Oral presentation 6

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· **Chairs:** Kwang Ha Yoo (Konkuk Univ.), Man Yong Han (CHA Univ.)

OP-56

Exposure to particulate matter impaired the lung function in children

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Background: Particulate matter is associated with asthma symptoms and respiratory tract infection in children. However, the longitudinal impact of exposure to air pollution on lung function of children is poorly understood yet. The purpose of this study was to investigate the effect of particulate matter on lung function in Korean school students.
Methods: A total of 2231 children (grade 1 and 2) from 33 elementary schools in 10 cities in 2005-2006 were included in a baseline survey of the Children's Health and Environmental Research (CHEER) study. Their children underwent pulmonary function test. Particulate matter (PM10) was measured by the ordinary kriging method. Ordinary kriging was implemented with the Geostatistical Analyst extension of Arc-GIS. We calculated the first year after birth, the 3 years after birth, and recent 2 years mean concentration at the individual level based on location of the residence.
Results: Higher exposure of PM10 had relationship with with FEF25-75% < 80% (aOR, 1.432; 95% CIs, 0.959-2.139; p-value, 0.079) during the first year after birth. We observed that higher level of PM10 was association with FEV1/FVC<80% (aOR, 2.081; 95% CIs, 1.015-4.268; p-value, 0.045) during recent 2 years. And continuous exposure (during the first year after birth and recent 2 years) to higher than mean levels of PM10 is associated with FEV1<80% (aOR, 23.129; 95% CIs, 1.536-348.379; p-value, 0.023)
Conclusions: These findings suggested that early-life and recent exposure PM10 impaired lung function in children. Effective reduction of air pollution may improve the lung function in childhood.

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Key Words: air pollution, particulate matter, lung function, children

OP-57

Profiles and Characteristics of Bronchial Responsiveness in Korean 7-year-old Children

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Introduction: Although bronchial responsiveness (BR) is used as a diagnostic tool for asthma, it does not exist in a dichotomy, but in a spectrum. We aimed to evaluate the distribution profile and characteristics of BR in the 7-year-old general population.
Methods: The 7-year-old birth cohort participants visited 16 regional study hospitals for skin prick test, standard spirometry, bronchial provocation test and a detailed history and physical examination. BR was categorized into five ordered groups and also log-transformed into a continuous marker response dose ratio (RDR). The distribution frequency, prevalence of recent wheezing, baseline lung function, and the prevalence of atopic sensitization across five groups and the association between RDR and allergic symptoms were assessed.
Results: Among 1577 birth-cohort participants, 559 subjects completed bronchial provocation test. 10.0% (56/559) of total population showed a provocative concentration of inhaled methacholine causing 20% fall in forced expiratory volume in 1 second (PC20FEV1)<4mg/mL (Group1) and 15.7% between 4 and 16 mg/mL (Group2). 14.7% showed PC20FEV1 ≥ 16 mg/mL but PC15FEV1 < 16mg/mL (Group3), 18.4% PC15FEV1 ≥ 16 mg/mL but PC10FEV1 < 16mg/mL (Group4), and 41.1% PC10FEV1 ≥ 16 mg/mL (Group 5). As the group number increases the proportion of subjects with wheezy episodes during the last year decreased (P for trend = 0.004), the proportion of those with allergic sensitization decreased (P for trend < 0.001), but the mean baseline FEV1percentage-predicted increased (P<0.001). RDR was significantly higher in current asthmatics than in others (P=0.022), and me RDR increased across the groups of control, allergic rhinitis only, asthma only, and combined allergic rhinitis and asthma (P=0.001).
Conclusion: The BR of 7-year-old general population showed a wide spectrum, associates with allergic symptoms, and correlates negatively with baseline lung function and positively with atopic sensitization.
Key Words: bronchial responsiveness, children, asthma

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Soluble CD93 as a novel biomarker for allergic asthma

