Poster

P-01

Effects of Weather and Air Pollutants on Emergency Department Use of Asthma Patients in Busan, Ulsan, and Gyeongsangnam-do

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Background: Weather and air pollution are associated with exacerbation of asthma. The purpose of this study is to analyze the effects of air pollution and meteorological factors on emergency department use of asthma patients based on residence in Busan, Ulsan, and Gyeongsangnam-do.
Methods: We analyzed the effects of weather and air pollutants on the use of emergency department for asthma patients in Busan, Ulsan, and Gyeongsangnam-do using Korea Health Insurance Review and Assessment data from 2007 to 2013.
Results: The medical use of asthma patients increased when mean temperature (incidence rate ratio [IRR] 0.984, P<0.001) and relative humidity (IRR 0.994, P<0.001) were lower, while temperature difference (IRR1.019, P<0.001) and atmospheric pressure (IRR 1.016, P<0.001) were higher. Analysis of the effect of air pollutants showed that the higher the concentration of PM10 (IRR 1.001, P<0.001) and ozone (IRR 1.002, P<0.001), the more medical use patterns of asthma were. In the interaction analysis, PM10 interacted with the mean temperature and relative humidity, thereby increasing the use of emergency medical care. Ozone interacted with mean temperature, temperature difference, and relative humidity. In the sensitivity analysis by age, it showed to be sensitive at ages 0-9 and ≥65 years.
Conclusion: PM10, ozone, and meteorological factors impacted the use of emergency department, especially in children and the elderly. Furthermore, their effects should consider the interaction of weather and air pollutants.

Key Words: Asthma, Weather, Air pollutant

P-02

Association of Pollen Sensitization Pattern with Pollen-Food Allergy Syndrome

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Background: Sensitization pattern is regionally different according to surrounding environments, such as temperature, moisture, CO2 concentration, and proportion of greenbelt. We analyzed sensitization pattern of our region and analyzed its impact on pollen-food allergy syndrome (PFAS).
Methods: We retrospectively analyzed questionnaire survey and skin prick test of Seongnam Citizens' Health Festival at Oct. 14th, 2018. Food hypersensitivity symptoms were asked to each subject, especially for fruits or vegetables, crustaceans, and wheat. When the subjects have hypersensitivity symptoms after exposure of fruits or vegetables, we asked additional questionnaires about pollen-food allergy syndrome (PFAS) which was used in previous nationwide survey.
Results: A total of 203 subjects completed both the questionnaire and skin prick test. Mean age was 47.0±18.8 (rage 7-81) years old and 39.6% were consisted of male. There were 84 subjects (41.4%) without any allergic diseases and the others have 1 (46.3%) or 2 or more (12.3%) allergic diseases. Sensitization rate to each allergen was 28.6% (D.p), 16.3% (birch), 15.3% (oak), 4.4% (timothy), 4.4% (ragweed), 8.9% (mugwort), 6.9% (Hop J), 11.3% (cat), and 10.8% (dog). Food hypersensitivity symptoms were noted in 5.9% (fruits or vegetables), 5.4% (crustaceans), and 2.5% (wheat). We analyzed clinical parameters associated with fruits or vegetables hypersensitivity. Sensitization of grass or weed pollen was associated with fruits or vegetables hypersensitivity along with BMI and comorbidity of chronic urticaria. Especially, when subject were sensitized to all of 3 weed pollens, 16-fold increased risk of PFAS was observed (OR=16.111, P=0.056). In addition, if subject has hypersensitivity to wheat, the risk of fruits or vegetables hypersensitivity was 9.167 (P=0.081) and that of crustacean was 19.667 (P=0.005).
Conclusion: Sensitization of grass or weed pollen was associated with PFAS in addition to history of food allergy to wheat.

Key Words: Pollen, Sensitization, Pollen-food allergy syndrome

P-03

Ozone-Induced Lung Injury Mouse Model Exhibits the Emphysematous Changes with Airflow Obstruction Mimicking Human Chronic Obstructive Pulmonary Diseases

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To understand the pathogenesis of chronic obstructive pulmonary diseases (COPD) and to screen new drug targets, the valid animal model is required. A cigarette smoke (CS)-induced model remains the most popular one. However, it usually requires 3-12 months to induce the COPD animal model by CS which is such a time-consuming and labor-intensive process. In this study, we aimed to establish the protocol for the ozone-induced COPD murine model and to differentiate the aging effects from the real ozone-induced detrimental effects on the lung in the mice. Ozone-induced COPD murine model was established by the exposure to 3 ppm of ozone twice a week for 7 weeks. Time-course analysis showed that the number of BAL cells was increased in air-exposed mice and ozone-exposed mice at the same age (i.e., 14 weeks) compared to young air-exposed mice (i.e., 6-7 weeks). The expression of TGF-β, IL-17, and IL-1β is gradually increased as ozone-exposed time goes by up to 7 weeks (TGF-β, IL-17) and 6 weeks (IL-1β), respectively. In addition, ozone-exposed mice for 7 weeks revealed that decreased lung function (FEV0.1) and increased alveolar destruction in lung tissues compared to air-exposed mice. Interestingly, old air-exposed mice (14 weeks) showed more severe lung destruction than young aged air-exposed mice (6-7 weeks). These findings suggest that ozone-exposed mice can be used for preclinical experiments regarding COPD as a better choice than CS-induced models and that this mouse model reflects the detrimental effects of aging as well as ozone on the lung more physiologically.

Key Words: Ozone, Airflow obstruction, Emphysematous changes

P-04

A Deep Learning Approach for Detecting the Effects Of Indoor Air Pollutants Concentrations on Pulmonary Function Test Results: Are Asthma Attacks Predictable?

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Background: Despite ample research on the association between indoor air pollution and asthma exacerbation, public health and environmental policies still lack predictive evidence for developing a preventive guideline for patients or vulnerable populations mostly due to limitation of real-time big data and model predictability. Recent popularity of IoT and machine learning techniques could provide enabling technologies for collecting real-time big data and analyzing them for more accurate prediction of allergic disease risks for evidence-based intervention, but the effort is still in its infancy.
Method: This pilot study explores and evaluates a predictability of the deep learning algorithm on detecting temporal correlation between indoor air indicators and pulmonary function by linking daily peak expiratory flow rate (PEFR) results for 16 asthmatic children visiting the Korea University Guro Hospital with outdoor air data and indoor air pollutants concentration data collected at their residence at every 10 minutes between June 1, 2017 and July 31, 2018. We interpolated the daily PEFR results for each patient throughout the day so that it can be matched to the indoor air data including temperature, humidity, radon, PM10, PM2.5, VOCs, CO2, NO2, and HCHO.
Results: It is found that the temporal patterns of PEFR results correspond better with many indoor air indicators,compared to a similar model using outdoor air data. The deep learning experiments using the first 10 months of the linked data revealed an acceptable level of predictability in the change of PEFR for the last 2 months during the study period.
Conclusion: Upon successful modifications of the algorithm based on a larger sample, this approach could potentially play a groundbreaking role for asthma exacerbation and scientific data-driven environmental health intervention.

Key Words: Indoor air pollutants, Pulmonary function test, Deep learning

P-05

The Effect of Mechanical Hot Dryer for Removing Pollens Allergens

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Rationale: Pollens may be spread to indoor by clothes contaminated during outdoor activity. This study aimed to evaluate the pollen removal efficacy of sanitize course from dryer (Samsung Electronics Co, Seoul, Korea)
Method: Test loads of 100% cottons were 2kg in dry and 4kg in wet condition and size of test fabric is 2x5cm. Birch, Japanese cider, ragweed, and timothy grass pollens were used. After spread pollen, there store for 8 hours at RT and counted pollen as control by Calberla's stain. The fabrics were fixed on test loads and proceeded the dry and wet sanitized course and counted pollen on the fabric to evaluate pollen removal rate on a loads. We measured remaining allergens in extracts from the contaminated fabrics after the dry and wet sanitize course. The concentrations of allergens (Amb a 1, Bet v 1, Crp j 1, and Phl p 1) in each extracted solution were measured by 2-site enzyme linked immunosorbent assay.
Result: Mean removal rate of pollen concentration was 99.9% for birch, 99.95% for Japanese cedar, 99.84% for timothy grass, and 99.91 for ragweed in dry condition and 96.04% for birch, 95.23% for Japanese cedar, 97.59% for timothy grass, and 98.63 for ragweed in wet condition. Mean removal rate of pollen allergens was 99.8% for birch, 99.8% for Japanese cedar, 99.9% for timothy grass, and 99.9% for ragweed.
Conclusion: Sanitize course of dryer removed more than 95 % of the pollens outside of the clothes when the load is dry and wet condition.

Key Words: Pollen allergy, Pollen, Mechanical hot dryer

P-06

Identification and Characterization of Allergen Homologues from Japanese Hop Pollen

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Background: Japanese hop is an important cause of seasonal pollinosis in East Asia. However, molecular characteristics of the major allergen have not been elucidated.
Method: cDNA library was constructed using In-Fusion SMARTerTM Directional cDNA Library Construction kit (Clontech) with 50 ng of total RNA from Japanese hop pollen. Allergen homologues were identified by the initial screening of 963 EST clones. Recombinant proteins of pathogenesis-related 1 (PR-1), pectin methyl esterase (PME), and profilin were produced and IgE reactivities were examined by ELISA.
Results: PME of Japanese hop shares amino acid sequence identity of 50.2% with Act d 7 (green kiwi allergen), 24.2% with Ole e 11 (olive), and 23.2% with Sal k 1 (Russian thistle). PR1 shows 43.3% of identities to Art v 1 (mugwort), 42.5% to Cuc m 3 (muskmelon), and 49.3% to Cyn d 24 (Bermuda grass). IgE antibodies from Japanese hop allergy patients' sera recognized 13.8% (4/29) of PME, 3.4% (1/29) of PR-1, and 13.8% (4/29) of profilin, respectively. Combination of three recombinant proteins showed only 27.5% (8/29) of IgE reactivity to the sera tested.
Conclusion: Novel allergens were identified, even though low IgE reactivity was displayed reflecting the low degree of cross-reactivity with other pollen allergens. In-Fusion SMARTer Directional Library Construction kit enables construction of full-length cDNA library for the identification of novel allergens only from nanograms of pollen RNA.

