is of clinical importance because it can predict COPD exacerbation.

PS362

YEARLY PROGRESSION OF LOW LUNG ATTENUATION AREA IN LOW DOSE CHEST CT FOR ASYMPTOMATIC CURRENT SMOKERS

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There is still no biomarkers idenfifying 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 I COPD. From March 2007 to October 2012, initial and annual follow-up low dose CT scans with the measurement of 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) at our institution. Visceral fat, body fat, BMI, and pulmonary function test(FEV1, FEV1/FVC(%)) were obtained. Only baseline FEV1/FVC% were 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 after one year. 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 changed($p > 0.05$) in smokers on the annual follow-up study. There were no significant differenced in th paired LAA_{-950}, BMI, visceral fat,body fat, FEV1% and FEV1/FVC% in non-smokers on the annual followup study. Measurement of LAA_{-950} in low dose chest CT may show individual yearly progression of microscopic emphysema in current smokers with normal lung function or GOLD stage I subjects who do not show significant annual changes in lung function.

PS363

AUDIT OF A HOSPITAL AT HOME SERVICE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background Clinical trials suggest that hospital at home (HaH) may be a safe and cost effective option in the management of chronic obstructive pulmonary disease (COPD) exacerbations. [Ref. 1] However, there is little information on the effectiveness of HaH care in secular practice outside some European centers. [Refs. 2 & 3].
Aim We describe the results of a HaH service for COPD in a university hospital in Singapore.
Methods We retrospectively analyzed the clinical outcomes of a HaH service which was implemented in 2005 within a comprehensive, integrated care program for patients with COPD.
Results From June 2011 to 2013, 257 home visits were performed for 201 patients with COPD. Hospital re-admissions were needed for only 9 episodes (4.5%). However, 55 (21%) were associated with adverse events (clinical deterioration, hospital attendance or death: 9 patients chose to die at home). The range of HaH services rendered included patient education, care giver training, drug adjustments, oxygen therapy(19), non-invasive ventilation(4), financial advice, palliative care(21), treatment of co-morbities(16), social and emotional support.
Conclusions A HaH service is effective in avoiding hospitalizations in the majority of cases. To optimize HaH outcomes, a wide repertoire of clinical skills and support services are required. The patients have advanced COPD and thus, HaH need capacity to cope effectively with adverse events.
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PS364

FREQUENCY OF COPD IN THE PATIENTS WITH HEARING LOSS

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Background and Aim of Study Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. COPD patients generally suffer from chronic hypoxemia. The aim of our study is to analyze effects of chronic hypoxia on hearing threshold.
Method Out-patient pulmonary medicine clinic records and pure tone audiogram records were analyzed and patients whose age over 50 were included in our study. Data was recorded in Microsoft Excel and analyzes were made in SPSS version 16. Hearing threshold of 30 dB. or more was defined as hearing loss. Independent Samples T test and Chi-Square tests were used for statistical analyses.
Results 96 pure tone audiogram records were analyzed in 1 year period (2011). 54 (65.1 ± 10.2 years) of patients were males and 42 (63.7 ± 8.5 years) of patients were females ($P > 0.05$). 70 (72.9%) patient had hearing loss and 6 (8.6%) of these cases had COPD diagnosis. 26 (27.1%) patient had normal hearing levels and 1 (3.8%) of these cases had COPD diagnosis ($P > 0.05$).
Discussion Our analyses showed that hearing loss was more frequent in COPD patients but differences between two groups were statistically insignificant. Low number of patients might be cause for these results. More future prospective controlled studies are needed.

PS365

THE OVERLAP SYNDROME OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE: ITS PREVALENCE AND CLINICAL CHARACTERISTICS

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Background and Aim Although asthma and chronic obstructive pulmonary disease (COPD) have been accepted as different diseases, many elderly patients show clinical features of both asthma and COPD, so called 'overlap syndrome (OS)'. The aim of our study was to examine the prevalence and clinical characteristics of the OS.
Methods We conducted a retrospective survey of patients above 40 years old who had visited our hospital from January 2005 to June 2009 because of obstructive lung diseases. Patients with structural lung diseases or short duration of follow-up period were excluded. Based on lung function profiles, we classified subjects into COPD or OS group, and analyzed their prevalence, demographics, and lung function profiles.
Results 2,105 subjects were included. 240 (11.4 %) and 630 (29.9 %) were found to have OS and COPD, respectively. The mean age was similar in both group (66.4 years old vs. 67.7 years, $p = 0.553$) but age of symptom onset was earlier in OS group than COPD group (38.4 years old vs. 58.2 years old, $p < 0.001$). The OS group showed lower baseline post-bronchodilator forced expiratory volume at 1 second (FEV_1) than the COPD group (50.9 % vs. 57.7 %, $p < 0.05$). After additional treatment with tiotropium, the OS and COPD groups showed significant improvement of post-bronchodilator FEV_1 (5.5 %, $p < 0.05$; 7.7 %, $p < 0.001$).
Conclusion Certain proportion of elderly patients has the OS. Although their symptoms develop earlier and baseline lung function is worse, intensive treatment can improve lung function.
Key Words asthma; chronic obstructive pulmonary disease; overlap syndrome; prevalence; clinical characteristics.

PS366

FACTORS ASSOCIATED WITH MALNUTRITION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: ANXIETY AND DEPRESSION

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Background and Aim Nutritional state is an important determinant of symptoms, disability, and prognosis in chronic obstructive pulmonary disease (COPD). Anxiety and depression are the major comorbidities in COPD. The Mini Nutritional Assessment® (MNA) questionnaire is a simple, validated questionnaire widely used to identify the elderly at risk for malnutrition; the MNA explores 4 components that affect malnutrition. We examined whether impaired nutritional status using the MNA is associated with anxiety and depression in COPD.
Methods A total of 105 clinically stable COPD patients (mean age, 73.7 years; Global Initiative for Chronic Obstructive Lung Disease stage I:18, II: 43, III: 39, IV: 5; male, 97), who were previously investigated in the association study between malnutrition assessed by the MNA and decreased exercise intolerance (presented in ATS 2013), were included in the study. Pulmonary function, exercise intolerance (6-minute walking distance test), anxiety and depression (Hospital Anxiety and Depression Scale [HADS]), and nutritional status (MNA) in addition to body composition were evaluated. We calculated the total score and scores for each of the 4 nutritional status domains from the MNA: anthropometric, functional, dietary and self-perception assessment.
Results Both depression and anxiety scores of the HADS were significantly correlated with the MNA total score (high scores indicates good nutritional status) ($p = 0.001$, and 0.018, respectively) (rho = –0.312, and –0.231, respectively). The depression score was also significantly correlated with the MNA self-perception score ($p < 0.001$, rho = –0.394).
Conclusions The malnutrition assessed by the MNA was associated with depression and anxiety in patients with COPD. Especially, depression was associated with self-perception affecting malnutrition in COPD. Treating depression may improve nutritional status in COPD patients.

PS367

RISK FACTORS OF COPD IN NEVER-SMOKERS VS. EVER-SMOKERS FROM KOREAN NHANES

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Background Although smoking is the strongest risk factor of COPD development, some patients have no history of smoking. Nonsmoker COPDs will present another characteristics and risk factors, compared with smoker COPDs.
Methods Dominant characteristics in never-smoker COPD compared to ever-smoker COPD using the data of 4th Korean National Health and Nutrition Examination Survey (KNHANES) 2007–2009 were evaluated. COPD was defined as FEV1/FVC < 0.7. Patients of known asthma or patients with restrictive lung function (FEV1 < 80% and FEV1/FVC > 0.7) were excluded. Never-smoker was defined as subject who had never smoked or had smoked in past less than 5 pack-years.
Results Among total 9,152 subjects who were enrolled during that period and performed pulmonary function test (PFT), 6,934 subjects showed acceptable PFT. Since exclusion criteria, finally 5,784 subjects were evaluated. The proportion of smokers was 60% and incidence of COPD was 14.3%. The prevalence of COPD in ever-smokers was much higher than in never-smokers (24.6% vs. 7.4%, $p < 0.0001$). History of tuberculosis (never-smokers: OR 2.42, CI 1.48–3.96 vs. ever-smokers: OR 1.85, CI 1.29–2.65) and presence of bronchiectasis (never-smokers: OR 9.05, CI 3.17–25.83 vs. ever-smokers: OR 2.58, CI 0.72–9.19) were more closely related with the existence of COPD in never-smokers, compared to ever-smokers. Besides those risk factors, age, educational levels, living with partner, and family income were also significant risk factors of COPD in both groups.
Conclusions When nonsmokers of no known asthma present PFT of obstructive pattern, history of tuberculosis or presence of bronchiectasis should be considered.

2-E1: COPD 10

PS368

EFFECT OF EUCALYPTOL, LIMONENE AND PINENE MIXTURE (AN' NINGPAI) ON AIRWAY MUCOCILIARY CLEARANCE FUNCTION IN RATS EXPOSED TO CIGARETTE SMOKE

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Objective To contrasted the effects between An' ningpai and its main component eucalyptol in chronic cigarette smoke-exposed rats, further explored its mechanism on airway MCC function.
Methods The models were established by continuously exposeing cigarette smoke for 12 weeks. An' ningpai and eucalyptol, intervened at the beginning of smoke exposed, were compared with after intervention treatment between different groups on rats general morphology, airway bacterial load, airway scavenging activity on exogenous H. influenzae, microstructure change under TEM, AB-PAS staining, airway mucin MUC5AC production and expression.
Results Compared with smoke exposed group, the pathological structure was relatively improved in An' ningpai intervention group, though obvious structural changes still exited compared with normal control group. Bacterial load was reduced in the rat airway of An' ningpai intervention group, and scavenging activity on exogenous H. influenzae was accelerated. TEM results showed airway epithelial cilia structure was relatively intact, that prompted medical intervention for cilia played a protective role. But for the damage of the cell structures and organelles the improvement was not obvious. The effect of An' ningpai on mucous secretion was manifested in regulating acid mucopolysaccharide proportion secreted by airway epithelium goblet cells, affecting the properties of mucus, and reducing airway MUC5AC expression level. The therapeutic effect of eucalyptol intervention group was similar to that of An' ningpai intervention group, no significant statistical difference showed. Glycerol as a drug control had no influence to the detection indexes.
Conclusions An' ningpai has the effects on reducing airway bacterial load in rats exposed to cigarette smoke, increasing bactiria scavenging activity by improving airway mucociliary clearance function. The effects are mainly performed by protecting airway epithelial cilia structure, regulating acid mucopolysaccharide ratio and mucin MUC5AC level secreted in goblet cells.
Key Words An' ningpai; Eucalyptol; COPD; Rats exposed to cigarette smoke; Mucociliary clearance; H. influenzae.

PS369

MECHANISM OF AN' NINGPAI AND EUCALYPTOL ON AIRWAY INFLAMMATION AND MUCOUS HYPERSECRETION IN RATS EXPOSED TO CIGARETTE SMOKE

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Objective and Methods To compare An' ningpai and eucalyptol on airway inflammation and mucous hypersecretion in cigarette smoked-exposed rats and to explore its mechanism, the indicators were compared between groups on rats airway inflammation, including bronchoalveolar lavage fluid (BALF) cell count, the expression levels of TNF-alpha, and IL-6, and detection of p38MAPK and p-p38MAPK protein levels. And combining with the MUC5AC expression level, the correlation between indicators were evaluated. To explore whether the effect of An' ningpai and eucalyptol on inflammatory mediators were related to p38MAPK phosphorylation.
Results The anti-inflammatory effects was found in An' ningpai intervention group, and the inflammation index improved levels were significantly related with mucin improved levels. Compared with normal control group, increased BALF inflammatory cell count and expression of TNF-alpha, IL-6, were shown in smoke exposed group rats, accompaning by higher p38MAPK and p-p38MAPK protein levels. Compared with smoke exposed group, BALF inflammatory cell ratio and expression of TNF-alpha, IL-6, were obviously reduced by An' ningpai intervention, accompanied with higher p38MAPK and p-p38MAPK protein levels. And the p38MAPK and p-p38MAPK expression decreased, more obviously drop of p-p38MAPK suggested that An' ningpai had the effect of p38MAPK dephosphorylation. The anti-inflammatory effect of eucalyptol intervention group was similar to that of An' ningpai intervention group, no significant statistical difference showed. Glycerol as a drug control had no influence to the detection indexes.
Conclusions During An' ningpai regulating airway mucociliary clearance function, the effects on inflammatory mediators were involved in at the same time. The induction dephosphorylated of p38MAPK may be the common mechanism of An' ningpai effect on regulation of mucin secretion and anti-inflammation, in it, eucalyptol played a main role.
Key Words An' ningpai; Eucalyptol; COPD; Rats exposed to cigarette smoke; MAPK.

PS370

FACTORS PREDICTING LUNG HYPERINFLATION OF PATIENT WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A COHORT STUDY FOR SIX MONTH

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Rationale Patients with chronic obstructive pulmonary disease (COPD) often have some degree of hyperinflation of the lungs. Hyperinflated lungs can produce significant detrimental effects on breathing. Static lung hyperinflation has important clinical consequences in patients with COPD. The power of lung hyperinflation as measured by the inspiratory capacity-to-total lung capacity ratio (IC/TLC) was an independent risk factor for mortality in cohort study of patient with COPD. In this study, we prospectively look for the factors that affect hyperinflation of the lung.
Methods Thirty eight COPD patients were grouped into two based on the ratio of IC/TLC. The IC/TLC value less than 25% was a predictor of higher mortality. The patients were analyzed for age, %FEV_1 (FEV_1/FEV_1 predicted), duration of smoking, Body Mass Index (BMI) and frequency of exacerbation after six months using Student T test.
Result Nine patients (23.7%) had ratio of IC/TLC ≤ 25% and 29 patients (76,3%) were more than 25%. Age, duration of smoking and frequency of exacerbations were not significantly related with lung hyperinflation. BMI and %FEV_1 correlated significantly with lung hyperinflation.
Conclusion Body Mass Index (BMI) and %FEV_1 correlated significantly with lung hyperinflation.
Keywords lung hyperinflation, IC/TLC.

