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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

CLINICAL AND LABORATORY PROFILES AND OUTCOMES OF CRITICALLY ILL CHEST DISEASE PATIENTS IN A TERTIARY CARE CHEST HOSPITAL

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Background Critical care in respiratory field has been introduced recently in Bangladesh. Last year total 429 patients were admitted in ICU. This prospective observational study conducted to observe presenting profiles and outcomes of treatment of critically ill chest disease patients.
Methods All ICU admitted patients were enrolled consecutively. Baseline demographic and laboratory characteristics including primary diagnosis, present clinical problem, arterial blood gas, electrolytes, sputum microscopic findings were noted. Types of intervention and outcomes of the patients in term of death, referral, discharged were noted.
Results Total 429 patients were enrolled. Male: Female was 1.66 : 1.294 cases (68.5%) had type-2 respiratory failure, mainly due to COPD (74.8%) followed by bilateral bronchiectasis (17.34%), and severe persistent asthma (7.24%). Type-1 respiratory failure was seen in 105 cases (24.4%); due to acute asthma in 42.6%, ARDS in 24.8%, ILD in 32% cases. Mean PCO_2 was 76 mm of Hg; range 60–158 mm of Hg. BiPAP was given in all patients. 88.75% was compliant and 72.58% had satisfactory improvement. Invasive ventilation was given to rest. No growth was seen in 46.86% patients on sputum or tracheal aspirates culture. Acinatobacter (36.8%) and pseudomonas (52.4%) were main culprit organisms. Acinatobacter was resistant to all antibiotics except colistin (88.5%). Mortality was 32.4%. 12.87% referred to other hospitals and 55.6% discharged. Among intubated patients, ventilation associated pneumonia (VAP) followed by septic shock seen in 64.7% and cardiac arrest due to arrhythmias or myocardial ischemia seen in 32.9% patients as cause of death.
Conclusion Type-2 Respiratory failure was the main cause of referral to ICU in this specialized chest hospital. BiPAP was very effective to reduce PCO_2. VAP was predominant cause of death in intubated patients.

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 postoperative 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

STUDY OF INCIDENCE, OUTCOME AND ANTIBIOTIC SENSITIVITY PATTERN OF VENTILATOR ASSOCIATED PNEUMONIA IN ICU OF TERTIARY CARE HOSPITAL IN NEPAL

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Background Ventilator Associated pneumonia (VAP) is an important intensive care unit (ICU)-acquired infection in mechanically ventilated patients. Early and correct diagnosis of VAP is difficult but is an urgent challenge for an optimal antibiotic treatment.
Aim of Study To evaluate the incidence, microbiology and antibiotic sensitivity pattern of Ventilator Associated Pneumonia.
Methods A prospective, open, epidemiological clinical study was performed in ICU of TUTH, Maharajgunj. 100 patients admitted to ICU and Mechanically Ventilated were evaluated with regard to VAP. Clinical Pulmonary Infection Score (CPIS) was used as tools to diagnose VAP.
Results Among 60 long-term ventilated patients, 25 (41.6%) developed VAP. The incidence was 25 VAPs per 100 ventilated patients or 26 VAPs per 1000 ventilator days during the period of study. Days on ventilator and duration in ICU were higher in the VAP group. There was a trend towards increasing mortality in the VAP group (p value 0.06). The VAP was caused predominantly by Klebsiella pneumonia in 34.5% of cases, followed by Acinetobacter calcoaceticus baumanni in 27.6%, Acinetobacter wolffi and Pseudomonas aeruginosa in 13.8% each and Escheresia coli in 10.3%. The most sensitive antibiotics were Colistin, followed by Polymyxin B and Amikacin with sensitivity rates of 67%, 60% and 58% respectively.
Conclusion There exists a high rate of VAP in our ICU. Targeted strategies aimed at reducing VAP should be implemented to improve patient outcome and reduce length of ICU stay and costs.