Key Words: Allergen, Pollinosis, Japanese hop

P-07

Diagnostic Values of Skin Prick Test and Allergen-Specific IgE in Evaluating Laboratory Animal Allergy among Korean Laboratory Animal Researchers

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Background: Diagnostic values of skin prick test (SPT) and allergen-specific IgE in evaluating laboratory animal allergy (LAA) is not fully investigated yet.
Methods: A total of 223 Korean laboratory researchers who attended 2018 annual symposium of Korean Association of Laboratory Animal Science responded to the questionnaires regarding animal allergy and to undergo SPT using animal allergens including mouse and rat epithelium allergen extract (Lofarma, Milano, Italy). In 51 subjects who showed positivity in SPT, bloods were drawn to measure serum levels of mouse- and rat-specific IgEs (ImmunoCAP, Thermofisher, Uppsala, Sweden).
Results: In whole subjects, 65 (29.0%) and 29 (13.1%) experienced respiratory or dermatologic allergic symptoms during exposure to mouse and rat, respectively. Sensitivity, specificity, positive predictive value, and negative predictive value were 52.5%, 83.9%, 57.1%, and 81.2% in SPT using mouse allergen, whereas 23.0%, 94.0%, 60.9%, and 74.9% in SPT using rat allergen. In 51 subjects whose bloods were drawn to evaluate allergen-specific IgEs, sensitivity, specificity, positive predictive value, and negative predictive value of allergen-specific IgEs were 81.5%, 33.3%, 57.9%, and 61.5% for mouse epithelium; 70.4%, 70.8%, 73.1%, 68% for mouse urine, 63.0%, 33.3%, 51.5%, and 44.4% for mouse serum; 57.1%, 51.4%, 30.8%, and 76.0% for rat epithelium; 71.4%, 35.1%, 29.4%, and 76.5% for rat urine; 42.9%, 48.6%, 24.0%, and 69.2% for rat serum.
Conclusion: Diagnostic values of SPT and allergen-specific IgE in evaluating laboratory animal allergy (LAA) are relatively low. Allergen extracts used in SPT and allergen-specific IgE are warranted to be qualified.

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Key Words: Skin prick test, Specific IgE, Mouse, Rat

P-08

Clinical Value of Detecting Specific IgE for Cat and Dog Allergens Including Major Allergen Components

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Background: Confirming the presence of specific IgE (sIgE) is important for diagnosis and management of pet allergy. However, cross-reactivity between cat and dog make difficult to interpret the sIgE. Therefore, the usefulness of IgE measurements for allergen extracts or allergen components of pets has been questioned.
Methods: One hundred eighty-eight patients with allergic rhinitis were enrolled. sIgE for cat (e1) and dog (e5) total allergen extracts and for allergen components (Fel d 1, Can f 1) were measured in the sera of patients. Then, the sIgE positivity for allergens were compared among groups (non-owners, cat owners, dog owners, and owners of both). In addition, positive concordance rates among sIgE for allergen extracts, sIgE for allergen components and results of skin prick test were calculated.
Results: Positivity of e1 were higher in cat owners (83.7%) than dog owners (63.8%) or non-owners (38.8%). However, positivity of Fel d 1 were not different between cat owners (63.3%) and dog owners (77.5%, p=0.080). Positive concordance rate of e1 and Fel d 1 was 80%. Positive concordance rate with skin prick test was higher at e1 than Fel d 1. (83.7% vs. 73.8%). Positivity of e5 in dog owners (41.3%) did not statistically differ with non-owners (38.8%), and it was even higher in cat owners (77.6%) than dog owners. Positivity of Can f 1 in dog owners (48.8%) were higher than non-owners (10.2%), however, it was not different from cat owners (40.8%, p=0.380). Positive concordance rate of e5 and Can f 1 was 54.8%. Positive concordance rate with skin prick test was higher at e5 than Can f 1. (74.5% vs. 54.6%).
Conclusions: Allergen extracts-based sIgE detection is suitable in cat allergy. However, in dog allergy, sIgE detection of allergen component should be considered in addition to testing for allergen extracts.

Key Words: Component resolved diagnosis, Specific IgE, Pet allergy

P-09

Role of PLUNC/AKAP350 Proteins in Allergen-Induced Airway Inflammation

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Introduction: Innate immunity has been involved in the mechanism of allergir rhinitis(AR). Epithelial cells act as inflammatory promoters inducing the Th2 response as well as barrier functions. We previously demonstrated that PLUNC (LPLUNC1/SPLUNC1) and AKAP350 proteins, which are known to be involved in barrier functions, showed significant expression differences in nasal fluids before/after the nasal provocation tests with HDM in patients with AR using a proteomic analysis. The present study was aimed to investigate the role of these proteins in the airway inflammation of AR.
Methods: To investigate the role of SPLUNC1/LPLUNC1/AKAP 350 proteins in airway epithelial cells (AECs), we evaluated their production patterns in A549 cells in response of toll-like receptor (TLR) 3 agonist/HDM exposure. Western blot and fluorescence microscopy were performed to evaluate their expression changes in AECs. ELISA was used to measure released levels of SPLUNC1/LPLUNC1/AKAP 350 in the culture supernatant of AECs. Correlations between these proteins and innate immune cytokines of HAECs, TSLP/IL-33 were explored.
Results: With TLR3 agonist/HDM exposure, expressions of SPLUNC1/ LPLUNC1 in AECs increased initially, and then, decreased at higher exposure doses; release of SPLUNC1 from AECs increased significantly in dose-dependent manners, while no significant changes were noted in LPLUNC1. HDM exposure significantly increased expression and release of AKAP350 in AECs. Furthermore, increased release of IL-33/TSLP was noted from AECs when exposed to HDM, which were significantly correlated with SPLUNC1/AKAP350 levels.
Conclusion: We have confirmed the increased production/release of SPLUNC1/AKAP350 in HEACs by HDM exposure. In addition, our results suggest that increased release of SPLUNC1/AKAP350 from AECs may be contributed to TSLP/IL33-derived airway inflammation.

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Key Words: Innate immunity, Airway inflammation, PLUNC, AKAP350

P-10

Effect of New-Types of Smoking Alternatives in Asthma and Allergic Rhinitis in Adolescent

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Background: Smoking is known to be one of the major risk factors for development of allergic rhinitis (AR) and asthma. Electronic cigarette (EC) and heated tobacco product (HTP) were developed as an alternatives to conventional cigarette (CC) but the health effect of EC and HTP is still under investigation.
Objective: To evaluate the effect of EC and HTP on asthma and AR.
Methods: This study was conducted using the 14th Korea Youth Risk Behavior Web-based Survey (KYRBWS), which represented Korean middle and high school students. Self-administered questionnaires were used to assess the presence of asthma and AR, and the status of CC, EC and, HTP use. The relationship between current asthma/AR and CC and EC use was evaluated using logistic regression modelling for complex survey data. Estimates were adjusted for age and sex (model 1), and further adjusted for other covariates such as BMI, residential area, regular exercise, sedentary time, exposure to secondhand smoke, and socioeconomic status (model 2).
Results: A total of 59,734 participants representing 2,850,118 Korean middle and high school students were analyzed. Of the total participants, 8.7% and 36.6% had current asthma and allergic rhinitis, respectively, and 6.7%, 2.7%, and 1.4% were current CC users, current EC users and ever HTP users (who had ever used HTPs), respectively. Current CC use was significantly associated with current asthma (odds ratio [OR] 1.5, 95% confidence interval [CI] 1.2-1.9) and AR (OR 1.3, 95% CI 1.2-1.5) in adjusted models. Current EC use was significantly associated with current AR (OR 1.5, 95% CI 1.2-1.8) but not with current asthma in adjusted models. The relationship between ever HTP use and current asthma was significantly increased (OR 1.5, 95% CI 1.0-2.3) in adjusted model.
Conclusion: CC and HTP use were related with current AR and asthma and EC use seemed associated with current AR but not asthma. Switching CC from EC may lower risk of current asthma.

Key Words: Electronic nicotine delivery systems, Asthma, Rhinitis, Allergic

P-11

Synergistic Effects of Prenatal Maternal Anxiety and Particulate Matter PM2.5 on the Risk of Atopic Dermatitis in the First Year of Life: COCOA Study

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Rationale: Maternal stress during pregnancy is associated with allergic diseases including atopic dermatitis (AD). Growing evidences have shown that prenatal particulate matter (PM) exposure may increase the risk of AD in the early life of children. We examined effects of prenatal PM2.5 and prenatal maternal anxiety on the risk of AD in infants.
Methods: The study included 802 infants from the COhort for Childhood Origin of Asthma and Allergic Diseases (COCOA) study, which is a general population-based birth cohort study. Maternal anxiety was measured based on mother's responses to the questioners about maternal state and trait anxiety (STAI) at 36 weeks during pregnancy and dichotomized as low and high. PM2.5 exposure during pregnancy was estimated using land-use regression models based on national monitoring system. A diagnosis of AD was based on physician's diagnosis at age 1 year. Logistic regression was used to estimate the effects of prenatal exposure to PM and maternal anxiety on the risk of AD in infants.
Results: Higher maternal STAI score was associated with an increased risk of AD at age 1. Higher PM2.5 exposure in first trimester was associated with an increased risk of AD. We observed an interaction between prenatal exposure to PM2.5 and maternal anxiety relation to AD risk in infants at age 1.
Conclusion: PM2.5 exposure and maternal anxiety during pregnancy synergistically effect on the risk of AD at age 1 year.