PS371

MEASUREMENT OF LUNG DIFFUSING CAPACITY FOR CARBON MONOXIDE WITH SINGLE BREATH METHOD (DLCO-SB) IN COPD PATIENTS IN PERSAHABATAN HOSPITAL JAKARTA

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Background and Aim of Study This is a pilot study to measure DLCO-SB in COPD patients in Persahabatan Hospital. The aim of the study is to know the magnitude of disturbance in diffusing capacity of the lung in COPD patients.
Methods This was an observational study in which COPD patients attending COPD-Asthma clinic in Persahabatan Hospital Jakarta were performed spirometry and DLCO SB consecutively from May 2013 to June 2013. Comorbid conditions were also identified.
Results Spirometry and DLCO-SB measurement were conducted on 17 COPD subjects of which 14 subjects (82.4%) were COPD grade I-II and 3 subjects (17.6%) were COPD grade III-IV. The mean age was 67.65 (39–81); mean FEV_1% was 58.12% (37.15–75.55), mean DLCO was 13.78 ml/min/mmHg (6.82–31.37) and the mean DLCO% was 85.85% (43.41–140.48). The prevalence of decreasing in diffusing capacity of the lung in COPD patients was 23.5% (4 subjects), while 13 subjects were normal. Thirteen subjects (76.3%) had comorbid conditions. There were 2 subjects with mild decrease in DLCO and there was no significant correlation between comorbidities, grade of COPD, and obesity with the lung diffusing capacity abnormality. There was no significant correlation between age, FEV_1% value, and Body Mass Index (BMI) with DLCO value.
Conclusion The prevalence of decreasing in DLCO in COPD patients was 23.5%. There was no significant correlation between comorbidities, grade of COPD and obesity with lung diffusing capacity abnormality. There was no significant correlation between age, FEV_1% value, and Body Mass Index (BMI) with DLCO value.
Keywords COPD, spirometry, DLCO-SB, comorbidities, FEV1, BMI.

PS372

ANALYSIS OF BONE QUALITY IN RATS WITH EMPHYSEMA BY FTIR IMAGING AND RAMAN SPECTROSCOPY

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Introduction Osteoporosis is one of the comorbidities of chronic obstructive pulmonary disease (COPD). However the pathogenesis of the osteoporosis in COPD has not been fully elucidated yet. Bone strength reflects the integration of two main features: bone density and bone quality. We have investigated bone qualities in rats and mice with renal failure by Fourier transform infrared (FTIR) imaging and microscopic Raman spectroscopy. In this study we investigated bone quality in rats with emphysema by FTIR imaging and Raman spectroscopy.
Methods Ten-week-old male SHR rats, fed with fiber free diet discontinuously were exposed to cigarette smoke twice a day for 8 weeks. After the last exposure, bone density in the femurs of the rats was measured by x-ray and DEXA, while bone quality was investigated by FTIR imaging and microscopic Raman spectroscopy (1064 nm).
Results In the cigarette smoke exposed rats, emphysematous lesions with destruction and enlargement of alveolar walls were found. In these rats, bone mineral density measured by DEXA was significantly lower than those in control rats (non-smoked, continuously fed with control diet). In femur head X-ray image revealed bone density was lower than control rats. FTIR imaging showed decreased calcification in rats with emphysema. The decrease in calcification was more severe in trabecular than in cortical bone. Microscopic Raman spectroscopy showed the increase in carbonate-substituted hydroxyapatite, in spite of the reduction of the crystallinity in bone of rats with emphysema.
Conclusion In rats with emphysema, bone quality as well as bone density was altered. The alteration in bone quality as well as the decrease in bone density may contribute to development of the osteoporosis in COPD.

PS373

ESTIMATION OF THE SITE OF WHEEZES IN PULMONARY EMPHYSEMA: AIRFLOW SIMULATION STUDY BY THE USE OF A 4D LUNG MODEL

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Rationale Although the textbook tells that expiratory airflow limitation in emphysema occurs at the peripheral airways and that wheezes are generated there, wheezes are often heard without stethoscope. Are they really generated periphery in the lung? We have recently revealed with 4D-CT images that expiratory airflow limitation in emphysema occurs at the intra-mediastinal airway (intra-thoracic trachea, main bronchi, right lobar bronchi) due to its dynamic compression enhanced by the surrounding overinflated lungs, because the membranous part there has no cartilage and highly deformable. We performed expiratory airflow simulation by the use of computational fluid dynamics (CFD), and investigated the relationship between the tracheal shape and the pressure fluctuation generated by the airflow.
Methods A 4D finite element model in which all nodes are displaced according to breathing motion was constructed. A cylindrical trachea opens to the atmosphere at the position of the subglottic cavity. The posterior wall of the trachea was deformed mimicking the 4D-CT images Airflow during expiration was computed by solving numerically incompressible Navier-Stokes' equation under moving boundary condition (solver: AcuSolve, Altair Engineerng, USA). Time step was assigned at 0.0001 sec, and dynamic LES (large eddy simulation) model was applied for turbulence.
Results Only slight pressure fluctuation beyond 1,000 Hz caused by turbulence was observed in the airflow simulations in the non-deformed trachea. However, in the deformed trachea, periodical vortex releases with 300–900 Hz at the end of protrusion of the membranous part was found with the range of flow rate between 0.5 L/s and 3.0 L/s. Airflow simulation through the peripheral airway was performed using the same model with the scale of 1/10, and no apparent pressure fluctuations were observed within the airway.
Conclusions The present simulation study strongly has suggested that wheezes are generated not at the peripheral but at the intra-mediastinal airway.

PS374

INTERLEUKIN-17 PLAYS A ROLE IN PULMONARY INFLAMMATION INDUCED BY CIGARETTE SMOKE EXPOSURE IN MICE

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Background Even short-term exposure to cigarette smoke causes airway inflammatory response, which were similar to characteristic neutrophilic inflammation seen in COPD or steroid-resistant asthma. IL-17 is a pro-inflammatory cytokine, provoking neutrophilic inflammation. The role of IL-17 on airway inflammation induced by cigarette smoke was investigated, using the murine model.
Methods Both IL-17 deficient mice and wild-type mice were exposed to tobacco smoke for 5, 8, 12 and 26 days, using the tobacco smoke exposure system. Mice were anaesthetized and sacrificed, and then bronchoalveolar lavage (BAL) fluid was collected, prior to obtaining lung tissues. Cellular responses in BAL fluid were determined. Protein levels of pro-inflammatory proteins in BAL fluid were measured using enzyme-linked immunosorbent assay, as well as mRNA levels in the lung tissues using quantitative RT-PCR. Sections of 3 mu m of paraffin-embedded lung tissue were stained with hematoxylin and eosin.
Result The number of neutrophils in BAL fluid reached the maximum on the 8th day, and then it was decreased on the 26th. The number of neutrophils in BAL fluid, and mRNA levels of KC, GM-CSF, and MMP-9 in lung tissue were lower in IL-17 deficient mice than those in wild-type mice ($p < 0.05$). No significant difference in mRNA levels of tumor necrosis factor-alpha was detected. These results indicated that IL-17 play a role in neutrophilic inflammation induced by cigarette smoke, probably via KC, GM-CSF and MMP-9.
Conclusion Using murine model, we demonstrated that IL-17 plays a role in the induction of neutorphilic inflammation evoked by cigarette smoke exposure.

PS375

ASSOCIATION OF TUMOR NECROSIS FACTOR ALPHA & LYMPHOTOXIN ALPHA GENE POLYMORPHISMS WITH THE PRESENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background Chronic Obstructive Pulmonary Disease (COPD) will be the highest cause of mortality and morbidity in the world. Data showed that 85–90% of COPD cases are caused by smoking, but only 15–20% of chronic heavy smokers who will develop COPD. This indicates a different susceptibility to damage from smoking that may be linked to genetic factors. The purpose of this study was to analyze the occurrence of Chronic Obstructive Pulmonary Disease role path of -308G/A, -238G/A TNFalpha gene polymorphism and +252A/G LTalpha gene polymorphism in smokers.
Method Case-control study, comparing the genetic group of people who have COPD (cases) and a group of people who do not suffer from COPD (control) with the same smoking history. Implementation of the study started from January 2011 to March 2012 at several locations, among others: Pulmonary Clinic RSUP. H. Adam Malik, RS. Pirngadi, RS. Tobacco Deli, RS. Siti Hajar in Medan and several health centers in the city of Medan. Examination of lung function using spirometry was performed and gene analysed by PCR-RFLP.
Result From the total of 227 people obtained, the sample that met the study inclusion, exclusion criteria and equalizing the age and history of smoking, there are as many as 186 people (93 people as the case group and 93 people as the control group). For polymorphism-308G/A TNFalpha gene OR = 0.436, CI = 0.224 to 0.850 and p = 0.014. For polymorphism -238G/A TNFalpha gene OR = 2.094, CI = 0.608 to 7.211 and p = 0.241. Polymorphism +252A/G LTalpha gene OR = 1,256, CI = 0.694 to 2.272 and p = 0.450.
Conclusion Polymorphism-308 TNFalpha gene shown to be a protective factor for the occurrence of COPD. Polymorphism -238 TNFalpha gene and +252 LTalpha gene has not been proven association with COPD.
Keywords Chronic Obstructive Pulmonary Disease, TNFalpha gene, LTalpha gene and polymorphism.

PS376

CIGARETTE SMOKE IMPAIRS ALVEOLAR MACROPHAGE PHAGOCYTOSIS FOR APOPTOTIC NEUTROPHILS VIA INHIBITION OF HISTONE DEACETYLASE/RAC/CD9 PATHWAYS

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Background and Aim of Study Efferocytosis, homeostatic phagocytosis of apoptotic cells, prevents the release of toxic intracellular contents and subsequent tissue damage. Impairment of efferocytosis was reported in alveolar macrophages (AMs) of patients with chronic obstructive pulmonary disease (COPD), a common disease caused by smoking. In COPD, histone deacetylase (HDAC) activity is reduced in AMs. We investigated whether the reduction of HDAC activity is associated with the impairment of efferocytosis.
Methods Murine AMs were collected by bronchoalveolar lavage. Pretreatment of AMs with cigarette smoke extract (CSE) or trichostatin A (TSA) and their ability of efferocytosis for apoptotic human polymorphonuclear leucocytes was assessed. RhoA or Rac activity was evaluated by enzyme-linked immunosorbent assay and colorimetric approaches. Surface expressions on AMs were analyzed by flow cytometry.
Results CSE or TSA reduced HDAC activity and suppressed efferocytosis. TSA inhibited the activity of Rac, a key mediator of efferocytosis. These TSA-induced impairments were restored by treatment of AMs with aminophylline, a potent activator of HDAC. To further elucidate the underlying mechanism, we explored a role of CD9 in TSA-induced impairment of efferocytosis. CD9 is a tetraspan transmembrane protein, that facilitates the uptake of several pathogens and materials. TSA profoundly down-regulated the expression of CD9 on AMs. The expression of CD9 was partly down-regulated by Rac inhibitor. Finally, pretreatment of anti-CD9 mAbs inhibited efferocytosis, which was attributable to the reduced binding of AMs to apoptotic cells.
Conclusion Cigarette smoking impairs efferocytosis via inhibition of HDAC/Rac/CD9 pathways. Aminophylline/theophylline is effective for restoring the impairment of efferocytosis and might have benefit for the treatment of patients with COPD.

PS377

ELASTASE INDUCES EMPHYSEMA VIA THE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS TRIGGERING OF AIRWAY STRUCTURAL CELLS

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Rationale Pulmonary emphysema is characterized by persistent inflammation and progressive alveolar destruction. The receptor for advanced glycation end products (RAGE) is a multi-ligand cell surface receptor, reported to be involved in the process of acute alveolar epithelial cell injury. However, the role of RAGE in pulmonary emphysema is not well defined. We investigated the role of RAGE in the development of elastase-induced pulmonary emphysema.
Methods RAGE sufficient (RAGE+/+) mice and RAGE deficient (RAGE-/-) mice were treated with intratracheal elastase on day 0. Airway inflammation, static compliance (Cst), lung histology and the levels of neutrophil-related chemokine and pro-inflammatory cytokines in bronchoalveolar lavage (BAL) fluid were determined on days 4 and 21.
Results Neutrophilia in BAL fluid, seen in elastase-treated RAGE+/+ mice, was reduced in elastase-treated RAGE-/- mice on day 4, which was associated with decreased levels of KC, MIP-2 and IL-1beta. Cst values and emphysematous changes in the lung tissue were decreased in RAGE-/- mice compared to RAGE+/+ mice on day 21 after elastase treatment. Experiments using irradiated chimeric mice showed that the mice expressing RAGE on radioresistant structural cells but not hematopoietic cells developed elastase-induced neutrophilia and emphysematous change in the lung. In contrast, the mice expressing RAGE on hematopoietic cells but not radioresistant structural cells showed reduced neutrophilia and emphysematous change in the lung.
Conclusions These data identify the importance of RAGE expressed on lung structural cells in the development of elastase-induced pulmonary inflammation and emphysema. Thus, RAGE represents a novel therapeutic target for preventing pulmonary emphysema.