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Background: CD93, a membrane-associated glycoprotein, has been studied as a novel biomarker for various inflammatory and immune associated disease. We aimed to evaluate the potential role of soluble form of CD93 (sCD93) as a novel biomarker for allergic asthma in vitro and in vivo.
Methods: We performed house dust mite (HDM) stimulation in BEAS-2B and U937 cell line. Dexamethasone was treated to reduce stimulation effect in vitro. We measured mRNA expression of various genes by qPCR. Level of protein was analyzed by ELISA. We investigate CD93 expression in ovalbumin (OVA)-induced asthma mice model. In addition, we measured serum sCD93 level using ELISA in 96 human subjects.
Results: HDM stimulated BEAS-2B cell showed increased mRNA expression of IL-6, TSLP and IL-33 whereas CD93 mRNA expression was decreased. In contrary, HDM stimulated U937 cell showed increased level of sCD93 in culture supernatant. This phenomenon was suppressed by dexamethasone treatment. In vivo, OVA sensitization and exposure led to reduce CD93 level in bronchial epithelial cell and lung homogenates; whereas it led to increased CD93 level in serum. In human, serum sCD93 level in asthma patients (155.3±9.1 μg/mL) was significantly higher than that in control (112.2±3.7 μg/mL, $P < 0.001$). When adjusted with age and sex, higher level of CD93 ($\geq$ 138.5 μg/mL) predicts asthma with moderate sensitivity (71.4%) and specificity (82.4%) (AUC = 0.787, $P < 0.001$).
Conclusion: The CD93 expression in bronchial epithelial cell is decreased after allergic stimulation; however, it is increased in serum in vitro and in vivo. We demonstrated sCD93 can be a novel biomarker for allergic asthma.

Key Words: asthma, biomarker, CD93

OP-59

Clinical characteristics of asthma patients with high level of leukotriene E4

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Background: The cysteinyl leukotrienes including LTC4/LTD4/LTE4 are important mediators for bronchoconstriction, inflammatory cell infiltration, mucus production, and smooth muscle proliferation in the airways of asthmatic patients.
Aim: This study was aimed to compare the serum and urine levels of LTE4 according to asthma control status and phenotype on regular anti-asthmatic medications including inhaled corticosteroid and leukotriene receptor antagonist.
Method: Peripheral venous blood and urine samples were collected from 137 asthmatics (72 well controlled ; 48 partly controlled; 17 uncontrolled by GINA guideline) and 20 healthy controls. The levels of serum and urine LTE4 were measured using LC-MS/MS.
Results: Serum and urine levels of LTE4 showed no significant differences according to the control status in total asthmatics and in patients with aspirin tolerant asthma (ATA). In patients with aspirin exacerbated respiratory disease (AERD), serum and urine levels of LTE4 were significantly higher in patients with uncontrolled status ($P=0.002$, compared to those with well controlled and partly controlled status; $P=0.047$ compared to those with partly controlled, respectively). Serum and urine levels of LTE4 were significantly higher in patients with eosinophilic asthma (peripheral eosinophil count $\geq$ 300 /μL) ($P=0.001$, $P=0.010$ in total asthma and $P=0.049$, $P=0.010$ in AERD). Significant positive correlations were observed between serum/urine levels of LTE4 and the level of FeNO in asthmatics ($P=0.005$, $r=0.243$ and $P<0.001$, $r=0.356$) while a negative correlation was noted between urine LTE4 level and FEV1/FVC ($P=0.042$, $r=-0.175$).
Conclusion: Taking into account the relation between high levels of LTE4 in uncontrolled asthmatics and eosinophilic inflammation with airway obstruction, there are unmet needs for development of new anti-inflammatory medications and leukotriene modulators.