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Key Words: Particulate matter, Prenatal maternal anxiety, Atopic dermatitis

P-12

Comparison of the Perceptions and Lifestyles Toward Pet Allergies: A Cross-Sectional Questionnaire Survey among Participants from the Pet Exhibition in Korea

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Background: The aim of this study was to investigate and compare the perceptions and lifestyles regarding pet (dog and cat) allergies.
Methods: We conducted questionnaire survey for subjects who participated in a pet exhibition. Self-reported questionnaires included pet related allergic symptoms, perceptions of pet allergies as well as lifestyles.
Results: A total of 582 participants who underwent questionnaire survey and testing included in this study (464 females, mean age 30.4 years). The prevalence of pet related symptoms were 19.6% in dog and 23.0% in cat. Physician diagnosed allergic rhinitis, asthma, atopic dermatitis and family history of allergic disease were more prevalent in the symptomatic group (SG) than the asymptomatic group (ASG). There was no difference in the frequencies of cleaning beds and home cleaning between two groups. SG thought pet allergies to be more common in proportion to duration and frequency of exposure, number of pets and comorbid allergic diseases, whereas ASG responded that there were no associations between pet exposure and allergies. SG reported that frequent shaving and washing pets could prevent allergies, and that pet hair removal from clothes was most effective measure to avoid allergic symptoms, along with washing the pet, using air purifiers and restriction of exposure. SG and ASG equally reported that physician prescription was regarded as the first action plan for allergic symptoms, followed by over-the-counter medications and receiving allergen immunotherapy. Moreover, SG had significantly more positive response to treatment, while many did not receive allergen immunotherapy.
Conclusion: There were differences in perception of pet allergies but not in lifestyle according to the presence or absence of pet allergy. Future efforts should focus on raising awareness of environmental control measures and treatment against pet allergies.

Acknowledgement: This research was supported by a grant from the KAAACI (2018).

Key Words: Questionnaire survey, Pet allergy, Perception

P-13

Clinical Manifestations and Risk Factors of Anaphylaxis in Pollen-Food Allergy Syndrome

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Objective: Many studies have reported that pollen-food allergy syndrome (PFAS) can cause anaphylaxis. No comprehensive investigations regarding anaphylaxis in PFAS have been conducted. In this study, we investigated the clinical manifestations and risk factors for anaphylaxis in PFAS in Korean patients with pollinosis.
Methods: Data obtained from the nationwide cross-sectional study previously reported regarding PFAS in Korean patients with pollinosis. Data of 273 patients with PFAS were collected, including demographics, list of culprit fruits and vegetables, and clinical manifestations of food allergy. We analyzed 27 anaphylaxis patients and compared them with patients with PFAS with oropharyngeal symptoms only (n=130).
Results: The most common cause of anaphylaxis in PFAS was peanut (33.3%), apple (22.2%), walnut (22.2%), pine nut (18.5%), peach (14.8%), and ginseng (14.8%). Anaphylaxis was significantly associated with the strength of sensitization to alder, hazel, willow, poplar, timothy, and ragweed (P<0.05, respectively). Multivariable analysis revealed that the presence of atopic dermatitis (odds ratio [OR], 3.58; 95% confidence interval [CI], 1.25–10.23; P=0.017), sensitization to hazel (OR, 5.27; 95% CI, 1.79–15.53; P=0.003), timothy (OR, 11.8; 95% CI, 2.70–51.64; P=0.001), ragweed (OR, 3.18; 95% CI, 1.03–9.87; P=0.045), and the number of culprit foods (OR, 1.25; 95% CI, 1.15–1.37; P<0.001) were related to the development of anaphylaxis in PFAS.
Conclusion: The most common culprit foods causing anaphylaxis in PFAS were peanut and apple. The presence of atopic dermatitis, sensitization to hazel, timothy, ragweed, and higher number of culprit foods were a risk factor for anaphylaxis in PFAS.

Key Words: Pollen-food allergy syndrome, Pollen, Food allergy, Anaphylaxis

P-14

Trends in Asthma-Related Mortality in Korea, 2002-2015

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Background: Asthmatic patients have higher prevalence of comorbid conditions contributing to mortality. There have been little data to report asthma-related mortality according to asthma severity in Korea.
Methods: Using the National Health Insurance Sharing Service (NHISS) database, we observed the prevalence of adult asthma, and defined asthma-related deaths (ARD) based on patients' prescription records if a patient has at least 1 prescription for ≥1 of the following prescription history; SABA ≥1 canister, ICS ≥1 canister, ICS/LABA ≥1 canister, LTRA ≥30 days or Xanthine ≥ 30 days within 3 months before all-caused-death. Then, NHISS data was linked to Causes of Death Survey (CDS) by Korean Statistical Information Service. We thoroughly examined the cause of deaths, and defined that asthma-caused deaths and asthma-contributing deaths (ACTD), if patient's cause of death on CDS was of diseases of asthma (J45-J46), the respiratory system (J00-J99), respectively, and compared it with ARD.
Results: The age-standardized (AS)-ARD seems to be increasing from 16.2 per 100,000 population (CI=15.75-16.56) in 2002. Since reaching its peak at 34.2 per 100,000 population (CI=33.76, 34.70) in 2012, the AS-ARD had slightly decreased. The AS-ARD of male was higher than that of female, and both of ARD and ACTD showed the increasing trends, which was the opposite of trends by the data from Statistics from Korea. It was noted that the ACTD increased more than 3 times and the age group over 80 years showed the highest ARD all the years. The leading cause of death was definitely neoplasms (30%-37%), followed by diseases of the respiratory system (27-33%) and the circulatory system (13%-18%).
Conclusions: The asthma mortality showed a steady rising trend while asthma-caused mortality by Statistics Korea displayed the trends to a steady decline. This is also derived from increasing population of elderly, as they have more comorbid conditions and are not active to treatments

Key Words: Asthma, Mortality, Cause of death

P-15

Associated Factors of Asthma Severity in Korean Children

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Background: Childhood asthma has a considerable social impact and economic burden, especially in severe asthma. This study aimed to identify the proportion of childhood asthma severity and to evaluate the associated factors for greater asthma severity.
Methods: This study was performed in 667 children aged 5–15 years with asthma from the nationwide 19 hospitals in the Korean childhood Asthma Study (KAS). Asthma was classified as mild intermittent, mild persistent, moderate/severe persistent groups according to the National Asthma Education and Prevention Program recommendations. Multinomial logistic regression models were used to identify the associated factors for greater asthma severity.
Results: Mild persistent asthma was the most prevalent (39.0%), followed by mild intermittent (37.6%), moderate persistent (22.8%), and severe persistent asthma (0.6%). Onset later than 6 years of age (adjusted odds ratio [aOR], 1.69 for mild persistent asthma; aOR, 1.92 for moderate/severe persistent asthma) was positively correlated with asthma severity. Exposure to environmental tobacco smoke (aOR, 1.53 for mild persistent asthma; aOR, 1.85 for moderate/severe persistent asthma), and current dog ownership with sensitization to dog dander (aOR, 5.86 for mild persistent asthma; aOR, 6.90 for moderate/severe persistent asthma) showed dose–dependent relationships with greater asthma severity. Lower maternal education levels (aOR, 2.32) and no usage of an air purifier in exposure to high levels of outdoor air pollution (aOR, 1.76) increased the risk of moderate/severe asthma.
Conclusions: Modification of the identified environmental factors associated with greater asthma severity might help better control childhood asthma, thereby reducing the disease burden due to childhood asthma.

Key Words: Childhood asthma, Severity, Risk factor

P-16

Identification of Severe Asthma Patients Eligible for Anti-IL-5 or Anti-IgE Treatment: Findings from a Korean Asthma Cohort, COREA

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Background: With the introduction of various biologic agents, clinicians have the important task of deciding the phenotype of the asthma patient and initiating the proper biologic when needed.
Objective: To evaluate the prevalence and characteristics of the candidates eligible for anti–IL–5 and/or anti Ig E among asthma patients from the Cohort for Reality and Evolution of Adult Asthma in Korea (COREA).
Methods: Patients with severe asthma were defined according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines. Among them, the eligibility for each biologic agent was determined by the regulatory labels of Korea Food and Drug Administration.
Results: Of the 4955 patients in the COREA database, 809 (16.3%) patients were defined having severe asthma. Among the severe asthma patients, 297 (297/809, 36.7%) were eligible for anti–IL–5, mepolizumab and 51 (51/809, 6.3%) were eligible for anti–Ig E, omalizumab. Twenty–seven patients were eligible for both biologics. When comparisons were made among the three groups, namely, only mepolizumab–eligible, only omalizumab–eligible, and the overlap groups, it was observed that the overlapping population had the youngest patients and most frequent use of triple inhaler therapy. Approximately 10% and 50% of the mepolizumab and omalizumab eligible patients, respectively, constituted the overlap group.
Conclusion: The present study identified the prevalence and described the characteristics of subgroups of severe asthma patients according to eligibility for mepolizumab and omalizumab. Since there was a considerable proportion of patients who could be responders for more than one targeting agent, further studies guiding the treatment for this overlap population are required.

Key Words: Severe asthma, Biologics, Anti–IL–5, Anti–Ig E

P-17

Lung Function Decline in Elderly Asthma: 3-Year Follow Up in Prospective Study

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Introduction: Asthma in the elderly (age ≥65 year-old) is increasing and poses a great socioeconomic burden on the health care system. We investigated annual lung function decline among in elderly asthma cohort during 36 months.
Methods: Three existing adult asthma cohorts in Korea merged into elderly asthma cohort with a unified protocol and database. We selected a total of 1,382 patients from the merged cohort to evaluate risk factors predicting acute exacerbation during one year prior to the enrollment. Baseline data were collected on clinical variables, smoking history and atopic status. Exacerbation and longitudinal lung function change was observed over a period of 3 years. Lung function decline was compared using a linear mixed effect model for longitudinal data.
Results: Overall, the elderly asthma patients experienced a rate of decline of lung function (Forced expiratory volume in 1 second, FEV1) of 49±5.8 ml per year. Among subjects who participated in 36 months, the adjusted decline in FEV1 among subjects with exacerbation in asthma was −64±5.32 ml per year, as compared with −46±5.71 ml per year in those without exacerbation (p=0.036). Independent factors associated with an accelerated decline of lung function were more frequent severe exacerbations, baseline fixed airway obstruction and chronic sinusitis.
Conclusion: In our prospective study, recurrent exacerbation and fixed airway obstruction are associated with lung function decline in elderly asthma.