2-E2: RESPIRATORY NEUROBIOLOGY AND SLEEP 1

PS378

OBESITY HYPOVENTILATION SYNDROME IN JAPAN AND INDEPENDENT DETERMINANTS OF ARTERIAL CARBON DIOXIDE LEVELS

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Backgrounds and Aim of Study That obstructive sleep apnea (OSA) occurs at a lower body mass index (BMI) in Asian population compared to those of European descent is well known. However, characteristics of Asian patients with obesity hypoventilation syndrome (OHS) have not yet been established. We aimed to reveal the prevalence of OHS and characteristics of individuals with OHS in Japan, which clarified the factors related to hypercapnia in OHS patients.
Methods We studied 983 consecutive patients hospitalized for examination of OSA from October 2008 to September 2012. Multiple regression analysis was performed to identify variables independently associated with arterial carbon dioxide pressure ($PaCO_2$) in the 162 obese OSA (BMI > 30 kg/m^2 and apnea-hypopnea index (AHI) > 5/h).
Results The prevalence of OHS in OSA and that in obese OSA were 2.3% and 12.3%, respectively. In addition to increased $PaCO_2$ and AHI, patients with OHS had a lower expiratory residual volume even after adjustment for waist circumference. Multiple regression analysis revealed that independent of age and BMI, arterial oxygen pressure (PaO_2) (contribution rate (R^2) = 7.7%), 4% oxygen desaturation index (ODI) (R^2 = 8.9%), %carbon monoxide diffusing capacity/alveolar volume (%DLco/VA) (R^2 = 8.3%), and hemoglobin concentration (R^2 = 4.9%) as well as waist circumference (R^2 = 4.9%) were independently associated with $PaCO_2$. With long-term continuous positive airway pressure (CPAP) treatment (12.3 ± 4.6 months), the $PaCO_2$ levels in 12 of the 14 patients with OHS improved.
Conclusions The prevalence of OHS in obese OSA in Japan was approximately the same as in the West, even at less obesity (BMI 36.7 ± 4.9 kg/m^2). Factors contributing to the elevation of %DLco/VA (hemoglobin concentration, cardiac output, etc.) should be considered in the management of OHS. And the long-term CPAP treatment was effective to attain $PaCO_2$ < 45 mmHg in OHS patients.

PS379

THE DOSE-RESPONSE RELATIONSHIP BETWEEN CPAP ADHERENCE AND THE DAILY PERFORMANCE IN SUBJECTS WITH OSA

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Background and Objectives Obstructive sleep apnea (OSA) affects our daily functional and cognitive performance. Continuous Positive Airway pressure (CPAP) treatment may improve our symptoms and quality of life to different extents. This study investigated the relationships between CPAP adherence and daytime sleepiness, quality of life, emotion, and adherence-related cognition in subjects with OSA, after 1 year of CPAP use.
Methods Subjects who were newly diagnosed of OSA and CPAP therapy navie were recruited. Epworth sleepiness scale (ESS), Calgary sleep apnea quality of life index (SAQLI), Depression anxiety stress scale (DASS21), and Self-efficacy measure for sleep apnea questionnaire (SEMSA), were assessed before and after 1 year of CPAP treatment. CPAP usage data were downloaded at the completion of this 1-year study. Regression analyses were performed to assess the dose-response relationship between CPAP adherence and daily performance in subjects with OSA.
Results 100 subjects with OSA indicated for CPAP treatment were recruited, with an average age of 52 ± 10 years, BMI of 29.0 ± 5.5 kg/m^2, and AHI of 36.2 ± 22 events/hour. After one year of CPAP treatment, average CPAP daily usage was 3.5 ± 2.7 hours per day and usage index (the percentage of days using CPAP for at least 4 hours per day) was 48% ± 38%. And, the CPAP usage index was found to have dose-response effects on the improvement of sleepiness [ESS score: β = –4.016 (–6.076, –1.956)], quality of life [total SAQLIscore: β = 0.468 (0.011, 0.924)], emotion [total DASS score: β = –5.432 (–10.836, –0.028); DASS stress score: β = –3.011 (–5.618, –0.404)], adherence-related cognition [SEMSA outcome expectation score: β = 0.661 (0.335, 0.987); SEMSA treatment self-efficacy score: β = 0.842 (0.470, 1.215)], even after adjustment for their baseline values. Similar findings were also shown with daily CPAP usage.
Conclusions After 1-year CPAP treatment, the CPAP adherence was shown significant dose-related improvements in the functional and cognitive performance in subjects with OSA.

PS380

PREVALENCE OF DIABETES AND IMPAIRED GLUCOSE TOLERANCE IN PATIENTS WITH SLEEP APNEA SYNDROME

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Background and Aim of Study Patients with sleep apnea syndrome (SAS) and patients with diabetes mellitus (DM) are increasing in Japan. We sought to assess the recent prevalence of DM and the glucose tolerance profile of patients with SAS.
Methods Data from 103 patients with SAS (apnea-hypopnea index > 5 events/hr; male 76, female 27; mean age 53.8, mean body mass index 28.6) were reviewed. A 75 gm oral glucose tolerance test (OGTT) was performed in SAS patients who had not been diagnosed with DM. Homeostasis model assessment insulin resistance index (HOMA-R) and insulinogenic index (II) were calculated. We adopted the diagnostic criteria of the Japan Diabetic Society and the American Diabetes Association.
Results 24 SAS patients (23.3%) had already been diagnosed with DM. 7 SAS patients (6.8%) were diagnosed with diabetes at the time of the current OGTT. 24 SAS patients (23.3%) were diagnosed with impaired glucose tolerance and/or impaired fasting glucose. 48 SAS patients (46.6%) were normal on OGTT, but 13 were found to have a one-hour serum glucose level higher than 180 mg/dl. Abnormal HOMA-R and abnormal II were found in 51.9% and 24.7% of subjects, respectively.
Conclusion 30.1% of SAS patients had DM and only 17.5% of SAS patients had intact glucose tolerance.

PS381

SLEEP ASSESSMENT OF COPD PATIENTS BY ACTIGRAPHY AND TYPE 3 PORTABLE MONITORING: A POPULATION-BASED STUDY OF MALE EMPLOYEES IN JAPAN

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Background and Objective Sleep disturbances in patients with chronic obstructive pulmonary disease (COPD) such as poor sleep quality, nocturnal oxygen desaturation, and the presence of coexistent obstructive sleep apnea (OSA), which is called overlap syndrome, have been described in several reports. However, in the majority of previous reports, sleep was assessed by polysomnography or subjective reports. This is the first population-based study that assessed sleep quality and hygiene in COPD patients using an actigraphy and type 3 portable monitoring in a home environment. This study aimed to determine the prevalence of COPD patients and patients with overlap syndrome in urban Asian male subjects by actigraphy and type 3 portable monitoring at home.
Methods A cross-sectional epidemiological health survey of 303 male employees (age 43.9 ± 8.2 y; body mass index 24.0 ± 3.1 kg/m^2: mean ± SD) was done. Sleep quality was measured by the Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI). A Respiratory Disturbance Index (RDI) of 5 and over indicated OSA.
Results Nineteen subjects (6.3%) had COPD and 181 (59.7%) had OSA. Eleven (3.6%) had overlap syndrome. Sleep duration, ESS, and PSQI scores were not significantly different between COPD patients and normal control subjects. However, COPD patients had significantly longer sleep latency ($P = 0.019$), lower sleep efficiency ($P = 0.017$), and a higher sleep fragmentation index ($P = 0.041$) and average activity ($P = 0.0097$) during sleep than control subjects. They also had a significantly higher RDI and more severe desaturation during sleep than control subjects ($P < 0.01$). The difference remained after adjustment for age and BMI, but disappeared following adjustment for RDI.
Conclusions From population-based data collected by actigraphy and type 3 portable monitor in the home environment, even patients with mild-to-moderate COPD had nocturnal desaturation and OSA-related impaired sleep quality although the ESS or PSQI revealed no significant symptoms.

PS382

LONG-TERM EFFECTS OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ON PULMONARY FUNCTIONS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA PATIENTS (OSAS)

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Background and Aim Nasal CPAP (nCPAP) has been a first-line treatment for patients with OSAS. Although nCPAP can completely abolish upper airway occlusion and apnea during sleep, substantial high pressure affects pulmonary systems of patients and may be harmful in long-term duration. However, long-term effects of nCPAP on pulmonary functions and arterial blood gases are still unclear. Therefore, we investigate the changes of pulmonary functions before and after nCPAP treatment on long-term duration in patients with OSAS.
Method Seventy-five male patients with OSAS who underwent nCPAP therapy more than 5 years were included in this study. Pulmonary function test and blood gas analysis were performed before and after 7 and 14 years after treatment. Pulmonary function tests consisted of spirometry, pulmonary volumes, diffusion capacity and flow-volume curve. Subjects were divided in two groups, high pressure group (nCPAP > 10 cmH2O) and low pressure group (nCPAP < 10 cmH2O) and the changes of pulmonary functions were compared between two groups.
Results There were no significant changes on pulmonary functions (%VC, FEV1.0%, %FEV1.0, %TLC, %FRC, %RV, and %DLco) and arterial blood gases (PaO2, PaCO2, and pH). before and after 7 years and 14 years of nCPAP treatment. There were no significant changes of pulmonary functions and blood gases between low pressure groups and high pressure groups.
Conclusion Long-term nCPAP treatment did not affect on pulmonary functions and arterial blood gases in patients with OSAS, even in patients with high pressure (>10 cmH2O). nCPAP is safe treatment for patients with OSAS in long-term duration.

PS383

SYSTEMIC INFLAMMATORY PATTERNS IN PATIENTS WITH OVERLAP SYNDROME (OSAS AND COPD)

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Background and Aim of Study Obstructive sleep apnea syndrome (OSAS) patients concomitant with chronic obstructive pulmonary disease (COPD), termed as overlap syndrome (OS), have a worse prognosis than patients with only one of these diseases. The aim of this study is to investigate alterations of systemic inflammatory mediators in patients with OSAS, COPD, and OS and to explore relations between serum levels of inflammatory mediators and polysomnography (PSG) variables, pulmonary function variables, and scores of health status questionnaires in OS patients.
Methods This prospectively observational study was implemented from March, 2012 to May, 2013 and designed with three groups as follows: COPD group included patients with naïve COPD alone; OSAS group included patients with moderate-to-severe OSAS alone; OS group included patients with OSAS and naïve COPD. Venous blood samples were obtained in the morning of PSG.
Results A total of 46 patients (13 OSAS patients, 13 COPD patients and 20 OS patients) were enrolled. High-sensitive C-reactive protein (hs-CRP) was elevated in OS patients as compared with OSAS patients and COPD patients ($p = 0.027$ and $p = 0.013$, respectively). Tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) were elevated in OS patients as compared with OSAS patients. Hs-CRP, TNF-α and IL-6 were similar between OSAS patients and COPD patients. Interleukin-8 (IL-8) was similar among three groups. In OS patients, IL-6 and IL-8 were negatively correlated with first second of forced expiratory volume/forced vital capacity(FEV1/FVC) and total lung capacity(TLC), respectively ($r = -0.48$, $p < 0.05$; $r = -0.83$, $p < 0.001$, respectively). The tested inflammatory mediators showed no correlation with PSG variables (Apnea-hypopnea index, lowest SaO2, and mean SaO2) and scores of health status questionnaires (COPD assessment test and modified Medical Research Council Dyspnea Scale).
Conclusion As compared with OSAS patients and COPD patients, OS patients had significantly higher systemic inflammatory mediators and were negatively correlated with FEV1/FVC and TLC.

PS384

DISSOCIATIVE IDENTITY DISORDER AND CENTRAL HYPERSOMNOLENCE: CO-MORBID DIAGNOSES, OR THE SAME PHENOMENA AT DIFFERENT ENDS OF A SPECTRUM?

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Introduction Dissociative Identity Disorder (DID), formerly known as Multiple Personality Disorder, is characterised by more than one personality state within an individual. Although the prototypical DID is distinguished by a dominant alternate identity(-ies) enforcing complete amnesia in the primary identity, there is a spectrum of amnestic qualities that are best described as 'overlapping identities'. The Polysomnographic (PSG) diagnosis of Idiopathic Hypersomnolence (IH) in an individual with DID has never been described. The symptomatic boundary state of DID has also never been described in sleep terms.
Method We report a case of DID, and co-morbid IH. Patient A had a normal Epworth Sleepiness Scale (ESS) of 9/24 with phenomena more akin to Hypersomnolences of Central Origin. She described daytime 'identity overlapping' similar to her primary identity 'falling asleep', streams of consciousness interrupting her sleep entry and exit, frequent abnormal tactile and visual hallucinations suggestive of Hypnagogic Hallucinations, and recurrent symptomatic Sleep Paralysis. Her PSG and MSLT (off medications) was consistent with IH. Both her daytime and boundary symptoms improved with modafinil.
Results The cardinal features of DID and Central Hypersomnolences may appear distinctly different, but some manifestations share common elements. Daytime sleepiness in DID may be misconstrued as the day-time shift in the dominant identity. Excessive Daytime Sleepiness and its psychiatric interpretations are amenable to modafinil.
Discussion This is the first unique reported case of co-morbid IH in DID. These diagnoses may mutually co-exist. Alternatively they could be the same phenomenon at different ends of one spectrum: one occurring in isolation at the boundary of sleep, another occurring intermittently in both wake-and-sleep. Questions remain regarding where her alternate entities reside, and if Modafinil is in fact simply suppressing these.