Key Words: leukotrienes, uncontrolled asthma, eosinophilic inflammation

OP-60

Age-of-asthma onset and characteristics of adult-onset asthma in the Korean general population

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Age-of-asthma onset is used to define asthma phenotypes. In particular, late- or adult-onset asthma is suggested as a distinct entity; however, the age criteria for the classification have been inconsistent in the literature. We aimed to examine the distribution of age-of-asthma onset and characterize subjects with adult-onset asthma in the Korean general population. A cross-sectional dataset from 56,632 participants in the Korean National Health and Nutrition Examination Survey 2010-2016 was analyzed. History of physician-diagnosed asthma and age-on-asthma onset were asked using structured questionnaires. Demographic and clinical parameters were also assessed. Estimated mean value of age-of-asthma onset was 15.27±0.49 years (mean ± standard error) among all subjects with physician-diagnosed asthma. Histogram showed a sharp edge peak in early childhood which became flat since around the age of 15 years. Based on the distribution pattern, we classified asthma into childhood-onset (onset age$<$15 years) and adult-onset asthma (onset age$\geq$15 years) for subsequent analyses. In multivariate logistic regression analyses (vs. childhood-onset asthma), adult-onset asthma had significant relationships with female, smoking history, obesity, allergic rhinitis and chronic rhinosinusitis with nasal polyps (CRSwNP). In explorative classification of adult-onset asthma into early-adult-onset (onset age 15-39 years) and late-adult-onset subgroups (onset age$\geq$40 years), obesity and CRSwNP were significant determinants for late-adult-onset asthma (vs. early adult-onset asthma). The present general population analyses suggest the age-of-onset around 15 years is a reasonable criterion for differentiating childhood-onset and adult-onset asthma. Adult-onset asthma in the general population were associated with female, obesity and CRSwNP, supporting the conclusions from clinic-based cluster analyses of asthma patients. Obesity and CRSwNP may have important roles in late-adult-onset asthma.

Key Words: Age-of-asthma onset, late-onset asthma, epidemiology

OP-61

Sputum gene expression analysis identifies two clusters in elderly asthma

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Background: Pathogenesis of asthma in the elderly has not been fully understood. Gene expression is tissue-specific and provides a clue for understanding disease pathogenesis. This study aimed to identify a sputum gene expression signature that specifies and discriminates asthma in the elderly.
Method: We enrolled 58 elderly asthmatics and 14 elderly controls and performed genome-wide gene expression analysis of their sputum. Sputum induction was done before starting treatments. Then we performed cluster and gene-set enrichment analysis using differentially expressed genes between elderly asthmatics and controls.
Results: Cluster analysis of 3,156 differentially expressed genes revealed two, distinctive gene expression clusters. One cluster (cluster 1) was characterized by more sputum eosinophil and worse lung function compared to the other cluster (cluster 2). Oxidative phosphorylation, P53, and unfolded protein response pathways were significantly enriched in the cluster 1, whereas epithelial-mesenchymal transition, KRAS signaling, and myogenesis pathways were significantly enriched in the cluster 2.
Conclusion: Our analysis suggested that there might be two different mechanisms underlying pathogenesis of asthma in the elderly.

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Key Words: Elderly asthma, Sputum, Gene expression, Cluster

OP-62

Severe asthma and high doses of corticosteroid use impair trabecular bone score more than bone mineral density

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Background: Corticosteroid treatment in asthmatic patients may lead to bone loss. Trabecular bone score (TBS) is a new, indirect parameter of bone quality. Studies have yet to evaluate TBS in asthmatic patients in relation to disease severity and corticosteroid use.
Objective: This study aimed to evaluate TBS in asthmatics in comparison to propensity score-matched controls and to investigate correlations between TBS and systemic and inhaled corticosteroid doses 1 year prior to bone mineral density measurement.
Methods: In total, 627 patients with asthma (193 severe, 101 non-severe, 333 non-active asthma) and the same number of non-asthmatic controls matched for sex and age were included in this retrospective cohort study. TBS was calculated in the lumbar region, based on two dimensional projections of dual-energy X-ray absorptiometry.
Results: Patients with severe asthma exhibited lower vertebral TBS values (1.33±0.11) than those with non-severe asthma (1.37±0.10, P=.004), with non-active asthma (1.38±0.10, P<0.001), and without asthma (1.39±0.10, P<.001). No significant differences in BMD were noted among the study groups (0.96±0.18 vs 0.98±0.25 vs 0.97±0.17 vs 0.97±0.18, all P-values>.05). TBS was significantly associated with cumulative systemic and inhaled corticosteroid doses, as well as lung function and airway hyper-responsiveness. A TBS of 1.42 was determined as a cut-off for osteoporosis. A multivariate analysis revealed that age, systemic corticosteroid dose ≥5mg/day and inhaled corticosteroid ≥90mg of fluticasone equivalent doses for a year prior to BMD measurement were significant predictors of reduced TBS in patients with asthma.
Conclusion: The present study demonstrates that TBS can be of use as an early indicator of alterations in bone quality resulting from glucocorticoid therapy and severe asthma.