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Key Words: Asthma, Lung function, FEV1

P-18

Development of an Accurate Operational Definition for Asthma Using Decision Tree Model

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Background: Analysis of the National Health Insurance data has been actively carried out for the purpose of academic research and establishing scientific evidences for health care service policy in asthma. However, there has been a limitation for the accuracy of the data extracted through conventional operational definition.
Aim: To establish an operational definition that predicts asthma more accurately.
Methods: From Jan 2017 to Jan 2018, we extracted patients with asthma using the conventional operational definition in St. Paul's Hospital at the Catholic University of Korea. Among these, 10% of patients were randomly sampled and analyzed. Using the decision tree model, we established the most accurate operational definition of asthma and validated it.
Results: Total 85 patients were enrolled in this study. Twenty-eight patients were not eligible for asthma. Of these, 22 patients were chronic obstructive pulmonary disease. By decision tree model, operational definition of asthma was most precise when it included inhaled corticosteroid and excluded long-acting muscarinic antagonists. As a result of validation of this model, the overall accuracy was 80.0 % (95 % confidence interval : 0.593-0.9317), sensitivity was 75.0 % and specificity was 82.4 %.
Conclusions: The conventional operational definition of asthma has limitation to extract true asthma patients in real world. Therefore, it is necessary to establish an accurate standardized operational definition of asthma.

Key Words: Asthma, Diagnosis, Validation

P-19

Relationship between Asthma and Sarcopenia in the Elderly Population: A Nationwide Cross-Sectional Study from KNHANES 2008-2011

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Background: The prevalence of asthma has been greatly increasing in the older population in recent years. With the previous study showing that regular physical activity was important for healthy aging, physical activity plays potential roles on healthy aging, and lowering the risk of development of several diseases, there has been no study on the relationships of asthma with that including physical activity. Therefore, we aimed to examine the relationships of asthma with sarcopenia including physical activity in a nationwide population.
Methods: A cross-sectional dataset from 28,758 participants in the Korean National Health and Nutrition Examination Survey 2008-2011 was analyzed. History of asthma, including asthma onset age, recent asthma exacerbation, and hospitalization due to asthma exacerbation was asked using structured questionnaires. Appendicular skeletal muscle (ASM) was calculated as the sum of the skeletal muscle mass, and physical activity was calculated as metabolic equivalents (METs) by using the International Physical Activity Questionnaire.
Results: Estimated proportion of asthma patients was 6.17±0.37% in the elderly, and those were older, female predominant, more obese, lower lung function, and myopenia than never asthma. Asthma with myopenia was significantly related to older age, younger asthma onset age, male predominance, less obese, lower lung functions, and lower physical activity, and had a higher proportion of admission and recent asthma exacerbation (vs. asthma with non-myopenia).
Conclusion: Muscle mass may play a more important role in lung functions and asthma controls than physical activity in the elderly asthma patients.

Key Words: Sarcopenia, Asthma, Physical activity

P-20

Comorbidities of Adult Asthma according to Severity: Analysis of NHISS Database

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Background: Asthma is a heterogenous disease with a variety of phenotypes and clinical courses, and therefore comorbidities vary with age and disease severity. The well known asthma comorbiditie include rhinitis, gastroesophageal reflux disease (GERD), hypertensive disease, obstructive sleep apnea, hormonal disorders and psychopathologies. However, comorbiditie of asthma is not studied in population base and difference in comorbidities according to severity is not studied well in Korea.
Methods: National Health Insurance claim records from July 1, 2005 and June 31, 2016 were analyzed in a retrospective, population-based study. Among those data, we conducted the analysis of frequent comorbidities in adult asthmatics. Patients were divided into the following groups according to severity of asthma; patients with non-severe asthma (NSA) and patients with severe asthma (SA). Risk of major comorbidities were analyzed according to morbidity and severity of asthma.
Results: Vasomotor and allergic rhinitis, bronchitis, upper respiratory infection, and GERD were common comorbid conditions in all patients with asthma. COPD was more common in SA than NSA according to asthma severity. In major comorbidities, patients with asthma had more risk in chronic diseases such as diabetes mellitus (odds ratio (OR): [95% CI] 1.21 [1.20, 1,22]) and hypertensive disease (OR 1.24 [1.23, 1.25]) as well as rhinitis (OR 7.42 [7.38, 7.46]), GERD (OR 2.29 [2.28, 2.30]) and osteoporosis. In addition, these trends were similar in comparison between SA and NSA. Patients with SA had more comorbidities than NSA and higher incidence of cardiovascular disease, cerebrovascular disease, dementia, and several psychological diseases.
Conclusions: Patients with asthma had a higher risk of chronic diseases than patients without asthma, and there was a tendency of higher risk of major comorbidities in severe asthma. Clinicians should consider influence of comorbid diseases in the asthma patient care.

Key Words: Asthma, Athma severity, Comorbiditie

P-21

Clinical Characteristics of Severe Eosinophilic Asthma: Analysis from the Korean Severe Asthma Registry (KOSAR)

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This study was performed to identify and analyze eosinophilic asthma from the Korean Severe Asthma Registry (KOSAR) in comparison with non-eosinophilic asthma. In the KOSAR, patients are registered since 2010 from 15 hospitals nationwide in Korea according to the severe asthma definition of the modified ERS/ATS criteria. We defined eosinophilic asthma to have more than 300 blood eosinophils per microliter and non-eosinophilic asthma to have less than 150 blood eosinophils per microliter. We identified 195 (40.8%) patients with eosinophilic asthma and 178 (37.2%) patients with non-eosinophilic asthma among 478 severe asthmatics. Mean blood eosinophil count was 779.5±577.6 cells/ul in the eosinophilic asthma and 70.7±45.2 cells/ul in the non-eosinophilic asthma. Age, sex, BMI, smoking history, presence of atopy were similar in both groups. Allergic rhinitis was notably more prevalent in the eosinophilic asthmatics, while medical history of diabetes mellitus and pulmonary tuberculosis was more reported in the non-eosinophilic group. FEV1 and FVC % predicted were significantly lower in the non-eosinophilic asthmatics. Fraction of exhaled nitric oxide was higher, as well as the percentage of sputum eosinophils in the eosinophilic asthma. Clinical control status was rated rather poor in both groups with no significant difference, as ACT score was 18.1±5.3, and unexpected medical seek was also high with admission rates of 23.7% (no difference). In terms of medication, concomitant usage of long acting muscarinic antagonists was higher in the non-eosinophilic asthma, and we found no difference in the usage of biologics such as anti-IgE and anti-IL5 antibodies in both groups. Systemic corticosteroid was used in higher dosage in the non-eosinophilic asthma. Eosinophilic asthma comprises nearly half of severe asthmatics in Korea, and efforts to better control asthma symptoms and disease burden should follow in this severe eosinophilic asthma subset.

Key Words: Asthma, Severe asthma, Severe eosinophilic asthma

P-22

Clinical Efficacy of Information and Communication Technology based Monitoring in Asthma

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Backgrounds: Wide application of Information and Communication Technologies (ICT) to health care have allowed the development of tele-medicine based programs of care with chronic diseases. The aim of this study was to evaluation the impact of ICT based monitoring of asthma.

Methods: We conducted a 6-month prospective randomized controlled trials for patients with asthma. Participants were centrally randomized to ICT group or control group. Primary outcome measures were changes of symptoms and quality of life, lung function. The ICT group provided ICT base monitoring system (daily recording and transmission of symptoms and FEV1, peak flow with immediate feedback promoting action according to an agreed plan). The control group was managing to visit the hospital every month.

Results: A total of 100 were enrolled. Ten were withdrawn from consent, resulting in 43 ICT and 47 control subjects. There was no difference in baseline characteristics. There was no significant difference in the change of symptoms score, quality of life, lung function between the two groups. The numbers of patients who had acute exacerbation was lower without significant in ICT group (4 vs.12, p=0.056). There was no statistically significant difference in drug compliance. The cost of hospitalization and transportation was low in the ICT group, but the total cost was higher in the ICT group because the cost of monitoring system was high in the ICT group.

Conclusions: This study did not demonstrate significant differences in asthma related outcomes between two group. The ICT based monitoring system was no cost effective.

Key Words: Asthma, Information technology, Telemedicine

P-23

Risk of a Severe Exacerbation Following Higher Reliever Use: Post-Hoc Analysis of SYGMA 1 in Mild Asthma

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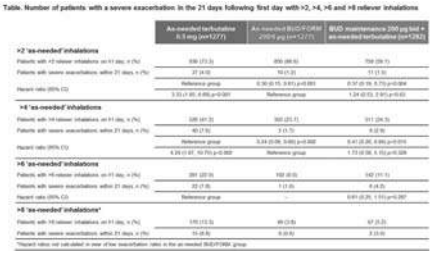
Introduction: In mild asthma, as-needed budesonide/formoterol (BUD/FORM) reduces long-term severe exacerbation risk vs terbutaline as-needed, with similar reduction as maintenance BUD + terbutaline as-needed. In a post-hoc analysis of SYGMA 1 (NCT02149199; O'Byrne et al. NEJM 2018;378(20):1865-1876) we examined the short-term risk of a severe exacerbation after a single day with various levels of reliever use, comparing terbutaline as-needed, BUD/FORM as-needed, and maintenance BUD + terbutaline as-needed.
Methods: In the SYGMA 1 study, 3836 patients with mild asthma were randomised to placebo twice daily (bid) + terbutaline 0.5 mg as-needed, placebo bid + BUD/FORM 200/6 μg as-needed, or maintenance BUD 200 μg bid + terbutaline as-needed. For patients with >2, >4, >6 or >8 reliever inhalations on any day, the proportions who had a severe exacerbation during the next 21 days were compared.
Results: The proportion of patients with >4, >6 or >8 as-needed inhalation use days was lower with BUD/FORM as-needed vs terbutaline as-needed and maintenance BUD + terbutaline as-needed, with reduced risk of severe exacerbation during the next 21 days vs terbutaline as-needed (Fig; Table). The safety of BUD/FORM as-needed was consistent across all inhalation groups, with no new safety findings.
Conclusions: In mild asthma, anti-inflammatory reliever therapy with BUD/FORM as-needed reduces higher reliever use days and reduces exacerbations within the next 21 days vs terbutaline as-needed.