2-E3: RESPIRATORY NEUROBIOLOGY AND SLEEP 2

PS385

IMPROVEMENTS IN PATIENT'S MOOD WITH DIFFERENT TREATMENTS IN OBSTRUCTIVE SLEEP APNE

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Background Obstructive sleep apnea (OSA) is a sleep disorder with repeated nocturnal desaturation and sleep fragmentation. It can lead to poor sleep quality, anxiety and depression. Our goal was to investigate short term (one month) and long term (six months) improvement of anxiety and depression in patients with different treatments of OSA.
Methods This was a prospective, non-randomized and hospital-based study. There were 44 patients (Male/female: 38/6) suffering from OSA with definition of apnea/hypopnea index (AHI) >15/hr. The studied subjects were divided into three groups: surgery group(Uvulopalatopharyngoplasty, UPPP), CPAP group (continuous positive airway pressure) and no treatment group(even under doctor's encouragement). All subjects completed Beck Depression Inventory II(BDI-II), Beck Anxiety Inventory(BAI) and Pittsburgh Sleep Quality Index(PSQI) before treatment, 1 and 6 months after treatment.
Result Compared to patients without treatment of OSA (no treatment group), surgery group and CPAP group had higher body mass index, scored higher in AHI and Epworth Sleepness Scale, whereas no difference in BAI, BDI and PSQI between group was registered. Only CPAP group had significant difference in BDI ($p = 0.03$) after one-month treatment. The surgery group and CPAP group had significant decrease in BDI (Surgery group: $p = 0.025$; CPAP group: $p = 0.011$) and PSQI (Surgery group: $P = 0.027$; CPAP group: $P = 0.001$) after six-month treatment. The CPAP group had significant difference in BAI ($P = 0.043$) after six-month treatment. However, no significant differences were present in BAI in surgery group after six-month treatment. No significant differences were either present in BDI, BAI and PSQI in no treatment group during 1 month or 6 months follow up.
Conclusion CPAP can improve OSA patient's mood within one month treatment, as well as decrease anxiety, depression and improve sleep quality in six-month treatment. OSA patients have also significant improvement in measures of depression and sleep quality after surgical treatment in six months.

PS386

INTERMITTENT HYPOXIC EXPOSURE ENHANCES THE RELEASE OF VON WILLEBRAND FACTOR FROM HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS

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Backgrand Patients with obstructive sleep apnea (OSA) have an increased risk of thrombotic cardiovascular events without CPAP therapy. We previously reported the loss of plasma high molecular weight-VWF multimers during sleep was related to the severity of OSA and low-level platelet consumption in patients with OSA (Koyama N et al, Eur Respir J, 2012). However, the relationships of intermittent hypoxia (IH) which characterize OSA and an increased risk of thrombosis have not been fully revealed.
Aims To reveal the relationships of IH and VWF, we evaluated VWF releasing from human umbilical vein endothelial cells (HUVEC) under circumstance of intermittent hypoxia (IH) or normoxia.
Methods HUVEC were exposed to 16 cycles/6 h, 32 cycles/12 h and 64 cycles/24 h of IH (5 min $1\%O_2$/10 min $21\%O_2$) or normoxia with cell culture system controlled by change of gases. After the exposure, the cell culture supernatants were collected. VWF antigens were measured with ELISA.
Results The increased ratio of VWF in IH was 2.11 ± 0.04 and in normoxia was 1.82 ± 0.14 after 6 hours exposure. The increased ratio of VWF in IH was 2.72 ± 0.16 and in normoxia was 2.19 ± 0.12 after 12 hours exposure. The increased ratio of VWF in IH was 2.98 ± 0.33 and in normoxia was 2.29 ± 0.21 after 24 hours exposure. The increased ratio of VWF showed significantly higher in IH than normoxia in all exposure periods.
Conclusion Intermittent hypoxic exposure enhances the release of von Willebrand factor from human umbilical vein endothelial cells.

PS387

THE ASSOCIATIONS AMONG ANTHROPOMETRIC INDEXES, METABOLIC SYNDROME AND OBSTRUCTIVE SLEEP APNEA IN A KOREAN POPULATION

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Background This study is to evaluate anthropometric indexes and metabolic syndrome (MetS) in patients with and without obstructive sleep apnea (OSA).
Methods Anthropometric indexes including neck circumference (NC), waist circumference (WC), and body mass index (BMI), and MetS were assessed in 191 consecutive subjects who visited the sleep clinic in St. Paul's Hospital for evaluating OSA. OSA was defined as >= 5 apnea-hypopnea index.
Results This study included 155 subjects with OSA (81%). The Prevalence of MetS was significantly higher in OSA group than in non-OSA group (58% vs. 33%, $p = 0.007$). NC ($r = 0.526$, $p = 0.01$), WC ($r = 0.570$, $p = 0.01$), and BMI ($r = 0.511$, $p = 0.01$), and the number of MetS components ($r = 0.268$, $p = 0.01$) were significantly correlated with AHI. The optimal cut-off values for predicting OSA were determined that the value of 34 cm in NC, 84 cm in WC, and 26.6 kg/m^2 in BMI were optimal for female, and that the value of 38 cm in NC, 88 cm in WC, and 25.0 kg/m^2 in BMI were optimal for male. After adjusting age, sex, alcohol consumption, and smoking, logistic regression models showed that NC (OR, 1.33, $p < 0.001$), WC (OR, 1.15,$p < 0.001$), BMI (OR, 1.39, $p < 0.001$), number of MetS components (OR, 1.47, $p = 0.029$), and MetS (OR, 2.36, $p = 0.004$) were significantly associated with the presence of OSA. Linear regression models showed that NC ($\beta = 3.954$, $p < 0.001$), WC ($\beta = 1.449$, $p < 0.001$), BMI ($\beta = 3.479$, $p < 0.001$), number of MetS components ($\beta = 5.833$, $p < 0.001$), and MetS ($\beta = 11.827$, $p = 0.004$) were significantly associated with the severity of OSA.
Conclusion Increased anthropometric indexes and number of MetS components were significant risk factors for the presence and severity of OSA.

PS388

ENHANCING LONG-TERM CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) COMPLIANCE WITH A SPECIALIST NURSE CLINIC

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Introduction In 2009, we demonstrated that acceptance rate of Continuous Positive Airway Pressure (CPAP) treatment in patients diagnosed with Obstructive Sleep Apnoea (OSA) was significantly higher with an additional 15-minute individual consultation after the "usual" structured educational talk than those having the talk alone.
Objective A Specialist Nurse-Clinic follow-up would be offered to all patients who agreed to receive CPAP therapy, where the use and compliance of CPAP treatment would be monitored and evaluated.
Methodology It's a retrospective study to evaluate 1-year CPAP compliance rate in 2011 after CPAP therapy from both medical and nursing consultation notes. Patients were all scheduled to the clinic one-month after initiation of CPAP therapy. Respiratory nurses would deal with problems associated with machine, accessories or interface. Data reading including average usage hours, mask leakage, residual Apnoea-Hypnoea-Index was recorded. Advices were frequently offered to enhance comfort and adherence. Overnight oximetry reports would be reviewed. Phone follow-up would be offered if necessary.
Results 90% of 259 patients attended the educational talk and 15-minute individual consultation. Although 77.4% patients initially agreed for CPAP therapy, only 140 patients attended the nurse clinic and the rest attended physician clinics. 84 patients (60%) reported problems related to CPAP during follow-up, of which 86% were eventually solved. Acceptable compliance was defined by Kribbs et al. as CPAP use at least 4 h/day for at least 70% of the nights per week. The CPAP compliance rates were significantly higher for patients attending specialist nurse-clinic (86.4%) than those who did not (52.1%) (physician follow-up only). ($p < 0.001$).
Conclusion A Specialty Nurse Clinic on CPAP therapy can improve patient compliance with CPAP therapy.

PS389

NOVEL HYPOTHESIS: PANIC DISORDER COULD BE A LUNG DISEASE

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Background Panic disorder (PD) is a complex condition that is further complicated by its numerous inducers, which include hypercapnia, hypoxia, sodium lactate, caffeine and cholecystokinin. It seems unlikely that there are specific suffocation receptors for each of these inducers in the brain. Novel hypothesis for the cause of panic disorder should be submitted without the brain.
Methods The pulmonary neuroepithelial bodies (NEBs), which are situated at the bifurcation point of the small bronchi, act as storage cells for 5-hydroxytryptamine (5-HT) and sensors for suffocation. If we suppose that PD might represent hyperfunction of inflammatory NEBs, bradykinin (BK) which augments the airway hyper-response to diverse indcers might cause these cells to release 5-HT along with peptides and panneuroendcrine markers from their dence-core secretory granules. It was revealed that BK with 5-HT could cross the blood-brain barrier (BBB).
Results When 5-HT released from these cells along with BK cross the BBB, the release of 5-HT at the axonal terminals in the serotonergic neurons in the brain will be inhibited by the 5-HT1A autoreceptor. The inhibition of 5-HT at the axonal terminal causes to suppress the periaqueductal gray matter, which inhibits flight reactions to impending danger, pain or asphyxia. In short, this serotonergic situation might bring about PD.
Conclusion According to this theory, the type of inducer that the PD patient is exposed to is unimportant as long as it stimulates the NEBs, and through the effect of 5-HT and BK, PD would be revaluated as a lung disease that directly and reversibly affects the brain.

PS390

CHRONIC INTERMITTENT HYPOXIA/REOXYGENATION FACILITATE AMYLOID-BETA GENERATION IN MICE

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Background and Aim of Study Previous studies have shown a high prevalence of obstructive sleep apnea (OSA) among patients with Alzheimer's disease (AD). However, it is poorly assessed whether chronic intermittent hypoxia (CIH), which is a characteristic of OSA, affects the pathophysiology of AD. We aimed to investigate the direct effect of intermittent hypoxia (IH) in pathophysiology of AD in vivo and in vitro.
Methods In vivo, 15 male triple transgenic AD mice were exposed to either CIH or normoxia (5% O2 and 21% O2 every 10 min, 8 h/day for 4 weeks). The amyloid-beta (Abeta) profile, cognitive brain function and brain pathology were evaluated. In vitro, human neuroblastoma SH-SY5Y cells stably expressing wild-type amyloid beta precursor protein were exposed to either IH (8 cycles of 1% O2 for 10 minutes followed by 21% O2 for 20 minutes) or normoxia. The Abeta profile in the conditioned medium was analyzed.
Results CIH significantly increased levels of Abeta42 but not Abeta40 in the brains of mice without the increase in hypoxia-inducible factor 1, alpha subunit (HIF-1alpha) expression. Furthermore, CIH significantly increased intracellular Abeta in the brain cortex. There were no significant changes in cognitive function. IH significantly increased levels of Abeta42 in the medium of SH-SY5Y cells without the increase in the HIF-1alpha expression. CIH directly and selectively increased levels of Abeta42 in the AD model.
Conclusion Our results suggest that OSA would aggravate AD. Early detection and intervention of OSA in AD may help to alleviate the progression of the disease.

PS391

THE POTENTIAL ROLE AND MECHANISM OF 17BETA-ESTRADIOL ON IH INDUCED ENDOTHELIAL CELL INJURY

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Objective to explore whether estrogen/Trx-1/Txnip-1 participates in protecting cells from injury under the condition of intermittent hypoxia.
Methods ECV304 human umbilical vein endothelial cells (HUVECs) was used in this experiment. After 16 h intermittent hypoxia, Endothelial impairment was assessed through detecting proliferation and apoptosis by WST-1 methods and flow cytometry respectively. MDA and GSH content were measured by TBA and DTNB method respectively. ELISA method is used for measuring IL-6 and IL-8. Trx and Txnip mRNA levels were measured by real time-PCR.
Results Compare with intermittent air(IA) group, apoptosis rate of HUVECs in intermittent hypoxia (IH), IH and estrogen administration (IHE2)group decreased ($P = 0.0363$), while the proliferation rate increased ($P = 0.00358$). The MDA levels in IH group were significantly increased and GSH decreased($P = 0.0038$, $P = 0.0006$ respectively); MDA levels in IHE2 group was significantly lower than IH group, while GSH levels were higher ($P = 0.0263$, $P = 0.0101$ respectively). Compare with IA group, IL-6 and IL-8 levels in IH group were significantly increased ($P = 0.0018$, $P = 0.0033$ respectively); while the IHE2 group was significantly decreased ($P = 0.0025$, $P = 0.0472$ respectively). Except for the IAE2 group (1.92 ± 0.72), Trx-1 mRNA expression of cells in IH group (2.47 ± 0.41) and IHE2 group (3.28 ± 0.45) was higher than IA group (1.72 ± 0.14) ($p < 0.05$) and Txnip-1 mRNA expression levels in IHE2 group (2.36 ± 0.55) was significantly lower than IA group (6.82 ± 0.66), IAE2 group (5.83 ± 0.26) and IH group (4.71 ± 0.59) ($p < 0.05$).
Conclusions Estrogen/Trx-1/Txnip-1 pathway may participate in reducing oxidative stress and inflammatory response to protect cells from IH-induced injury.

PS393

CRITICAL ILLNESS POLYNEUROMYOPATHY PRESENTING AS BULBAR PALSY: A CASE REPORT

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Critical illness polyneuromyopathy is a clinical disorder which is a significant source of ICU- related morbidity. It usually affects the lower limbs and leads to skeletal muscle weakness, leading to neuromuscular impairment, difficulty weaning from the mechanical ventilator and prolonged rehabilitation. We present a case of a 58 year old female admitted due to dysphagia with recent history of acute myocardial infarction, on statin and steroids for joint inflammation. Upon admission, patient was stable complaining of dysphagia and cough with difficulty in expectoration. At the wards she had dyspnea and hypotension and was intubated. Videofluoroscopic studies showed motility dysfunction. Total creatine kinase and creatine kinase MM were elevated. Electromyography nerve conduction studies showed severe motor and sensory denervation of the limbs indicating axonal dysfunction compatible with critical illness polyneuropathy. Patient was treated for sepsis from pneumonia, had aggressive glycemic control, weaned from the ventilator, referred to rehabilitation and improved. She was discharged with improved muscle strength with resolution of dysphagia. This case is unusual since it presented initially with bulbar palsy rather than weakness of the lower extremities.