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

HUMAN RHINOVIRUS INFECTION OF ASTHMATIC AIRWAY EPITHELIAL CELLS CAUSES TIGHT JUNCTION DISASSEMBLY RESULTING IN INCREASED PERMEABILITY

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Introduction Human rhinovirus (HRV) has been identified as a major contributor of asthma exacerbations in children and has been suggested to occur by epithelial tight junction (TJ) protein modification and barrier integrity disruption. This study aimed to directly correlate live viral infection with TJ disassembly and whether this leads to barrier compromisation.
Methods Polarised human epithelial colorectal adenocarcinoma cells (Caco-2), modified human airway epithelial cell (NuLi-1) and primary human airway epithelial cells (pAECs) were infected with HRV-1B at various multiplicity of infection (MOI) over 24 hours. HRV receptor and viral replication were assessed via qPCR while cell viability and apoptosis was assessed via proliferation and apoptotic assays. TJ protein expression of occludin, claudin-1 and zonal occludin-1 (ZO-1) was assessed using in-cell western assays. Transepithelial permeability assays were performed to assess effects on barrier integrity.
Results Elevated basal LDL receptor expression was observed in asthmatic pAECs compared to healthy, but no significant change was seen in both cohorts following HRV-1B infection. Interestingly, viral replication was significantly higher in asthmatic pAECs compared to the healthy. A MOI-dependent effect on cell viability was observed in both healthy and asthmatic pAECs. Despite a significant 400-fold increase in apoptosis, no significant difference was detected in the apoptotic response between healthy and asthmatic pAECs 24 h post infection. Although disassembly of tight junctions occurred with increasing MOI in the pAECs, a greater effect occurred within the asthmatic cohorts. A marked increase in transepithelial permeability was concurrent with this disassembly following infection.
Conclusion Primary airway epithelial cells more susceptible to HRV-1B infection. At lower MOI, this causes a disassembly of TJ proteins, especially exaggerated in the asthmatic pAECs that is concomitant with increased transepithelial permeability. This may facilitate trafficking of small sized aeroallergens into the sub-epithelial space which could lead to the initiation of asthma exacerbation.

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 promot 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.
Funded by GlaxoSmithKline (HZC113684, NCT01376245)

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 ($70.57 \pm 26.80\%$), FEV1 ($81.57 \pm 23.71\%$), TLC ($75.71 \pm 20.20\%$), RV ($64.00 \pm 10.41\%$), RV/TLC ($35.14 \pm 7.90\%$) as compared to autoimmune/connective tissue disorder related pulmonary fibrosis group [FVC ($75.40 \pm 20.29\%$), FEV1 ($87.10 \pm 24.11\%$), TLC ($88.20 \pm 23.54\%$), RV ($89.40 \pm 37.64\%$) and RV/TLC ($36.20 \pm 12.31\%$)]. Autoimmune/connective tissue disorder related pulmonary fibrosis had lower DLCO ($52.80 \pm 13.86\%$) than IPF group ($65.71 \pm 39.30\%$).
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 intrapulmonary 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 $60.73 \pm 6.03\%$, $92.59 \pm 1.52\%$, $68.29 \pm 6.16\%$ and $163.6 \pm 14.17\%$, respectively. DLco % pred and DLco/VA % pred at first visit were $66.36 \pm 7.20\%$ and $84.48 \pm 7.09\%$ ($n = 12$). Annual decrease in FVC was -295.8 ± 73.1 mL ($-16.25 \pm 2.73\%$) ($n = 13$), and annual decrease in DLco was $-20.28 \pm 6.95\%$ ($n = 6$).
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.

[Correction added on 23 October 2013, after print publication and first online publication: Author name HAJIME TAKIAWA was corrected to HAJIME TAKIZAWA in abstract OS163.]

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

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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 $HLA\text{-}DR^+$). 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.
Acknowledgments This study was supported by grants from the Guangzhou Medical University Youth Fund Projects (No. 2010A26) and National Nature Science Foundation (No. 30872358).

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.