Key Words: Asthma, Asthma-management, Exacerbation

P-24

Dupilumab Benefits in Uncontrolled, Moderate-to-Severe Asthma with High and Low Baseline FEV1

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Background: Dupilumab, a fully human anti-IL-4 receptor α monoclonal antibody, inhibits IL-4 and IL-13, key drivers of Type 2 inflammation, and is approved for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis. In the phase 3 LIBERTY ASTHMA QUEST study, dupilumab 200 mg and 300 mg every 2 weeks vs matched placebo reduced annualized severe exacerbation rates and improved pre-bronchodilator FEV1, quality of life measures, and was generally well tolerated in patients with uncontrolled moderate-to-severe asthma. This analysis assessed the efficacy of dupilumab in subgroups by baseline percent predicted FEV1 (high [60%-90%] or low [<60%]).
Method: Annualized severe exacerbation rates during the 52-week treatment period and change from baseline in pre-bronchodilator FEV1 (L) at Week 12 were stratified and analyzed by baseline FEV1 (60%-90%/<60%).
Results: Dupilumab 200 mg and 300 mg vs matched placebo significantly reduced annualized severe exacerbation rates in both high (43% and 49% reduction) and low (53% and 44% reduction) baseline FEV1 subgroups (nominal P<0.01). Placebo groups with low FEV1 experienced higher annualized rates of severe exacerbations (1.046/1.160) than those with high FEV1 (0.734/0.814). Dupilumab 200 mg and 300 mg improved pre-bronchodilator FEV1 at Week 12 (LS mean change from baseline in FEV1 [L] vs placebo): high FEV1, 0.22 (0.02 SE) vs 0.13 (0.03), and 0.23 (0.02) vs 0.14 (0.03); low FEV1, 0.43 (0.03) vs 0.25 (0.04), and 0.45 (0.03) vs 0.28 (0.04), respectively (nominal P<0.01). The most frequent adverse event in the dupilumab-treated groups vs placebo was injection-site reactions (15%/18% vs 5%/10%).
Conclusions: Dupilumab significantly reduced severe exacerbation rates and improved FEV1, regardless of baseline percent predicted FEV1, in patients with uncontrolled moderate-to-severe asthma. Improvements in FEV1 were greater in patients with low baseline FEV1. Treatment was generally well tolerated.

Key Words: Asthma, Dupilumab, Baseline FEV1

P-25

Dupilumab Benefits In Uncontrolled, Moderate-to-Severe Asthma on Both High- and Medium Dose ICS

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Background: Dupilumab (DPL), a fully human antibody against IL-4 receptor α subunit that inhibits IL-4 and IL-13, key drivers of type 2 inflammation, is approved for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). In a double-blind, placebo (PBO) controlled phase 3 study (NCT02414854), asthmatics aged ≥12 years, without a minimum baseline eosinophil requirement, uncontrolled with medium-to-high-dose inhaled corticosteroids (ICS) plus up to two additional controllers, received add-on DPL 200/300 mg or matched PBO every 2 weeks (q2w) for 52 weeks. For the overall intent-to-treat (ITT) population, both DPL regimens significantly reduced annualized severe exacerbation rates during the 52-week treatment period, improved pre-bronchodilator (BD) FEV1 at Week 12, improved asthma symptoms/quality of life measures, and were generally well tolerated. This pre-specified analysis assessed the efficacy of DPL by disease severity determined by baseline ICS dose.
Methods: Annualized severe exacerbation rates during the 52-week treatment period and change from baseline in pre-BD FEV1 (L) at Week 12 were analyzed by baseline ICS dose (high/medium) subgroups.
Results: Both DPL q2w doses vs PBO significantly reduced annualized severe exacerbation rates over the 52 week treatment period (P<0.01) and improved pre-BD FEV1 at Week 12 (P<0.01) regardless of baseline ICS dose. Overall, reduction in exacerbation rate and improvement in FEV1 appear similar between high- and medium-dose ICS subgroups. The most frequent adverse event (AE) occurring at higher frequency in the DPL-treated groups vs PBO was injection site reactions (15%/18% vs 5%/10%, respectively). Conjunctivitis AEs were similar between DPL and PBO, in contrast to DPL studies in AD.
Conclusions: Dupilumab significantly reduced the rate of severe exacerbations, and improved FEV1 regardless of disease severity (as measured by ICS dose at baseline) in patients with moderate-to-severe asthma.

Key Words: Asthma, Dupilumab, Baseline ICS dose

P-26

EQ-5D Utility in Respiratory Allergy According to Disease Control

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Background: The EuroQol Five-Dimensional Questionnaire (EQ-5D) is a standardized instrument applied for measuring health outcomes across various diseases. To investigate the health impact of allergic diseases, the EQ-5D was assessed in patients with bronchial asthma (BA) and allergic rhinitis (AR) and was analyzed in accordance with disease control status.
Methods: In total, 253 patients with BA (54), AR (92), or BA + AR (107) were enrolled for to undergo EQ-5D assessment. Patient-oriented outcome measures, such as asthma control test and rhinitis control assessment test, were obtained. A generalized estimating equation was used to identify factors affecting EQ-5D.
Results: The overall mean EQ-5D scores in subjects with BA, AR, and BA + AR were 0.842, 0.914, and 0.869, respectively. EQ-5D scores differed significantly according to disease control status (well, partly, and uncontrolled) assessed by physicians (0.889 vs. 0.803 vs. 0.770, P<0.001 for BA, 0.933 vs. 0.873 vs. 0.868, P<0.001 for AR, 0.900 vs. 0.859 vs. 0.693, P<0.001 for BA + AR). The EQ-5D was significantly associated with patient-oriented outcome measures and responded well to changes in the control states of patients with BA and AR.
Conclusions: EQ-5D scores in BA and AR differed according to disease entity and were significantly associated with control test scores and disease activity. This study may be helpful for future modeling of quality-adjusted life years in pharmacoeconomic evaluation of allergic diseases.

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Key Words: Quality of life, Allergic diseases, Health impact

P-27

Characteristics and Risk Factors of Patients with Acute Asthma Exacerbation Visiting Pediatric Emergency Department

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Purpose: Acute asthma exacerbation is a major cause of children visiting pediatric emergency department (ED). The purpose of this study is to investigate clinical characteristics and risk factors of acute asthma exacerbation in pediatric ED.
Methods: We investigated medical records of patients who visited pediatric ED with acute asthma exacerbations from July 1, 2015 to June 31, 2018, retrospectively. The patient's history, family history, symptoms, treatment, hospitalization, laboratory tests and allergic tests were analyzed.
Results: Asthma (53.2%) was the most common history and allergic conjunctivitis (43.3%) was the most common family history. The symptoms and signs were as follows: wheezing (93.8%), cough (93.4%), dyspnea (89.2), tachypnea (55.6%) and chest retraction (41.8%). Asthma exacerbations occur most frequently in April and October and rhinovirus was also most commonly detected in April and October. History of asthma [adjusted odds ratio(aOR)]=4.197, p=.014) and neutropenia (aOR=2.722, p=.007) were the risk factors for oxygen administration in ED and neutrophilia (aOR=2.634, p=.040) and chest retraction symptom (aOR=7.335, p=<.001) were the risk factors for hospitalization. There were statistically significant relations in sensitization to food allergens with symptom persisting after 1 hour in ED (aOR=1.719, p=.019), oxygen supply (aOR=2.045, p=.004) and hospitalization (aOR=1.819, p=.010) in multivariable regression analysis.
Conclusion: History of asthma and rhinovirus infection were risk factors for visiting pediatric ED due to acute asthma exacerbations. History of asthma, neutropenia, chest retraction sign and sensitization to food allergen were important risk factors for more severe asthma exacerbation. Further studies are needed to identify more various risk factors for acute asthma exacerbation.

Key Words: Asthma, Children, Emergency department

P-28

Clinical Significance of Serum MRGPRX2 as a New Biomarker in Allergic Asthma

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Background: Although several biomarkers have been proposed for allergic asthma, parameters are still controversial as biomarkers to reflect the efficacy of treatment. Mas-related G protein-coupled receptor-X2 (MRGPRX2) is a newly emerging molecule in allergic and inflammatory disease.
Objective: The aim of this study was to analyze the MRGPRX2 concentrations in asthmatic patients, evaluating its role as a predictor of outcomes in allergic asthma.
Methods: We enrolled 102 healthy controls (CON), 164 allergic (AL), and 78 nonallergic asthmatic (NA) patients from the Cohort for Reality and Evolution of adult Asthma in Korea (COREA). We measured MRGPRX2 concentration (ng/ml) using an ELISA kit.
Results: The mean serum MRGPRX2 level in the allergic asthma was higher than nonallergic and healthy groups (AL: 102.4±54.5 vs. NA: 79.8±52.5 vs. CON: 12.9±9.8, p<0.001). Allergic asthmatic patients with higher MRGPRX2 levels required moderate-to-high dose than low dose inhaled corticosteroid (ICS) (108.1±52.9 vs.76.6±43.9, p=0.033) and had good response of ICS (well-controlled) than the uncontrolled group (113.4±55.2 vs.75.7±49.1, p=0.035). Furthermore, the optimal predictive cut-off value of MRGPRX2 level by ROC curve associated with ICS treatment response was 100 ng/ml (p=0.020, AUC=0.711).
Conclusion: Allergic asthmatic patients with MRGPRX2 levels≥100 ng/ml had good response of ICS although they need higher dose of ICS to treatment. This is the first study demonstrating the role of MRGPRX2 as new biomarker to predict treatment dose and response of ICS in allergic asthmatic patients.