2-E4: CRITICAL CARE MEDICINE 1

PS392

MANAGEMENT OF RESPIRATORY FAILURE IN SEVERE NEUROPARALYTIC SNAKE BITE, EXPERIENCE OF AN INDIAN TERTIARY CARE HOSPITAL

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Background Poisonous snake bites are a common, fatal emergency in India. The aim was to treat patients with neuroparalytic snake bite using polyvalent Anti snake venom(ASV) along with ventilatory support and to assess outcome with respect to hospital survival, duration of mechanical ventilation, amount of ASV given and complications associated with mechanical ventilation or ASV.
Methods The study included 58 patients with neurotoxic evenomation requiring mechanical ventilation for respiratory failure. They were administered 200 ml of polyvalent ASV. Outcome measures studied included hospital survival, duration of mechanical ventilation, amount of ASV given and complications associated with mechanical ventilation or ASV ventilation.
Result All patients were administered an initial bolus dose of 200 ml ASV, followed by repeated doses of 100 ml ASV every six hours until signs of neurological recovery. Mean total dose of ASV administered was 412 ml. All patients were initially ventilated using Assist control(A/C) mode of ventilation. Mean duration of ventilation on A/C mode was 30.89 hours. 56 patients were weaned off successfully using pressure support ventilation. Mean duration of weaning was 7 hours. 4 patients developed Ventilator associated pneumonia 2 patients expired, one due to ventilator associated pneumonia and the other due to septicaemia.
Conclusion We conclude that in the management, administration of a high initial bolus dose of 200 ml ASV and repeated doses of 100 ml ASV every six hours until signs of neurological recovery, supported by Assist control mode of ventilation resulted in an early recovery, a reduced total dose of ASV consumed, reduced the duration of mechanical ventilation, reduced the incidence of complications and was more cost effective.

PS394

CHARACTERISTICS OF PNEUMOTHORAX PATIENTS INCIPTO MANGUNKUSUMO NATIONAL CENTER GENERAL HOSPITAL

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Background and Aim of Study Factors cause pneumothorax is very important. Data about pneumothorax patients in Indonesia is still limited. The aim of the study was to determine the characteristics of pneumothorax patients during hospitalization in Cipto Mangunkusumo Hospital.
Methods Retrospective cohort study design conducted on 104 pneumothorax patients who were admitted 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 ($SD \pm 16.2$ years) with a male to female ratio of 3:1. Commonest symtoms of pneumothorax was shortness of breath 103(53.3%) and abnormalities on physical examination was hypersonor 101(57.3%). Plain chest X-ray of pneumothorax patients showed hyperlucent avascular only 95(91.4%) and hyperlucent avascular with infiltrates 79(88.7%). Risk factors for the incidence 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%). Commonest type of pneumothorax was secondary spontaneous pneumothorax 49(47.1%). Most of pneumothorax patients were successfully managed by chest thoracoscopy 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%). Factors that worsen the survival rate of pneumothorax patients were chest trauma (HR = 3.49 (95% CI 1.52 to 8.04)) and pulmonary tuberculosis (HR = 3.33 (95% CI 1.39 to 7.99)).
Conclusions Etiology of 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 thoracostomy. Outcome of pneumothorax patients were live. Cause of death in pneumothorax patients was respiratory failure.

PS395

SURVIVAL OF PNEUMOTHORAX PATIENTS INCIPTO MANGUNKUSUMO GENERAL HOSPITAL NATIONAL CENTER

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Background and Aim of Study Factors cause pneumothorax is very important. Implementation of proper guidelines in cooperation of an interdisciplinary medical science and overall management of pneumothorax is necessary. aim of the study was to determine the characteristics of pneumothorax patients and factors affecting survival in Cipto Mangunkusumo National Center General Hospital.
Methods Retrospective cohort study design was conducted on pneumothorax patients admitted in January 2000 to December 2011. Patients observed for 7 days regarding survival and factors influenced. Cumulative survival rate for 7 days was analyzed by Kaplan Meier and log-rank test. Cox proportional hazard regression was assign to calculate hazard ratio (HR).
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. Commonest symtoms of pneumothorax was shortness of breath 103(53.3%) and abnormalities on physical examination was hypersonor 101(57.3%). Plain chest X-ray of pneumothorax patients showed hyperlucent avascular only 95(91.4%) and hyperlucent avascular with infiltrates 79(88.7%). Risk factors for the incidence 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%). Commonest type of pneumothorax was secondary spontaneous pneumothorax 49(47.1%). Most of pneumothorax patients were successfully managed by chest thoracoscopy 98(82.3%). Outcome of pneumothorax patients were live 69(66.3%), died 35(33.7%). Causes of death was respiratory failure 16(45.8%) and factors that worsen the survival rate were chest trauma (HR = 3.49 (95% CI 1.52 to 8.04)) and pulmonary tuberculosis (HR = 3.33 (95% CI 1.39 to 7.99)).
Conclusions Factors that worsen the survival rate of pneumothorax patients were chest trauma (HR = 3.49 (95% CI 1.52 to 8.04)) and pulmonary tuberculosis (HR = 3.33 (95% CI 1.39 to 7.99)).

PS396

THE VALUE OF PERIPHERAL OXYGEN SATURATION AS A PROGNOSTIC TOOL FOR CRITICALLY ILL MEDICAL EMERGENCY PATIENTS

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Background and Aim of the Study Oxygen supply impairment due to acute physiological deterioration may increase the risk of poor prognosis, particularly in critically ill patients with inadequacy to compensate such changes. Pulse oxymeter is a rapid, simple and inexpensive tool that can be used to measure patient's initial oxygen saturation. The aim of the study was to evaluate peripheral oxygen saturation (SpO2) at admission in predicting the mortality of critically ill medical emergency patients in Cipto Mangunkusumo Hospital (CMH), a tertiary hospital referral center in Indonesia.
Methods We performed a prospective cohort study of critically ill medical patients in resuscitation room, Emergency Department (ED) of CMH from October to November 2012. Subjects were divided into 2 groups according to their SpO2 which meassured at admission: group with admision SpO2 95% or above (1) and SpO2 less than 95% (2). The outcome was 30-day mortality. Log-rank test was used to analyze survival between groups. The risk of 30-day mortality was analyzed with Cox proportional hazard model.
Results A total of 172 patients were included during the study. 30-day mortality was observed in 68 patients (39.5%). Patients with SpO2 less than 95% had a significantly lower survival rate [mean survival 22.8 (SE 3.77) days] compared to patients with SpO2 95% or above [mean survival 28.6 (SE 2.96) days], log-rank test $p = 0.011$. The hazard ratio of 30-day mortality was 1.8 (95% CI 1.10 to 2.87) in patients whose SpO2 fell below 95%.
Conclusions Peripheral oxygen saturation below 95% at admission was significantly associated with increased risk of 30-day mortality. Given the ease of its measurement, SpO2 can be considered as a predictor of mortality in critically ill medical emergency patients.

PS397

THE IMPACT OF NATIONWIDE EDUCATION PROGRAM IN SEPSIS CARE AND MORTALITY OF SEVERE SEPSIS: A POPULATION-BASED STUDY IN TAIWAN

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Objectives We investigated the effect of a nationwide educational program following surviving sepsis campaign (SSC) guidelines. Physicians' clinical practice in sepsis care and patient mortality rate for severe sepsis were analyzed using a nationally representative cohort.
Methods Hospitalizations for severe sepsis with organ failure from 1997 to 2008 were extracted from Taiwan's National Health Insurance Research Database (NHIRD), and trends in sepsis incidence and mortality rates were analyzed. A before-and-after study design was used to evaluate changes in the utilization rates of SSC items and changes in severe sepsis mortality rates occurred after a national education program conducted by the Joint Taiwan Critical Care Medicine Committee since 2004. A total of 39,706 hospitalizations were analyzed, which consisted of a pre-intervention cohort of 14,848 individuals (2000–2003) and a post-intervention cohort of 24,858 individuals (2005–2008).
Results The incidence rate of severe sepsis increased from 1.88 per 1,000 individuals in 1997 to 5.07 per 1,000 individuals in 2008. The cumulative mortality rate decreased from 48.2% for the pre-intervention cohort to 45.9% for the post-intervention cohort. The utilization rates of almost all SSC items changed significantly between the pre-intervention and post-intervention cohorts. These changes of utilization rates were found to be significantly associated with the reduction in mortality rate.
Conclusion The nationwide education program through a national professional society has a significant impact on physicians' clinical practice and resulted in a reduction of severe sepsis mortality rate.

PS398

USE OF SALMETEROL/FLUTICASONE IN PROLONGED MECHANICAL VENTILATION PATIENTS CONCOMITANT WITH POTENTIALLY UNDER-DIAGNOSED CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aim of Study Patients with prolonged mechanical ventilation (PMV) may be under-diagnosed of chronic obstructive pulmonary disease (COPD). The purposes of our study are to evaluate the efficacy of use of Salmeterol/Fluticasone on the rate of ventilator weaning, respiratory care center (RCC) hospitalization length and the incidence of ventilator associated pneumonia (VAP) in PMV patients concomitant with potentially under-diagnosed COPD and to perceive if under-diagnosed/un-treated COPD is a barrier for ventilator weaning in the RCC, a subacute ventilator dependency setting.
Methods This retrospectively observational study is implemented from January, 2010 to April, 2013. Patients admitted to RCC were enrolled. Salmeterol/Fluticasone is given only to those patients who were diagnosed of COPD during the period of Jan 2010 to Dec 2010 (control group) but given to those who fulfill all of the following criteria: 1. Age over 40-year-old, 2. Smoking over 10 pack-year and/or presence of other risk factors for COPD, 3. presence of copious sputum production, 4. Unsuccessful weaning attempt at intensive care units during the period of Jan 2011 to Apr 2013 (experimental group). Those who were diagnosed of bronchial asthma or enrolled in any other study were excluded.
Results A total of 516 patients were enrolled. 67.6% (349/516) patients were male and 32.4% (167/516) patients were female. 34.0% (50/147) patients received Salmeterol/Fluticasone in the control group and 57.3% (211/396) patients in the experimental group ($p < 0.001$). The rate of ventilator weaning was 57.1% (84/147) in the control group and 68.0% (251/396) in the experimental group ($p = 0.025$). The incidence of VAP (2.0% v.s. 1.9%, $p = 1.000$) and RCC hospitalization length (21.4 ± 17.4 v.s. 19.5 ± 14.7, $p = 0.207$) were similar in both groups.
Conclusion Treatment with salmeterol/fluticasone in PMV patients concomitant with potentially under-diagnosed COPD significantly improved the rate of ventilator weaning without increasing the incidence of VAP.

PS399

CLINICAL CHARACTERISTICS OF PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME ASSOCIATED WITH SCRUB TYPHUS

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Background Acute respiratory distress syndrome (ARDS) is a serious and unusual complication of scrub typhus. This study was conducted to evaluate the clinical characteristics of patients with ARDS associated with scrub typhus.
Methods This study retrospectively reviewed the medical records of patients diagnosed with scrub typhus at Pusan National University Hospital in Korea from January 1995 to December 2010. Nine patients with ARDS who were admitted to an intensive care unit (ICU) were included.
Results The mean age of patients was 73.2 ± 7.3 yr and 7 patients (77.8%) were male. Seven patients (77.8%) were hospitalized at November (autumn in Korea) and the most common symptom was dyspnea (55.5%). ARDS was diagnosed 1.7 ± 2.4 days after hospitalization. Acute Physiology and Chronic Health Evaluation II score and Sequential Organ Failure Assessment score of patients was 20.7 ± 4.6 and 8.8 ± 3.0, respectively. Shock was developed in 5 patients (55.5%). 7 patients (77.8%) started treatment with doxycycline at the day hospitalized. The ICU and hospital mortality was 33.3% and 33.3%, respectively.
Conclusion ARDS associated with scrub typhus occurs mainly in old aged persons at autumn. Due to high mortality, careful assessment and active treatment is needed in these patients.

2-E5: CRITICAL CARE MEDICINE 2

PS400

SMALL-BORE CATHETER IS SAFE AND EFFECTIVE FOR MANAGEMENT OF PLEURAL EFFUSION IN THE INTENSIVE CARE UNIT

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Background and Aim of Study Pleural effusions (PEs) are common in critically ill patients managing in intensive care unit (ICU). Recently, various small-bore catheters (SBCs) have been tried to drain PEs over chest tube (CT) thoracostomy. This study was conducted to evaluate effectiveness and safety of SBCs comparing with CT thoracostomy in ICU patients.
Methods We reviewed medical records of the adult patients admitted in the ICUs of our tertiary care hospital from May 2011 to September 2012. PEs drained with SBCs (7F standard single lumen central venous catheters) or CT thoracostomy (>28 F).
Results Two hundred thirty four were drained with SBC in 146 patients and 48 were drained with CT in 31 patients. Bilateral drainages were 32/146 (21.9 %) and 8/31 (25.8%) in SBC and CT group ($p = 0.814$). In SBC group, there were more patients of transudate (63.7% vs. 29.0%; $p = 0.001$) and heart failure (43.1% vs 6.4%; $p < 0.001$). In CT group, there were more patients of empyema (0.7% vs. 22.6%; $p < 0.001$) and hemothorax (2.7% Vs. 12.9%; $p = 0.013$). Mean duration of drainage was 8.1 ± 8.4 and 9.2 ± 6.7 days in SBC and CT group ($p = 0.443$). Mean hs-CRP and APACHE-II score were comparable in the two groups. Complication occurred in 13 (8.9%) and 4 patients (12.9%) in SBC and CT group ($p = 0.505$). Twelve were pneumothorax in SBC group. One was blockage and improved with urokinase. In CT group, 1 catheter infection, 2 subcutaneous emphysema and 1 malposition occurred. There was no procedure related mortality in both groups.
Conclusions The use of an SBC was as efficacious as CT in draining PEs in ICU. It was well tolerated by patients and was associated with no significant complications. It may be helpful to avoid repeated thoracentesis or the use of CT to drain uncomplicated PEs in an ICU.