Funding: This research was funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HI17C0970).
Key Words: Asthma, Trabecular bone score, Glucocorticoid

OP-63

Serum periostin level: a potential serologic marker for toluene diisocyanate-induced occupational asthma

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Background: Toluene diisocyanate (TDI) is a leading cause of occupational asthma (OA). Periostin is a matricellular protein which is implicated in the type 2 immunity driven asthma. Its pathogenic roles in TDI-OA have not been studied yet. The present study was performed to investigate the pathogenic role of periostin in TDI-OA
Methods: Serum levels of periostin were measured by ELISA in patients with TDI-OA and compared to those of asymptomatic TDI-exposure controls (AECs) and unexposed normal controls (NCs). To understand the mechanism by which TDI induces periostin production, we cultured airway epithelial cells including primary small airway epithelial cells (SAECs) under the stimulation of TDI and neutrophils from asthmatic patients.
Results: Fifty three patients with TDI-OA, 82 AECs and 83 NCs were enrolled. Serum level of periostin was significantly higher in TDI-OA subjects than in AECs (P=0.025) and NCs (P<0.001). When clinical parameters were compared between subjects with high periostin level and those with lower periostin among TDI-exposed subjects (TDI-OA and AEC), significantly lower PC20 methacholine level was noted in high periostin responders. TDI exposure could not increase periostin production directly from SAECs, however, periostin production increased significantly after the co-culture with TDI and neutrophils, which were suppressed by an anti-oxidant. In addition, increased release of TGF-β1 was noted from SAECs when exposed to TDI and neutrophils, which was also suppressed by anti-oxidant.
Conclusions: These findings suggest that increased periostin level may contribute to progression of airway inflammation to remodeling in TDI-exposed workers. High serum periostin level is a potential serologic marker for representing the phenotype of TDI-OA.

Key Words: Diisocyanate, occupational asthma, periostin

OP-64

Inhaled corticosteroid related tuberculosis in real world among the patients with asthma and COPD

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Background: To investigate the occurrence of tuberculosis (TB) in the real world among inhaled corticosteroids (ICS) users according to underlying respiratory diseases and different types of ICS including budesonide and fluticasone.
Methods: A 12-year population cohort (from 2002 to 2013) comprising about one million subjects collected from the Korean National Health Insurance Research Database was used. Enrolled patients included new adult users of ICS (budesonide or fluticasone) between January 1, 2003, and November 31, 2012. Temporal relationship between TB development and ICS usage were evaluated among them. TB was defined with ICD codes and use of anti-TB medication within 3 months of TB diagnosis. And then a nested case-control (1:4) study was performed. ICS users with TB development were identified as cases and control individuals were matched for age, sex, and initiation date of ICS.
Results: There were 18,300 ICS users and 175 ICS users with TB development during study period. 80% (140/175) of them got tuberculosis within 3 years after last prescription of ICS. In the nested case-control study, type of ICS was not related with occurrence of tuberculosis. However, the patients with TB showed higher annual admission rates and higher Charlson Comorbidity Index (CCI) score. After adjustments with age, sex, OCS dose, CCI score, and annual admission rates, the risks of ICS-related TB were higher in patients with COPD than those with asthma (OR: 2.31, CI 95%: 1.39-3.38, p = 0.0011). In the subgroup analysis for patients with each underlying respiratory diseases such as asthma, COPD, and ACOS, there were no differences between budesonide and fluticasone in the risk of TB developments.
Conclusion: Type of ICS was not related with ICS-related TB. Severity of underlying respiratory and higher burden of comorbidities seemed to be related with TB developments. Patients with COPD showed higher risk of TB than those with asthma and ACOS.