Key Words: MRGPRX2, Allergic asthma, Biomarker

P-29

Antiasthmatic Effect of A. lwoffii Via Modulation of Macrophage Activation

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Background: Microbes have dual effects on the inception and aggravation of asthma and innate immune response initiated with diverse pathogen-associated molecular pattern such as lipopolysaccharides may play a role. Acinetobacter lwoffii (A. lwoffii) commonly found in stables is known to have a protective effect on asthma inception. However, its impact on macrophage activation in relation to asthma has not been addressed.
Objective: The aim of this study was to investigate in vivo and in vitro anti-asthmatic effects of A. lwoffii associated with macrophage activation.
Method: Six-week-old female C57BL/6 mice were sensitized and challenged with OVA with or without intranasal treatment of A. lwoffii during the sensitization periods. In the in vitro study, alveolar macrophages collected from bronchoalveolar lavage fluid were treated with A. lwoffii before or after IL-13 stimulation and analyzed with real-time quantitative PCR to evaluate the impact of A. lwoffii on M2 differentiation.
Result: In a murine asthma model, the number of inflammatory cells, especially macrophages decreased in mice treated with A. lwoffii (A. lwoffii/OVA group) compared to those untreated (OVA group). Among macrophage subsets, antigen presenting cells were significantly reduced. In A. lwoffii/OVA group, expression of IL-12, M1 marker, increased, whereas CD206 and Arg1, typical M2 markers, decreased. Expression of relm-α, a protective M2 marker, presented further enhancement by A. lwoffii. In vitro experiment, macrophages pretreated with A. lwoffii, showed upregulation of IL-12 and relm-α expression. However, these changes were not observed when A. lwoffii were treated after IL-13 stimulation. Although expression of iNOS, M1 marker, was not altered by IL-13 stimulation, A. lwoffii treatment upregulated iNOS expression when combined with IL-13 stimulation.
Conclusion: A. lwoffii has an anti-asthmatic effect, which seems to be mediated by the modulation of M1/M2 differentiation in part.

Key Words: Asthma, Acinetobacter lwoffii, Macrophage activation

P-30

Effectiveness of Pressurised Metered Dose Inhalers in Older Asthmatics

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Background: Asthma control in older patients is often less effective. Poor responses to treatment in older asthmatics may be associated with longer asthma duration and poor adherence/inhalation technique.
Methods: We conducted a 12-week, randomized, open-label, parallel-designed trial involving older patients (over 55 years) with moderate to severe asthma, and compared the efficacy of 2 different forms of inhalers (fluticasone propionate/formoterol <FP/FOR> via to pressurised metered dose inhalers <pMDI> vs. fluticasone propionate/salmeterol <FP/SAL>) via dry powder inhaler<DPI>) on asthma control. Their clinical parameters including treatment/disease durations, changes of lung function parameters (airway obstruction evaluated by spirometry and air trapping evaluated by body plethysmography), adherence and inhalation techniques were compared with monitoring adverse reactions.
Result: A total of 69 patients underwent randomization, and 63 (30 in the FP/FOR group and 33 in the FP/SAL group) completed this study. FP/FOR pMDI was non-inferior to FP/SAL DPI with regard to the rates of well-controlled asthma (56.7% vs 36.4% at 4 weeks, 40.0% vs 36.4% at 8 weeks, 53.3% vs 45.5% at 12 weeks between the FP/FOR and the FP/SAL, respectively, P <0.001; the predefined non-inferiority limit of 17%), A general estimating equation model demonstrated that age (OR: 0.945) and longer treatment duration (over 15 years) were significant predictors for well-controlled status, whereas inhaler type and asthma duration did not affect asthma control. No significant differences were observed in lung function parameters, adherence, inhalation techniques and adverse reactions between the 2 groups.
Conclusion: These findings suggest that pMDI is found to be noninferior to DPI in the management of older asthmatics in aspects of efficacy, adherence and safety.

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Key Words: Older asthmatics, Pressurised metered dose inhaler, Dry powder inhaler

P-31

Potential Role of CD93 in in vitro and in vivo Allergic Asthma Model

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Background: CD93 exists as a membrane-associated glycoprotein on the surface of cells, including endothelial and myeloid cells, involved in the inflammatory cascade. CD93 is receiving renewed attention as a biomarker of inflammation in various inflammatory and immune-mediated diseases. We aimed to evaluate the potential role of soluble form of CD93 (sCD93) in allergic asthma.
Methods: We performed house dust mite (HDM) extract (D. pteronyssinus) stimulation in BEAS-2B and U937 cell lines with and without dexamethasone or against CD93 siRNA treatment. We investigated CD93 expression and level in HDM-induced asthma mouse model.
Results: BEAS-2B cell stimulated by HDM extract showed increased mRNA expression of IL-6, IL-33, TSLP, and CD93. CD93 level in culture supernatants steadily increased for 24 hours after HDM stimulation, dexamethasone and CD93 siRNA treatment significantly suppressed it. The siRNA treatment led to increase of IL-6 and TSLP level in culture supernatants, whereas it did not affect IL-33 level. In HDM asthma mouse model, CD93 decreased in lung tissues and lung homogenates, whereas it increased in serum.
Conclusion: These data showed that level of sCD93 significantly increased after HDM stimulation in vitro and in vivo. We suggest potential role of sCD93 as a novel biomarker in allergic asthma.

Key Words: Asthma, Soluble CD93, House dust mite, U937 cell, BEAS-2B cell, Biomarker

P-32

Human Mesenchymal Stem Cells Prevent Chronic Allergic Airway Inflammation and Remodeling

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Purpose: Various models of experimental allergic asthma have shown that mesenchymal stem cells (MSCs) are a potential therapeutic treatment for TH2 cell-mediated inflammation. However, the long-term effects of hMSCs in chronic asthma are still unidentified. Using a mouse model of experimental allergic asthma, we investigated the long-term effects of human adipose-derived MSCs (hADSCs) and human bone marrow-derived MSCs (hBMSCs).
Materials and Methods: We examined five groups of female BALB/c mice (control; ovalbumin [OVA]-sensitized and -challenged mice; OVA-sensitized and -challenged mice treated with phosphate-buffered saline, hADSCs or hBMSCs). Airway hyperresponsiveness (AHR), cytokine production, and lung pathology were compared among the groups.
Results: The systemic administration of human ADSC and BMSC during the challenge protected the mice from the characters of the chronic allergic airway inflammation, in particular improving the airway remodeling and preventing fibrosis. In addition, hBMSC treatment significantly decreased AHR, but hADSC did not change AHR value.
Conclusions: The study demonstrated that human MSCs are capable for preventing chronic allergic airway inflammation and remodeling, which further proved the hMSCs therapeutic potential for allergic airway inflammation and remodeling. These data suggest that hBMSC may be more effective that hADSC in therapies for allergic asthma.
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Key Words: Asthma, Human mesenchymal stem cells, Animal model

P-33

Gut Clostridiales Regulates Airway Inflammation Via Modifying Acetate Production in Allergic Asthma

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Background: Gut microbiota is known to be involved in the pathogenesis of allergic asthma. However, the direct links between gut microbiota and the airway inflammation of allergic asthma have not yet been fully understood.
Objective: To determine the effect of gut microbiota on asthma control, we observed changes in gut microbiota during allergen challenges in an OVA-challegned asthma model.
Methods: Composition of microbiota in fecal and lung samples and their changes after 2 antibiotics (cefixime or azithromycin) treatment analyzed using 16S rRNA metagenomic analysis were compared between OVA-treated allergic (OVA-treated group) and PBS-treated mice (control group). Levels of short-chain fatty acids in feces were measured by gas chromatography-mass spectrometry. The effect of gut microbiota on airway inflammation was confirmed by fecal microbiota transplantation.
Results: Significantly higher bacterial load and lower bacterial diversity were found in feces of the OVA-treated group than in those of the control group, while no differences were found in bronchoalveolar lavage fluid between the 2 groups. Azithromycin (not cefixime) treatment suppressed airway hyperresponsiveness (AHR) and Th2-airway inflammation in the OVA-treated group along with significant increases in fecal Clostridiales and acetate levels. Acetate treatment attenuated AHR and Th2 airway inflammation in the OVA-treated group. Fecal microbiota transfer from azithromycin-treated mice reduced AHR and Th2-airway inflammation in the lungs.
Conclusions: These findings suggest that gut microbiota, Clostridiales regulates AHR and allergic airway inflammation via increasing production of acetate, which could be a novel therapeutic approach in the management of allergic asthma.

Key Words: Allergic asthma, Gut microbiota, Clostridiales

P-34

Airway Short Chain Fatty Acids Alleviate Allergic Airway Inflammation

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Purpose: While it has been recognized that airway microbiome in asthma is different from healthy subjects, much is not known well regarding the mechanisms how this microbiota affects airway inflammation in asthma. Short chain fatty acids (SCFA), such as sodium acetate (SA), sodium propionate and sodium butyrate, produced by bacteria, exert various immune modulating effects. In this experimental study, we examined the effects of locally administered SCFA into airway on the allergic inflammation using in vivo and in vitro model of asthma.
Methods: Ovalbumin (OVA) induced asthma was induced by sensitizing mice using the intraperitoneal injection of OVA and intranasal administration of OVA afterward. Each of three kinds of SCFA were administered into airway via intranasal route at the time of OVA challenge. Airway inflammation was compared between each SCFA group and controls in terms of inflammatory cell counts in bronchoalveolar lavage (BAL) fluids and lung histology and cytokine expression. In addition, the effects of SCFA was also examined in house dust mite (HDM) treated BEAS-2B cells.
Results: SCFA (SA, SP and SB)-treated mice showed significant decrease in total inflammatory cell counts and eosinophil counts in BAL fluid and lung histology. Airway hypreresponsiveness was significantly attenuated in the SP administrated group. OVA-specific IgE level and the expression of IL-1 beta, inflammasome cytokine, were also significantly decreased with administration of SCFA. Moreover, SCFA attenuated the synthesis of IL-1 beta in HDM treated BEAS-2B cells.
Conclusions: These findings suggest that airway SCFA have anti-inflammatory effects in asthma by downregulating allergic immune response and inflammasome pathway.