PS401

PROSPECTIVE CORRELATION OF ARTERIAL VS VENOUS BLOOD GAS ANALYSIS IN METABOLIC ACIDOSIS WITH CHRONIC KIDNEY DISEASE PATIENTS

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Backgroud Acid-base unbalance is most common problem in severe ill patient, especially in condition of abnormal renal function state. Especially, metabolic acidosis is the most important clinical situation in patients with chronic kidney disease (CKD). The objective of this study is assess if venous blood gas (VBG) results are numerically similar to arterial blood gas (ABG) in acutely metabolic acidosis with CKD.
Methods We prospectively correlated paired ABG and VBG in these patients from March, 2011 to september, 2012. We hypothesized that ABG results could be predicted by VBG results using a regression equation.
Results We analyzed 125 patients (Women53) and mean arterial minus venous difference for pH, pCO2, and bicarbonate was- 0.0170, 2.6528, and 0.6124. Bland-Altmanplot was done for predicting agreement of two groups, and the scale was pH-2.95 to 4.17, pCO2–4.45 to 9.76, bicarbonate-2.95 to 4.16, in 95% relative. Correlations between ABG and VBG were strong, at $p = 0.90$ for pH, 0.9 for pCO2 and 0.94 for bicarbonate.
Conclusion The peripheral blood gas pH, pCO2, bicarbonate level is almost same as arterial blood gas analysis results. Therefore, VBG samples could be obtained in metabolic acidosis with CKD patients instead of ABG.

PS402

A REVIEW OF PATIENTS TREATED WITH PROTOCOLISED NON-INVASIVE VENTILATION FOR ACUTE RESPIRATORY FAILURE

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Background and Aim of Study Non-Invasive Ventilation (NIV) has been shown to be promising for selected patients with acute respiratory failure. By eliminating the need for endotracheal intubation, NIV avoids complications such as ventilator-associated pneumonia. This study is a retrospective review of the indications and immediate outcomes of patients treated according to the acute NIV protocol during its first year of implementation. The protocol was created by this institution according to the American Thoracic Society guidelines, to promote the appropriate management of patients on NIV.
Methods The institutional review board waived consent and approved this study. 193 patients were initiated on NIV for acute respiratory failure. A respiratory physician had to review each patient for appropriateness before NIV was initiated. NIV settings were reviewed at timed intervals, guided by the work of breathing and arterial blood gas results. The patients continued to be reviewed until they were weaned off NIV, intubated or died.
Results The indications for NIV support were exacerbation of COPD [50,(25.9%)], APO [53,(27.5%)], immunocompromised patient [26,(13.5%)], restrictive lung disease [10,(5.2%)], neuromuscular weakness [8,(4.1%)], obesity hypoventilation syndrome or obstructive sleep apnoea [14,(7.3%)] and facilitation of extubation [19,(9.8%)]. 13(6.7%) had other indications. By indication, the average initial pH ranged from 7.26 (neuromuscular weakness) to 7.44 (immunocompromised patient). The initial PaO_2/FiO_2 ratio ranged from 98 (immunocompromised patient) to 316 (neuromuscular weakness). Overall, 163 patients (84.5%) were successfully weaned off NIV within a median of 1.6 days (0.6–19.8), 23 (15.5%) were intubated and 7 died. The majority of those intubated, 11 patients, were immunocompromised patients.
Conclusion Although NIV benefits immunocompromised patients by avoiding the complications of endotracheal intubation, the high failure rate (50%) of NIV in this group suggests that stricter criteria should be used when deciding between NIV and endotracheal intubation for an immunocompromised patient in acute respiratory failure.

PS403

ANTIBIOTIC EXPOSURE AND EVOLUTION OF ANTIBIOTIC RESISTANCE IN PROLONGED MECHANICALLY VENTILATED PATIENTS

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Background and Aim of Study Antibiotic-resistant nosocomial infections are increasing rapidly. Selection pressure caused by previous antibiotic exposure is the major cause of drug resistance. Most previous studies on the emergence of resistance have focused on class of antibiotics, rather than considering more complex patterns of use. This has led to a paucity of data on dose-cumulative effects of long-term antibiotic exposure on the emergence of subsequent resistant infections This study was aimed to test the hypothesis that the antibiotic used to treat the initial infection and the time between antibiotic exposure and the onset of subsequent infection would have a significant correlation with the emergence of nosocomial drug resistant infections.
Methods We retrospectively analyzed 167 mechanically ventilated patients with nosocomial infections over a 3-year period in our chronic respiratory care units, with focus on infections in the bloodstream, urinary tract, lower respiratory tract, and surgical sites.
Results Of 167 patients, 62% were confirmed as antibiotic resistant. The most common isolated pathogen was extended-spectrum β-lactamase Enterobacteriaceae (43.9%), followed by methicillin-resistant Staphylococcus aureus (22.8%), and carbapenem-resistant Acinetobacter baumannii (17.5%). Multivariate analysis revealed that the association between resistance and the time interval increased within 10 days (odds ratio [OR] 2.45; $P = 0.133$) and peaked at 11 to 20 days (OR 7.17; $P = 0.012$). The data were categorized into 2 groups: when the time interval since exposure was more than 20 days, there was a 23.9% reduction in resistance rate compared with when the time interval was 20 days or less (OR 0.36; $P = 0.002$).
Conclusions Although antibiotic exposure increased resistance rate in nosocomial infections, this association decreased as time interval increased. We suggest that future research use the time interval since the last day of previous antibiotic exposure as an important reference while investigating the evolution of subsequent antibiotic-resistant infections.

PS404

RAPID BRADYCARDIA AFTER NON-INVASIVE VENTILATOR REMOVAL

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A 89 y/o female patient suffered from progressive shortness of breath for one month due to acute renal failure. Respiratory failure was occurred after admission and non-invasive ventilator was placed. However she suffered recurrent episodes of rapid bradycardia on removal of the mask. We have reviewed the literature and offer a potential mechanism for this phenomenon.

PS405

NON-INVASIVE MECHANICAL VENTILATION (NIMV) AT UST HOSPITAL A CROSS SECTIONAL DESCRIPTIVE STUDY

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Background and Aim Non-Invasive Mechanical Ventilation is a modality that gives ventilatory support without bypassing the upper airway with the use of devices such as tracheal tube, laryngeal mask or tracheostomy. This paper aims to describe the practice of instituting NIMV in UST Hospital. It will review the outcomes as well as the appropriateness of use and adherence to the guidelines in this institution.
Methods We reviewed the charts of all inpatients placed on non-invasive mechanical ventilation from July 2011 to March 2013 with emphasis on the following variables: demographic and clinical profile, clinical course and outcome. Patients from the pediatric age group and patients placed on CPAP for management of Obstructive Sleep Apnea were excluded.
Results A total of 76 patients were included in the study. There were 35 patients (46%) who failed NIMV. Out of this, 12(34%) were intubated but were eventually discharged, 10(28%) were intubated and subsequently died, and 13(37%) died while on NIMV. The most common indication for instituting NIMV was pneumonia. The success rate was 53.9%. Success was highest among patients placed on NIMV because of cardiac causes, asthma and metabolic acidosis.
Conclusion The failure rate of NIMV in our institution is high compared with previous studies even if we exclude those patients placed on NIMV because of advance directives. Many of those who failed NIMV died, therefore, the importance of patient selection is emphasized. Aside from patient selection, standard of care should be taken into consideration. Its impact in the outcome should be investigated in future studies.

2-F1: INTERSTITIAL LUNG DISEASE 3

PS406

EPITHELIAL INJURY ON HISTOLOGIC FINDING OF CELLULAR NONSPECIFIC INTERSTITIAL PNEUMONIA

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Background and Aim of Study Idiopathic nonspecific interstitial pneumonia (NSIP) most frequently develops in middle-age, showing a good long-term prognosis. NSIP was originally subcategorized into cellular NSIP (cNSIP) and fibrotic NSIP (fNSIP). cNSIP consists primarily of mild to moderate interstitial chronic inflammation, usually with lymphocytes and a few plasma cells. However, some cNSIP incorporates alveolar epithelial changes. Then we have recognized epithelial injury pattern as a histologic pattern, which does not meet the histologic criteria for acute lung injury pattern in DAD and OP. To investigate the clinical characteristics of the epitherial injury pattern, we performed this retrospective analysis.
Methods We regarded a pathological findings in cNSIP as epithelial injury pattern if there are at least one parameter as noted below. 1) Alveolar epithelial shedding and regenerative hyperplastic epithelia. 2) Obscured border between alveolar walls and lumen. 3) Membranous organization of the alveolar ducts and/or alveolar sac. A review of medical records between 2000 and 2010 identified patients who met the histological criteria with surgical biopsy and clinical criteria for cNSIP. Patients were divided into two groups: cNSIP with pathological epithelial injury and without.
Results Of the 28 patients with cellular NSIP included in the study, 14 were with pathological epithelial injury and 14 were without. Five-year survival rate was 100% in both two groups. There seemed to be lower %FVC, lower %FEV1, lower %DLCO and lower PaO2 in cNSIP patients with epithelial injury pattern at the initial visit. Neutrophil count in blood test ($P = 0.037$) and neutrophil count in BALF ($P = 0.037$) were significantly higher in those patients.
Conclusion The pathological findings of epithelial injury in cNSIP differ from the classic patterns of epithelial injury on acute lung injury pattern (DAD and OP). cNSIP patients with epithelial injury pattern were found severe at diagnosis, but showed good prognosis.

PS407

TEN CASES OF IDIOPATHIC UPPER LOBE FIBROSIS; CLINICAL AND PATHOLOGICAL CHARACTERISTICS

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Background and Aim of Study Idiopathic pulmonary upper lobe fibrosis (IPUF) is a unique condition first described by Amitani, et al. in 1992. IPUF presents idiopathic and progressive pulmonary fibrosis predominantly in the upper lobe and subpleural regions. This study was performed to examine clinical and pathological characteristics.
Patients and Methods Clinical, radiological, functional and pathological characteristics of 10 patients (7 males and 3 females) with IPUF were evaluated, restrictively excluded infections like *Mycobacterium*spp.
Results Body weight loss, history of pneumothorax and restrictive impairment of pulmonary function test were observed in 8, 9 and 9 patients respectively. In all patients predominant upper lobe volume loss was observed. Pathological findings were obtained in 8 patients. The fundamental histological features in the upper lobe were pleural thickening, parenchymal fibroelastosis, and the abrupt border between the fibroelastosis and the underlying normal lung parenchyma. In 6 of the 10 patients, however, interstitial changes were observed not only in the upper lobes, but also in lower lobes.
Conclusion IPUF is a new concept, and it may also include subtypes with and without interstitial change in lower lobes that result in pulmonary fibrosis predominantly in the upper lobe.

PS408

SIGNIFICANCE OF SERUM SURFACTANT PROTEIN D FOR COMBINED PULMONARY FIBROSIS WITH EMPHYSEMA IN IDIOPATHIC PULMONARY FIBROSIS

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Background Some patients with idiopathic pulmonary fibrosis (IPF) are classified in novel disease concept, combined pulmonary fibrosis and emphysema (CPFE). In spite of the disease progression, vital capacity (VC) trends to be preserved in patients with CPFE. VC therefore may be not important parameter for predicting prognosis of IPF showing characteristics of CPFE. We previously reported that high levels of serum surfactant protein (SP)-D predict poor prognosis in IPF. Aim of this study is to evaluate value of SP-D in this subset of IPF.
Subjects and Methods Seventy-two patients (pts) diagnosed as IPF according to the ATS/ERS statement were enrolled from 107 pts with interstitial pneumonia who visited Sapporo Medical University Hospital and Teine Keijinkai Hospital from 2007 to 2012. We defined "CPFE"pts who showed >25% emphysema on HRCT scan. The IPF pts were divided within two subsets; 34 of "CPFE" and 38 of "non-CPFE". Their medical records including pulmonary function tests and serum markers including SP-D were reviewed.
Results In "CPFE", VC was preserved but diffusing capacity was decreased stronger than compared to "non-CPFE". "CPFE" showed significantly worse survival than "non-CPFE". Particularly, "CPFE" with severe worsening in annual change of diffusing capacity showed poor prognosis. Moreover, in "CPFE", higher serum SP-D group (more than 150 ng/ml) showed significantly worse survival than another group ($p = 0.0089$).
Conclusion In IPF, "CPFE" pts showed significantly worse survival than "non-CPFE", especially the patients with high serum SP-D showed poor prognosis. It is suggested IPF patients with emphysema on HRCT and high SP-D level in sera should be needed careful observation.