Key Words: inhaled corticosteroids, tuberculosis, budesonide, fluticasone, COPD, asthma

OP-65

Characteristics of clinical phenotypes of childhood atopic dermatitis depending on the timing of onset: PSKC study

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Background: Atopic dermatitis (AD) is an inflammatory, pruritic skin disease that often occurs in early infancy with a chronic course. However, a specific description of subtypes of AD depending on the timing of onset and progression of the disease in childhood is lacking. We aimed to investigate different clinical phenotypes of AD using a definition based on symptoms before age 2 years and to determine risk factors of each phenotype.
Methods: This study includes 633 seven-year-old children from the Panel study on Korean Children (PSKC). We divided AD into early onset (onset before the first 2 years of life) and late onset according to the time of onset, and early onset group was divided into a persistence group and remission group according to whether they persisted AD symptoms until age 7. All subjects were performed laboratory tests and skin prick tests. Pediatric allergists confirmed the history of AD symptoms and the presence of recent AD symptoms by physical examination. Current AD was defined as having AD symptoms within the last 12 months and physician-diagnosed AD.
Results: The prevalence of physician diagnosed AD and current AD was 25.1% (158/633) and 13.2% (83/629) in 7-year-old children. Among children with AD, early onset(<2yr) AD was 52.0% (53/102). Children with early onset AD had higher rates of parental history of allergic disease, history of bronchiolitis and sensitization to aeroallergen than children with late onset AD. In early onset AD, AD symptoms improved in 52% children until 7 years of age. There was no difference in the remission group compared with the persistence group in ratio of atopy and comorbidity of other respiratory allergic diseases.
Conclusion: Early onset AD is likely to be associated with allergic sensitization and other respiratory allergic diseases regardless of remission. These findings are important for the development of strategies in allergy prevention.

Key Words: Atopic dermatitis, Prevalence, Risk factors

OP-66

Absorbance ratio of toxocara ELISA is useful for the prognostic prediction of pulmonary toxocariasis

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Background: Toxocariasis is a common cause of eosinophilic lung infiltration in Korea. Due to difficulty of obtaining biopsy tissue containing the toxocara larvae, diagnosis of pulmonary toxocariasis is based on patient history and serologic detection of IgG antibodies against larval antigens. However, positive serologic test does not necessarily indicate current clinical toxocara canis infection and may result in overdiagnosis. In addition to the limited diagnostic tool, there are yet no useful parameters to predict prognosis of pulmonary toxocariasis.
Materials and Methods: We retrospectively reviewed 102 patients with both pulmonary infiltration and positive enzyme immunoassay (ELISA) of specific IgG antibodies against toxocara larval antigens. We have used index value of toxocara ELISA which is defined by the ratio of absorbance of sample to absorbance of the weak positive control serum. We analyzed the correlation between the index with other laboratory tests, findings of imaging studies, and interval improvement in chest computed tomography scan (CT) of 1 month.
Result: The index value of toxocara ELISA correlated with the peripheral blood eosinophil counts and total IgE levels ($r = 0.354$; $P < 0.001$, $r = 0.314$; $P = 0.04$, respectively). Higher index value was related with progression of lung infiltration while lower index value was related with partial or complete remission of lung involvement in chest CT (OR = 2.37; 95% CI 1.08 - 5.20; $P = 0.031$) after one month.
Conclusion: Our study suggested that the index value of toxocara ELISA may be useful to improve the diagnosis and predict prognosis of pulmonary toxocariasis.

Key Words: Toxocariasis, eosinophilia, lung infiltration, ELISA