Key Words: Short chain fatty acid, Asthma, Inflammation

P-35

Role of Basophils in the Classification of Asthma Phenotype and the Relationship between the Cytokines in Exhaled Breath Condensate

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Background: Although basophils are major effector cells involved in the asthma, they remains unclear what exact role it plays in the pathophysiology of asthma. Therefore, we investigate the relationship between blood basophils and clinical features in asthmatics and to support the mechanism, we measured cytokines in exhaled breath condensate (EBC) which was relatively easy to obtain and noninvasive.
Methods: We have been enrolled the asthma patients in the Ewha Medical Center from 2017 to 2018 and defined asthma as followings: patients who have asthma symptoms with positive bronchodilator response or proven airway hyperresponsiveness. Information for demographics, comorbidities, smoking history, family history, pulmonary function test, and skin prick test were collected. The exhaled breath condensates were obtained from all registered patients and cytokines were measured in these specimens.
Results: A total of 13 patients were enrolled with a mean age of 60.2 years and 23% men. Non-smokers were 77%. Family history of allergic diseases was found in 61.5%. The mean FVC, FEV1, and FEV1/FVC were 83.1%, 75.9% of predicted value, and 74.4%, respectively. Bronchodilator response was proven in 60% and 66.7% of patients were atopic. Patients with high basophils ($\geq 50/\mu L$) had more frequent asthma exacerbations and absence from work due to asthma, and asthma control status and quality of life scores were worse, even though they had better pulmonary function than the patients with low basophils ($<50/\mu L$). In addition, IL-17 and IL-33 from EBC showed positive correlations with blood basophil counts in these asthma patients.
Conclusions: Basophils are thought to be a marker associated with frequent exacerbations of asthma independently of pulmonary function, which were also related to EBC IL-17 and IL-33. Although larger studies are needed in the future, it is likely that basophil is another criterion for asthma phenotyping.

Key Words: Asthma, Basophils, Breath tests

P-36

Pharmacologic Effects of a Novel PI3K-δ Inhibitor, YH25487 on Steroid-Resistant Eosinophilic Asthma in Mice

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Phosphoinositide 3-kinase (PI3K)-δ-dependent Akt activation play critical roles in various immune responses and PI3K-δ isoform is principally expressed in leukocytes. The restricted expression profile of PI3K-δ makes it an attractive drug target for various inflammatory conditions such as chronic airway disorders. Nowadays, it is believed that PI3K-δ contributes to the steroid resistance of severe respiratory diseases and more specifically that oxidative stress directly induces PI3K-δ-dependent Akt activation. With understanding the role of PI3K-δ in airway inflammatory disorders, recent developed PI3K-δ inhibitors are applying to control bronchial asthma or COPD in preclinical and clinical trials. In this study, we aimed to define the pharmacologic effects of YH25487, a newly developed PI3K-δ selective inhibitor on the steroid-resistant eosinophilic asthma using Aspergillus fumigatus (Af)-sensitized and -challenged mice. Our results showed that the intratracheal administration of YH25487 attenuated the Af-asthmatic manifestations including inflammatory signs and airway hyperresponsiveness in mice, while oral dexamethasone did not affect the asthmatic features. Moreover, when the pharmacologic effects are compared to the positive control GSK2269557, we found that the anti-asthmatic effects of YH25487 are superior to those of GSK2269557 in the severe eosinophilic asthma animal model. These findings suggest that a novel compound targeting PI3K-δ-isoform, YH25487 can be a promising therapeutic agent for the severe eosinophilic asthma, specifically as an inhalation formulation.

Key Words: Novel PI3K-δ inhibitor, YH25487, Severe asthma

P-37

Association of Obesity, Gender, and Age with Lung Function Changes in Adult Asthmatics

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Purpose: Obesity and asthma are chronic and prevalent disease. It is well known that asthma is related with obesity, but lung function changes in obese asthmatics in association with gender and age are not well understood. We investigated the association of obesity, gender and age with lung function changes after maintenance therapy in adult asthmatics.
Methods: In total, 937 newly diagnosed adult asthmatics were enrolled from the Cohort for Reality and Evolution of Adult Asthma in Korea (COREA). Asthma was diagnosed by positive result of methacholine bronchial provocation test (PC20≤25 mg/mL) or bronchodilator test (≥12% and 200mL improvement in FEV1 after inhalation of a bronchodilator. Follow-up spirometry was performed after 3 months of asthma treatment with controller medication. Percent change between spirometry before and aftertreatment was defined as {[(value after treatment-value before treatment)/value before treatment]×100}. Patients were categorized into four classifications based on body mass index (BMI,weight [kg]/height [m^2]): underweight (<18.5), normal weight (18.5-22.9), overweight (23.0-24.9), and obese (≥25.0).
Results: There was no consistent correlation between BMI and each lung function parameter. However, there was significant association between BMI and percent change of FEV1/FVC (%) after 3months of controller medication (P=0.013). Obese asthmatics showed significantly lower percent change of FEV1/FVC (6.0±13.5%) than underweight (12.6±21.4%) or normal weight patients (9.1±14.6%) (P<0.05, respectively). As a result of analyzing according to gender and age, women aged 45 to 60 years had increased BMI (22.39±3.52 vs. 24.11±3.60) and decreased percent change of FEV1/FVC (%) (8.9±14.3% vs. 5.7±11.9%) than women under 45 years.
Conclusions: Obesity is negatively correlated with percent change of FEV1/FVC (%) after controller medication. Gender seems to contribute differentially to the relationship between BMI and pulmonary function.

Key Words: Asthma, Obesity, Pulmonary function, Gender, Age

P-38

The Effect of Tirofiban in Mouse Model of Asthma

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Background: It is becoming apparent that the interaction of platelets with eosinophil in allergic inflammation and asthma. Previously, our team reported that increased platelet-eosinophil complex (PEC) in asthma, and showed the treatment of P2Y12 antagonist reduced PEC formation and allergic inflammation using the same model. Tirofiban is another potent antiplatelet drug and a small molecule inhibitor of the protein-protein interaction between fibrinogen and the platelet integrin receptor GP IIb/IIIa. We aimed to investigate the effects of tirofiban in an ovalbumin (OVA)-induced eosinophilic asthma mouse model.
Methods: BALB/c mice were sensitized by intraperitoneal injection of OVA (with alum) on days 0 and 14, followed by 3 nebulized OVA challenges on days 28-30. On each challenge day, 5mg/kg tirofiban was administered through intragastric administration 30 minutes before challenge. 48 hours after the last OVA challenge, mice were assessed for airway hyperresponsiveness (AHR) with a series of dilution of methacholine, differential cell count in bronchoalveolar lavage fluid (BALF). Th2 cytokines (interleukin-(IL)-4, IL-5, IL-13) in BALF were measured by ELISA.
Results: Tirofiban treatment decreased AHR to methacholine and airway inflammatory cell numbers including eosinophil in BAL fluid following OVA challenge (P<0.01). This treatment also decreased levels of Th2 cytokines such as IL-4, IL-5 and IL-13, but not Th1 cytokine in the BAL fluid. In histological analysis, the inflammatory cells in peribronchial and perivascular areas, including eosinophils, as well as mucus-containing goblet cells were also decreased in the tirofiban administered mice compared to vehicle group (P<0.01).
Conclusion: These findings revealed that tirofiban was effective in preventing the development of AHR, airway inflammation, and cytokine production in allergen-sensitized and challenged mice, and could be a potential candidate drug in the treatment of asthma.

Key Words: Asthma, Tirofiban, Platelet

P-39

Evaluation of Neutrophil Activation Status According to the Phenotypes of Adult Asthma

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Background: Neutrophils are considered key effector cells in the pathogenic mechanisms of airway inflammation in asthma. This study assessed the activation status of neutrophils in adult asthmatics, and the therapeutic potential of FTY720, a synthetic sphingosine-1-phosphate analog on activated neutrophils using an in vitro stimulation model.
Methods: We isolated peripheral blood neutrophils (PBNs) from 59 asthmatic patients (including 20 aspirin-exacerbated respiratory disease [AERD] and 39 aspirin-tolerant asthma [ATA] groups). PBNs were stimulated with N-formyl methionyl-leucyl-phenylalanine (fMLP) or lipopolysaccharide (LPS) and their activation status was determined based on reactive oxygen species (ROS) production, cell surface expression of CD11b, interleukin (IL)-8 and matrix metallopeptidase (MMP)-9 release. PBNs were primed with FTY720 to evaluate its anti-inflammatory action.
Results: In vitro PBN stimulation with fMLP or LPS treatment induced a significant increase in ROS/CD11b/IL-8/MMP-9 levels ($P<0.05$ for all). In asthmatics, fMLP-induced ROS level was significantly correlated with values of FEV1/FVC ($r=-0.278$, $P=0.036$), MMEF ($r=-0.309$, $P=0.019$) and PC20 methacholine ($r=-0.302$, $P=0.029$). In addition, ROS levels were significantly higher in patients with AERD and in those with severe asthma than in those with ATA or non-severe asthma ($P<0.05$ for all). FTY720 treatment could suppress ROS/CD11b levels, and LPS-induced IL-8 and MMP9 levels ($P<0.05$ for all). Responders to FTY720 treatment had significantly higher neutrophil counts in sputum ($P=0.004$).
Conclusions: Our findings suggest a useful in vitro PBN stimulation model for evaluating the neutrophil functional status and the therapeutic potentials of neutrophil-targeting candidates in asthmatics.