PS409

HCMV INFECTION TRIGGERS DEVELOPMENT OF INTERSTITIAL LUNG DISEASES IN AUTOIMMUNE DISORDERS

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Background and Aim Interstitial lung disease in connective tissue diseases (CTD-ILD) is a leading cause of death in these patients. Herpesviruses infection has been associated with autoimmune diseases. However, it is still unknown whether infection with some of the viruses could initiate ILD in patients with CTDs. The aim is to determine the role of herpesviruses infection in initiation of ILD in connective tissue disorders.
Methods Herpesviruses(HCMV,EBV,and HSV) infection was tested in the peripheral blood mononuclear cells (PBMCs), plasma and lung tissues of 62 patients with CTD-ILD, 19 patients with CTD(RA) and 33 healthy controls using quantitative PCR. T lymphecytes subsets and cytokines profile were analyzed by flow cytometry and liquid Chip.
Results In patients with CTD-ILD, the detection rate of HCMV was significantly higher than that in healthy controls (41.94% vs. 6.06%, $p = 0.000$). The increased HCMV infection was not associated with administration of immunosuppressors and with different types of CTD-ILD. The patients with RA-ILD appeared to have a remarkable augment of HCMV infection compared with those with RA alone(50.00% vs. 10.53%, $P = 0.022$). The High frequencies of cytotoxic T cells accompanied with a reduced regulatory T cells (Tregs) were observed in the peripheral blood of CTD-ILD patients with HCMV infection, concomitant with markedly increased IL-6 and IL-10 levels and with a decreased ratio of TGFbeta to IL-6 level compared with those in the patients without HCMV($P = 0.003$,$p = 0.008$,$p = 0.017$,respectively). The association of HCMV infection with the preceding indices to substantiate a pathogenic role for pulmonary function was assessed in the enrolled patients, showing lower percentages of FVC and DLCO observed in HCMV positive patients than in HCMV negative ones. High frequencies of cytotoxic T cells and reduced Tregs level combined with an increased IL-6 correlated highly with impaired lung function parameters.
Conclusions HCMV may initiate ILD in situation of autoimmune disorders.

PS410

SERUM HEME OXYGENASE-1 AS THE NEW BIOMARKERS FOR ACUTE EXACERBATION OF INTERSTITIAL PNEUMONIA PATIENTS

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Background and Aim of Study Heme oxygenase-1 (HO-1) is a 32-kDa heat shock protein known as the heme-splitting enzyme with pulmonary cellular protection against oxidative stress and inflammation. It has been reported that HO-1 is upregulated in the lung of diffuse alveolar damage patients. Therefore, we examined whether serum HO-1 could be the biomarker for acute exacerbation of interstitial pneumonia (AE-IP) patients.
Methods We measured serum HO-1 levels using sandwich ELISA method. First, we compared serum HO-1 levels of AE-IP patients with those of control subjects. Second, we evaluated the correlations between serum HO-1 and other biomarkers including serum LDH, WBC, CRP, SP-A, SP-D, KL-6 and PaO2/FiO2 ratio. Third, we evaluated the variations of serum HO-1 levels of AE-IP patients by treatments and compared serum HO-1 levels of AE-IP patients who needed the steroid pulse therapy with those of who did not needed.
Results 10 IP-AE patients were enrolled (M: F = 9:1). The mean age was 69.7 ± 10.3 yrs. 7 patients of AE of idiopathic pulmonary fibrosis and 3 patients of AE of collagen vascular disease were included. Serum HO-1 levels of AE-IP patients were higher than those of control subjects (61.7 ± 31.3 ng/mL, 33.2 ± 13.2 ng/mL ($p = 0.0004$)). Serum HO-1 levels of AE-IP patients before the treatment closely correlated with serum SP-A and LDH levels ($R = 0.95$, $R = 0.84$). Serum HO-1 levels of AE-IP patients significantly decreased in 7 days and 14 days after the treatment (both was $p < 0.05$). The mean serum HO-1 level of AE-IP patients who needed the steroid pulse therapy was 73.3 ± 11.9 ng/mL and that of those who did not needed was 44.3 ± 14.6 ng/mL.
Conclusion Serum HO-1 might be able to serve as one of the biomarkers for the disease activity of AE-IP patients.

PS411

PROGNOSTIC FACTORS AND CAUSE OF DEATH IN JAPANESE PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Rationale Idiopathic pulmonary fibrosis (IPF) has an unknown etiology and poor prognosis. Several large-scale epidemiological studies have been previously conducted in western countries predominantly. It is important to determine the current IPF status in the Japanese population and compare it to that of western countries in order to evaluate racial and regional differences.
Objectives To provide the epidemiological status of IPF and identify prognostic factors and causes of death in Japanese IPF patients.
Methods We selected the island of Hokkaido (population, 5.5 million) as the epidemiological cohort of IPF among Japanese. On the basis of the clinical records of 553 IPF patients who were accepted the application of the Certificate of Medical Benefit between 2003 and 2007, we performed a retrospective epidemiological and prognostic analysis.
Measurements and Main Results The prevalence and incidence of IPF was 10.0 and 2.23 per 100,000 people, respectively, with 72.7% predominance of males and the frequency increases with age. The median survival time was 35 months, and the most common (40%) cause of death was acute exacerbation. The most important factor influencing IPF prognosis was the percent vital capacity.
Conclusions The status of IPF in the Japanese population was clarified for the first time through our report. Our results showed a lower prevalence and incidence rate in Japan compared with western countries. In men, the incidence of death due to acute exacerbation was higher in Japan than in western studies. These results may suggest racial and regional differences in IPF cases.

PS412

CLINICAL FEATURES OF SJÖGREN'S SYNDROME COMPLICATED WITH ANTI-AMINOACYL-TRNA ANTIBODIES SYNDROME

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Background The frequency of pulmonary complications among patients with Sjögren's syndrome (SS) is 21–65%. Although about 50% of SS patients have other autoimmune diseases, reports on patients with SS complicated with anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies syndrome are rare.
Objective To better understand the clinical features of SS complicated with anti-ARS antibodies syndrome.
Results We investigated 32 patients with SS diagnosed from 1976 to 2012. Anti-ARS antibodies were detected in 8 patients (25%) (anti-Jo-1 in 1 patient, anti-PL-7 in 1 patient, anti-PL-12 in 2 patients, anti-EJ in 3 patients and anti-KS in 1 patient). Five patients (62.5%) in the anti-ARS-antibodies-positive group showed erythema suggestive of myositis such as a mechanic's hand, periungual erythema and nail fold bleeding; on the other hand, no patients in the anti-ARS-antibodies-negative group showed erythema suggestive of myositis. As to radiological findings on high-resolution CT, the anti-ARS-antibodies-positive group showed a significantly higher rate of cystic formations, while the anti-ARS-antibodies-negative group showed significantly higher rates of consolidations and thickening of bronchovascular bundles. The anti-ARS-antibodies-positive group had significantly shorter duration from diagnosis to the beginning of treatment than the negative group, although there were no significant differences in resistance to treatment and survival between the 2 groups. There were also no significant differences in bronchoalveolar lavage fluid and results of pulmonary function tests.
Conclusions We detected anti-ARS antibodies in 25% of SS patients. This investigation suggests that anti-ARS antibodies modify the clinical features of SS. Therefore, we should measure anti-ARS antibodies in patients diagnosed with SS.

PS413

ANGIOPOIETIN-2 EXPRESSION IN PATIENTS WITH ACUTE EXACERBATION OF IDIOPATHIC INTERSTITIAL PNEUMONIAS

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Background We hypothesized that increased pulmonary vascular permeability may play a role in the pathogenesis of acute exacerbation of idiopathic interstitial pneumonia (AE-IIP). Angiopoietin-2 (Ang-2) promotes endothelial activation, destabilization, and inflammation. We examined whether Ang-2 expression would be associated with the pathogenesis of AE-IIP.
Methods Twenty-three patients with AE-IIP, 18 patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS), 37 patients with idiopathic pulmonary fibrosis (IPF), and 33 healthy volunteers (HV) were enrolled. Serum levels of Ang-2 were measured by an enzyme-linked immunosolbent assay.
Results Serum levels of Ang-2 in patients with AE-IIP and ALI/ARDS were higher than those in IPF and HV, and BALF Ang-2 levels were also higher than those in IPF. There was a positive correlation between serum Ang-2 levels and CRP in patients with AE-IIP, whereas a significant positive correlation was found serum Ang-2 levels and CRP or SOFA score in the patients with ALI/ARDS. Although the baseline Ang-2 levels did not relate to survival, Ang-2 levels significantly declined during treatment in survivor, but not in non-survivor.
Conclusions Increased pulmonary vascular permeability and inflammation due to Ang-2 may play a role in the pathogenesis of AE-IIP.

PS414

CLINICAL CHARACTERISTICS IN PATIENTS WITH INTERSTITIAL PNEUMONIA WITH MORE THAN 10 YEARS OF FOLLOW-UP

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Background and Aim of Study Clinical course of interstitial pneumonia is often progressive with a poor prognosis. However, some groups of patients have relatively a stable clinical course. Clinical characteristics in patients with interstitial pneumonia whose respiratory functions had been monitored for more than ten years were retrospectively examined.
Methods Nineteen patients admitted in our hospitals were enrolled in this study. Clinical background such as age, sex, underlying diseases and prognosis were examined. Respiratory function parameters at the first visit and annual changes were also examined.
Results Patients consisted of 7 males and 12 female with 51.0 ± 2.2 years old, and follow-up periods were 15.11 ± 0.98 years. Eleven patients had collagen vascular disease, among which 6 patients had RA, and idiopathic nonspecific interstitial pneumonia was found in 6 patients. There were no patients with idiopathic pulmonary fibrosis (IPF), but one patient with idiopathic pulmonary upper lobe fibrosis and one with combined pulmonary fibrosis and emphysema (CPFE) were included in the study group. Annual decline of FVC in entire follow-up periods in all patients was 20.36 ± 8.66 mL, that was not significantly different from that of normal population.
Conclusion Patients with interstitial pneumonia who survived more than 10 years had a stable ventilatory function. There were no patients with IPF who survived more than 10 years with the exception of a patient with CPFE.

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PS415

THE ROLE OF BAX IN LUNG FIBROSIS

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Background Alveolar epithelial cell apoptosis is involved in the pathogenesis of lung injury and pulmonary fibrosis. On the other hand, 'Epithelial Mesenchymal Transition (EMT)' of alveolar epithelial cells, that is induced by TGF-beta has been reported to play promoting role in the development of lung fibrosis. Bax is a pro-apoptotic member of Bcl-2 family proteins, and plays central role in mitochondria-dependent apoptosis. It is reported that Bax expression is increased in pulmonary alveolar epithelial cells of the patients of Idiopathic pulmonary fibrosis (IPF). However, the relation between Bax and EMT still remains unknown.
Aim The purpose of this study is to investigate whether the control of Bax activity reduces apoptosis and EMT of alveolar epithelial cells in vitro.
Method Murine pulmonary alveolar epithelial cells (LA-4 cells) and human pulmonary alveolar epithelial cells (A549 cells) were stimulated with bleomycin (BLM) for induction of apoptosis and EMT. The cells were pretreated with Bax inhibiting peptide V5 (BIPV5) before adding BLM. BIPV5 is designed to prevent the translocation of Bax into mitochondria by binding the N- terminal of the Bax in cytosol. Apoptosis was assayed with Flow cytometry. EMT was analyzed with Western blotting and Immunostaining.
Results LA-4 cells and A549 cells underwent apoptotic change at 24 hours after stimulation of BLM. BIPV5 pretreatment decreased those apoptotic changes significantly. LA-4 cells and A549 cells underwent EMT change at 48–72 hours after stimulation with BLM. BIPV5 pretreatment decreased those EMT changes significantly.
Conclusion Control of Bax activation has an anti-apoptotic effect and an anti-EMT effect on lung epithelial cells.

PS416

DEPLETION OF CLARA CELLS ATTENUATES LUNG INJURY AND FIBROSIS INDUCED BY BLEOMYCIN IN MICE

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The role of bronchiolar epithelial cells in the pathogenesis of idiopathic pulmonary fibrosis has not been addressed, although bronchiolar epithelial cells are known to compensate for alveolar epithelial cell loss and express various cytokines. We previously demonstrated that DNA damage and apoptosis were found at early phase of the bleomycin-induced pulmonary fibrosis in mice in bronchiolar epithelial cells, whereas at later phase in alveolar epithelial cells. Clara cells, which are dominant epithelial cells in peripheral airways, play progenitor roles for bronchial epithelial cells, and also play protective roles by expressing Clara cell 10 kD protein (CC10) against lung injury. The aim of this study is to elucidate the role of Clara cells in the development of pulmonary fibrosis. C57BL/6J mice were given intraperitoneal injections of naphthalene on day 0 to deplete Clara cells, and were given intratracheal injections of bleomycin or vehicle on day 2. Bronchoalveolar lavage fluids and lung tissues were obtained on day 16. Surprisingly, naphthalene-induced Clara cell depletion protected mice from bleomycin-induced lung injury and fibrosis. It has been reported that bleomycin upregulates the expressions of transforming growth factor (TGF)-β1 and high mobility group box 1 (HMGB1) in bronchiolar epithelial cells. Interestingly, naphthalene pretreatment suppressed the expressions of these molecules. These results suggests that depletion of Clara cells by naphthalene pretreatment reduces the production of profibrotic mediators by regenerated bronchiolar epithelial cells in the development of bleomycin-induced pulmonary fibrosis in mice. We conclude that Clara cells are likely to play a promoting role in the pathogenesis of lung injury and fibrosis.

PS417

INCREASED OF RECEPTOR TYPE TYROSINE KINASE ROS1 IN INTERSTITIAL LUNG DISEASE

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Background Gene-expression profile analyses of interstitial lung diseases (ILDs) revealed that ROS1 was transactivated in majority of ILDs. ROS1 is a receptor type tyrosine kinase which is known as a driver mutation of human lung cancer. However, the biological significance of ROS1 in ILDs and its clinical potential as a therapeutic target for ILDs were not yet been studied.
Methods ROS1 immunoreactivities were quantitated 23 lung biopsy specimens obtained from patients with ILDs (7 idiopathic pulmonary fibrosis, 6 non-specific interstitial pneumonia and 10 chronic hypersensitivity pneumonitis). In addition, immunoreactivities of ROS1 in the lung specimens obtained from bleomycin-induced pulmonary fibrosis and control lung were also evaluated.
Results In lung biopsy specimens obtained from patients with ILDs, ROS1 was detected mainly in the alveolar epithelium surrounding areas of fibrosis in ILDs. Immunohistochemical positivities of ROS1 were correlated to gene expression profiles of ROS1 in microarray. ROS1 was remarkably expressed in the lung specimens obtained from bleomycin-induced pulmonary fibrosis than those from control.
Conclusion We conclude that ROS1 is up-regulated in the lung epithelium of ILDs. The results of this study support the potential of ROS1 to be a therapeutic target for ILDs.

PS418

FAMILIAL INTERSTITIAL LUNG DISEASE IN A FAMILY WITH FAMILIAL JUVENILE IDIOPATHIC ARTHRITIS: CLOSE FAMILY TIES

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Background Interstitial lung disease (ILD) includes a large, heterogeneous group of mostly rare pulmonary conditions that cause derangements of the alveolar walls and loss of functional alveolar capillaries. Familial ILD is a rare type of hereditary disease. It becomes explicitly rare and multifaceted when the main cause is another familial type of disease, familial juvenile idiopathic arthritis. Several factors should be considered, since it is exceptionally atypical in nature and are rarely encountered in practice. Proper treatment should be given to decrease the mortality among children.
Case This is a case of an 8 year old girl, presented with difficulty of breathing, with swelling of fingers, ankles and knees and had respiratory distress when she was 2 years old. Initially diagnosed as miliary tuberculosis however workups done such as Chest CT scan and open lung biopsy revealed ILD. RF factor was increased, and antidsDNA was equivocal. She had relatives who died with unknown cause, her eldest sister died of unknown diagnosis presented with respiratory distress when she was 1 year and 3 months old. Her 3rd sibling was diagnosed with SLE with overlapping JIA at 3 years old and was diagnosed with ILD. Presently maintained on steroids and sildenafil for the pulmonary hypertension.
Conclusion The diagnosis of interstitial lung disease is challenging. In this report we describe a rare type of familial ILD in Filipino children. Searching for the known etiology of such disease requires a thorough history and a complete physical examination. Presently underreported and misdiagnosed cases are usually seen in our clinical settings, thus vigilant actions should be done in order to decrease morbidity and mortality among children.

PS419

AMPHIREGULIN ATTENUATES LIPOPOLYSACCHARIDE-INDUCED ACUTE LUNG INJURY IN MICE

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Background Alveolar epithelial cell damage and apoptosis has been reported to play important roles in the pathogenesis of acute lung injury (ALI) in various animal models and human cases of ALI. Amphiregulin (AR) is a member of the epidermal growth factor family that contributes to regulate cell proliferation. We previously reported that AR attenuates BLM-induced lung injury. And AR was found to be upregulated in lung epithelial cells in ventilator-associated lung injury model. However, the role of amphiregulin in lung injury still remains elusive.
Aim The aim of this study is to investigate into the effect of AR in murine model of lipopolysaccharide (LPS)-induced acute lung injury. We investigated the effect of AR in vitro using the murine lung alveolar type II epithelial cell line LA-4 as well.
Methods 7-wk-old female C57BL/6 mice were treated with intraperitoneal injection of human recombinant AR or phosphate buffered saline, three times before and after (–6h r, –0.5 hr, +3 hr) intranasal administration of LPS. Histological evaluation of the lung tissue and analysis of the bronchoalveolar lavage fluid (BALF) were performed at 6 and 24 hours after LPS injection. LA-4 cells were cultured in the presence of 0, 10 or 100 nM of AR. After 3 hours incubation, LA-4 cells were rinsed and 50 μg/ml of LPS was added. After 24 hours incubation, cells were harvested and used for apoptosis analysis on a flow cytometer and western blotting.
Result Human recombinant AR significantly decreased TUNEL-positive cells in lung tissues. AR also decreased total cell counts, neutrophil counts and protein concentration in BALF from of LPS-injected mice. LPS induced apoptosis on LA-4 cells, and AR suppressed this apoptosis rate through inhibiting a caspase-8 activity.
Conclusion AR is likely to have a protective effect on acute lung injury. AR treatment might be one of new therapeutic approaches for ALI.

PS420

MEASUREMENT OF INFLAMMATORY CYTOKINES BY MULTICYTOKINE ASSAY IN PATIENTS WITH AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Introduction Autoimmune pulmonary alveolar proteinosis (APAP) is a rare lung disease characterized by dysfunction of alveolar macrophages and neutrophiles by neutralizing anti-granulocyte/macrophage colony-stimulating factor (GM-CSF) autoantibody. It is well known that levels of autoantibody against GM-CSF indicate remarkable increase in serum and bronchoalveolar lavage fluid. In this study, we focused on serum cytokines that decreased in APAP.
Subjects and Methods We enrolled 75 patients with APAP (54 (25–78) years old) and 89 healthy volunteers (41(21–62) years old). Multicytokine assay was performed with commercially available kit (Bio-Plex). The cytokine levels were analysed with several clinical measures.
Results Serum level of autoantibody against GM-CSF was positive in all APAP patients who enrolled this study. And serum levels of granulocyte colony-stimulating factor (G-CSF, $p < 0.01$) and macrophage colony-stimulating factor (M-CSF, $p < 0.01$) decreased compared with healthy volunteers. Twenty-two patients received GM-CSF inhalation therapy. Forty-one % of patients responded well and alveolar-arterial oxygen difference improved significantly ($p < 0.05$) after GM-CSF inhalation therapy, however, most of these cytokine levels did not significantly changed.
Conclusion The roles of serum G-CSF and M-CSF were not clear, but they did not recover by GM-CSF inhalation therapy. However, these cytokines are involved in proliferation and differentiation of precursor of macrophage. Measurement of cytokine/chemokine level in BALF as regional area of disease may be important to evaluate effects of GM-CSF inhalation therapy carefully in APAP. This study was supported by a grant for "Rare lung diseases (pulmonary alveolar proteinosis, congenital interstitial lung disease and hereditary hemorrhagic telangiectasia){H24-Nanchitou(Nanchi)-Ippan-035}." from the Ministry of Health Labour and Welfare, Japan.

PS421

PROTEOMICS ANALYSIS OF BALF IN RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASE WITH USUAL INTERSTITIAL PNEUMONIA PATTERN

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Background and Aim of Study Rheumatoid arthritis associated interstitial lung disease (RA-ILD) occurs 10% to 30% of patients with rheumatoid arthritis (RA) and is associated with increased mortality in up to 10% of patients with RA. However, little is known about the mechanisms of pathogenesis in RA-ILD. Gelsolin is one of actin binding proteins which regulate cell structure and metabolism. Recently, increased gelsolin expression is shown to have a role in pulmonary inflammation and fibrosis. The aim of this study is to investigate the proteins related to UIP pattern by comparing to OP pattern in RA-ILD using proteome analysis of bronchoalveolar lavage fluid (BALF).
Methods BALF samples were obtained from 13 patients with RA-ILD in our hospital between 1999 and 2011. We divided them into two groups, namely UIP pattern and OP pattern by findings of high resolution computed tomography. Five patients with UIP pattern and 8 patients with OP pattern were examined. BALF samples were concentrated by acetone precipitation and separated by 2-dimensional electrophoresis. Gels were stained with SYPRO Ruby Protein Gel Stain and scanned with FluoroPhoreStar 3000. Proteins were identified by referring to the published BALF maps and/or by LC-MS/MS.
Results In comparison of individual BALF samples, gelsolin and immunoglobulin kappa chain C were significantly higher in the patients with UIP pattern than OP pattern. In contrast, C-reactive protein, haptoglobin, surfactant-associated protein A, and alpha-1 antitrypsin were significantly higher in the patients with OP pattern than UIP pattern. Gelsolin, which was significantly higher in UIP pattern, was shown to be C-terminal half of gelsolin.
Conclusion We identified several proteins that might have roles in the clinical differences between UIP and OP patterns of RA-ILD. C-terminal half of gelsolin might contribute to pulmonary fibrosis in RA-ILD.

PS422

FIBROCYTE REGULATES LUNG FIBROBLAST ACIVATION VIA PRODUCING GROWTH FACTORS

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Rationale Circulating fibrocytes are thought to contribute the fibrogenesis in the lungs. However, the function of fibrocytes in pulmonary fibrosis remains unclear. Here we examined whether fibrocytes regulate the function of lung fibroblasts. In particular, we focused on production of growth factors from fibrocytes.
Methods We used 3H-thymidine incorporation assay to examine the growth of fibroblasts co-cultured with fibrocytes. Western blotting was performed to evaluate the myofibroblast differentiation. The concentrations of growth factors in fibrocyte culture medium were measured by ELISA. The inhibitory responses by neutralizing antibodies for each growth factor were examined. Immunofluorescence staining was performed to detect fibrocytes and growth factors in fibrotic lung tissues of patients with idiopathic pulmonary fibrosis.
Results Fibrocyte co-culture induced the growth and myofibroblast differentiation of human lung fibroblasts. Increased levels of growth factors were observed in fibrocyte culture medium. PDGF-BB and FGF-2 contribute to the growth-stimulating activity of fibrocytes, and TGF-beta and FGF-2 played roles in the stimulatory activity of fibrocytes in myofibroblast differentiation of fibroblasts.

PS423

THE CALPAIN INHIBITOR CALPEPTIN PREVENTS BLEOMYCIN-INDUCED PULMONARY FIBROSIS IN MICE

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Background Pulmonary fibrosis is characterized by progressive worsening of pulmonary function leading to a high incidence of death. Currently, however, there has been little progress in the therapeutic strategies for pulmonary fibrosis. There have been several reports on cytokines being associated with lung fibrosis, including IL-6, TGF-β1. We recently reported two substances (ATRA and thalidomide) had preventive effects on pulmonary fibrosis by inhibiting IL-6-dependent proliferation and TGF-β1-dependent transdifferentiation of lung fibroblasts. Rheumatoid arthritis is a chronic autoimmune disorder, and its pathogenesis is also characterized by an association with several cytokines. It has been reported that Calpain, a calcium-dependent intracellular cysteine protease, plays an important role in the progression of Rheumatoid arthritis. In this study, we examined the preventive effect of Calpeptin, a calpain inhibitor, on bleomycin-induced pulmonary fibrosis.
Methods We performed histological examinations and quantitative measurements of IL-6, TGF-β1, collagen type Iα1, and angiopoietin-1 in bleomycin treated- mouse lung tissues with or without the administration of Calpeptin.
Results Calpeptin histologically ameliorated bleomycin-induced pulmonary fibrosis in mice. Calpeptin decreased the expression of IL-6, TGF-β1, angiopoietin-1, and collagen type Iα1 mRNA in mouse lung tissues. In vitro studies disclosed that Calpeptin reduced 1) production of IL-6, TGF-β1, angiopoietin-1 and collagen synthesis from lung fibroblasts, and 2) both IL-6-dependent proliferation and angiopoietin-1-dependent migration of the cells, which could be the mechanism underlying the preventive effect of Calpeptin on pulmonary fibrosis.
Conclusions These data suggest the clinical use of Calpeptin for the prevention of pulmonary fibrosis.

PS424

LEUKOTRIENE C4 AGGRAVATES BLEOMYCIN-INDUCED PULMONARY FIBROSIS IN MICE

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Background and Objective Synthesis of cysteinyl leukotrienes (cys-LT) is thought to cause inflammatory disorders such as bronchial asthma and allergic rhinitis. Recent reports have suggested that leukotriene C4 (LTC4) is an important regulator of pulmonary fibrosis. This study examined the effect of LTC4 in LTC4 synthase-overexpressed transgenic mice with bleomycin-induced pulmonary fibrosis. The function of lung-derived fibroblasts from transgenic mice was also investigated.
Methods Bleomycin was administrated to transgenic mice and wild-type (WT) mice by intratracheal instillation. Concentrations of interleukin (IL)-4 and -13, interferon-gamma, and transforming growth factor (TGF)-beta1 in bronchoalveolar lavage fluid were measured 1, 3, 7 and 14 days after the administration of bleomycin. Lung tissue was examined histopathologically on day 14. In addition, lung-derived fibroblasts from transgenic and WT mice were cultured for 7 days. Expression of TGF-beta1 mRNA was measured by real-time polymerase chain reaction.
Results Both the pathological scores for pulmonary fibrosis and the levels of IL-4, IL-13 and TGF-beta1 on day 14 were significantly greater in transgenic than in WT mice. Furthermore, the reduction of LTC4 by pranlukast hydrate, a cys-LT1 receptor antagonist, in fibroblasts from transgenic significantly decreased the expression of TGF-beta1 mRNA compared with those from WT mice.
Conclusions Overexpression of LTC4, amplifies bleomycin-induced pulmonary fibrosis in mice. Our findings suggest a role for LTC4 in lung fibrosis.

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