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Key Words: Neutrophil, Asthma, FTY720

P-40

Serum Eosinophil-Derived Neurotoxin (EDN) Level: A Biomarker of Adult Severe Asthma

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Background and Purpose: The prevalence of severe asthma (SA) consists of only about 10% of that of total asthma, but the patients with SA undergo frequent asthma exacerbations and rapid decline of lung functions. Eosinophil activation is the key component of airway inflammation of SA, and serum EDN level has been suggested as a biomarker of eosinophil activation in childhood asthma and atopic dermatitis. We evaluated serum EDN level as a serum biomarker of SA.
Materials and Methods: A total of 1,258 subjects constituted of severe asthmatics (n=235), nonsevere asthmatics (n=898), and healthy controls (n=125) were recruited from Ajou University Medical Center. Serum EDN levels were measured by 2 different ELISA kits (MBL®; K-EDN® by SKIMS-BIO); serum periostin level was measured by ELISA. Their associations with various clinical parameters were evaluated.
Results: Severe asthmatics were older and had a longer duration of asthma and upper airway comorbidities such as chronic rhinosinusitis and nasal polyps with lower baseline FEV1(%) and methacholine PC20 values. Significantly higher blood/sputum eosinophilia with higher serum periostin levels were noted in severe asthmatics. In addition, serum EDN levels measured by both MBL® and K-EDN® were significantly higher in severe asthmatics than in nonsevere asthmatics as well as healthy controls. Total eosinophil counts in blood showed better significant correlations with serum EDN levels by K-EDN® than those by MBL® or serum periostin levels. Multivariate analysis demonstrated that serum EDN level by K-EDN was found to be a single marker for predicting the phenotype of SA (OR 1.004, $P=0.003$).
Conclusion: Serum EDN level measured by K-EDN® can be applied as diagnostic biomarker of SA distinguishing from nonsevere asthmatics.

Key Words: Eosinophil-derived neurotoxin, Severe asthma, Biomarker

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DNA Damage and Methylation of Peripheral Bloods in Adult Asthmatics: Relation with Persistent Airway Obstruction of Asthma

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In this study, we characterized lung underlying mechanism in plasma and gDNA of asthmatics and to assess the effect of different mechanism compositions on the changes of lung function in F/U duration.
We analyzed lung ROS, SOD, TAC, 8-OHdG and 5mC by using ELISA of the plasma and the gDNA paired sample of 60 asthmatics who were followed up for 1 year; 20 subjects with normal post-bronchodilator FEV1 (A), 20 patients with decreased FEV1 under 60% which showed a substantial increase lung function (B), and 20 patients with decreased FEV1 under 60% which did not increase during the follow up period (C).
Compared with A, B groups, C groups had higher the relative increase of the SOD and TCA for F/U duration ($p<0.01$) in the plasma sample. However, the ROS was lower ($p=0.014$). Compared with A, B groups, C groups had a higher relative decrease of the 5mC for F/U duration in the gDNA sample ($p=0.001$).
Significant alteration of oxidant, antioxidant, DNA damage and methylation in plasma and DNA were observed according to the refractory state of asthmatics. The asthma trajectory profiles may provide novel aspects for investigating pathophysiology and for developing a biomarker for refractory asthma.

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Key Words: ROS, Asthma, DNA damage, Methylation

P-42

Leukocyte Telomere Length Alone Cannot Reflect the Elevated Risk for Asthma Development

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Purpose: Exposure to prenatal stress is associated with offspring's allergic disease development, the oxidative stress is regarded to mediate the relationship. In this pilot study, we aimed to explore the clinical significance of the leukocyte telomere length (LTL), a marker for exposure to oxidative stress, in predicting the asthma development of preschool children.
Methods: We had measured the cord-blood LTLs and those of 1-year peripheral blood from a sample of birth-cohort participants (the COhort for Childhood Origin of Asthma and allergic diseases). We followed up those subjects' clinical courses and evaluated whether the LTLs can predict their development of bronchial asthma, defined by the presence of physician-diagnosed asthma or recurrent wheezing, in their preschool period.
Results: In a total of 84 subjects information on both the cord-blood/1-year peripheral-blood LTLs and the presence of bronchial asthma were available. Among them, 14 subjects developed bronchial asthma at the age of 2 to 4. Prenatally stressed subjects presented marginally increased odds of developing asthma (4/41 versus 10/43, chi-square test, $p=0.097$). Subjects with shorter cord-blood LTL showed no increased odds of developing asthma (3/17 versus 9/58, chi-square test, $p=0.833$). Finally, subjects with both higher prenatal stress and the shorter cord-blood LTL presented marginally increased odds of developing asthma (3/8 versus 11/76, chi-square test, $p=0.096$).
Conclusions: In this pilot study, LTL alone could not reflect the elevated risk of asthma development in their preschool period. It can marginally reflect the elevated risk only when it is combined with the history of prenatal stress exposure.

Key Words: Prenatal stress, Preschool asthma, Telomere length

P-43

Clinical Features of Asthma and Their Serum Biomarkers according to 3 Different Cutoffs of Total Eosinophil Counts in an Adult Asthmatic Cohort

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Background: Eosinophils are major effector cells in asthma and blood eosinophils are closely associated with asthma severity. Three kinds of anti-IL-5 antibodies are introduced, however, they provide 3 different cutoffs of blood eosinophils to begin treatment. This study aimed to evaluate various serum biomarkers and clinical parameters according to each eosinophil count and to suggest the ideal cutoff to define eosinophilic airway inflammation.
Methods: A total of 1,965 adult asthmatic patients who received asthma treatment for at least 1 year were enrolled. Serum biomarkers related to eosinophilic inflammation/airway remodeling (serum eosinophil-derived neurotoxin <EDN>, periostin, TGF-β1) were measured using ELISA. Clinical characteristics and serum biomarkers were compared according to 3 cutoffs of blood eosinophils (150, 300 and 400 cells/μL).
Results: In patients with higher eosinophils (>3 cutoffs), the prevalences of severe asthma and chronic rhinosinusitis and/or nasal polyp, and sputum eosinophil counts were significantly higher than those with lower eosinophils, while proportion of female/ever smoker, values of FEV1%, PC20 methacholine and sputum neutrophils were significantly lower. Although serum levels of EDN/periostin/TGF-β1 were significantly higher in patients with higher eosinophils (> all 3 cutoffs), those levels in patients with severe asthma and mean plus 2 standard deviations of those levels in healthy normal controls were comparable with those levels in patients with higher eosinophils (>300 cells/μL).
Conclusion: These findings suggest that eosinophil 300 may be the ideal cutoff to be used in real practice reflecting critical eosinophilic inflammation and to expect treatment efficacy of anti-IL-5 antibodies.

Key Words: Eosinophil, Severe asthma, Periostin

P-44

Differences in Aspergillus Fumigatus (Af)-Induced Allergic Lung Inflammation between Male and Female Mice

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Females are known to be more susceptible to many immunological disorders in humans. Several immunologic features in female gender have been suggested as the cause of this phenomenon. As for allergic lung inflammation, it has been reported that female mice are also more susceptible to the development of allergic inflammation against a typical experimental aeroallergen, ovalbumin, than male mice. We investigated whether there is also a gender gap regarding the degree of immune response against a potent fungal allergen, Aspergillus fumigatus (Af) in mice. Respiratory Af exposure led to the increases in the numbers of total cells, eosinophils, and lymphocytes in bronchoalveolar lavage (BAL) fluids from both genders compared to those of control mice. Furthermore, inhibition of phosphoinositide 3-kinase (PI3K)-δ significantly reduced the Af-induced increases in the numbers of total cells and eosinophils in BAL fluids from both male and female mice. Interestingly, female mice showed a tendency toward the more severe allergic lung inflammation than male mice. Intratracheal administration of IC87114, a potent inhibitor of PI3K-δ, into mice remarkably ameliorated the Af-induced increases of airway inflammatory cells infiltration, airway hyper-responsiveness, and pulmonary TH2 cytokines (IL-4, IL-5, and IL-13) in the lung. These findings suggest the presence of a gender gap in the severity of allergic lung inflammation against Af and PI3K-δ may play a key role in Af-induced allergic lung inflammation regardless of gender in mice.

Key Words: Fungal asthma, Gender, PI3K-δ blockade

P-45

Systematic Review and Meta-Analysis for Effects of PI3K Inhibitors on Allergic Lung Inflammation in Mice

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It has been recently reported that meta-analysis can be applied to the assessment of the efficacy of the summary estimate in experimental settings. We investigated therapeutic effects of phosphoinositide-3-kinase (PI3K) inhibitors in allergic murine models using meta-analysis. PubMed, EMBASE and Web of science were utilized for the literature search, and the search term was "PI3K inhibitor" and "Allergy" or "Asthma". Experimental studies were included only when experiments were performed using mice. The primary outcome of the inflammatory profile is as follows: numbers of total cells with differentials in bronchoalveolar lavage (BAL) fluids, levels of serum total Ig E and pulmonary pro-inflammatory mediators (IL-4, IL-5, IL-13, eotaxin, IFN-γ, IL-6, TNF-α, TGF-β. IL-1β, and VEGF). We evaluated effects of PI3K pan-inhibitors and PI3K-δ specific inhibitors as subgroups. Total of 16 articles were selected. PI3K pan-inhibitors significantly reduced total cell counts, eosinophils, and neutrophils in BAL fluids. PI3K-δ inhibitors also reduced total cells count, eosinophils, neutrophils, and lymphocytes. PI3K pan-inhibitor effectively reduced the serum total Ig E and pulmonary IL-4, IL-5, eotaxin, TGF-β, IL-1β, and VEGF. PI3K-δ inhibitor effectively reduced the serum total Ig E and pulmonary IL-4, IL-5, IL-13, TNF-α, IL-1β, and VEGF. These data suggest that inhibition of PI3Ks, especially PI3K-δ specific blockade, effectively abrogated the various features of allergic lung inflammation in murine models, and thus may be effective for treating allergic lung inflammation in humans.

Key Words: Asthma, Meta-analysis, PI3K isoforms

P-46

The Gut Microbiome Alteration in Adult Asthmatics

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Background: The human microbiome is now recognized as playing an imperative role in the pathogenesis of asthma. However, the effects of changes in gut microbiota on adult asthma have not explored yet.
Objective: We characterized the gut microbiome between subject diagnosed with asthma and healthy controls.
Methods: Total 105 fecal samples from 39 healthy subjects and 66 asthmatics (mild: 40, severe: 26) were obtained for microbiome analysis using 16S ribosomal RNA gene sequencing methods. Bacterial DNA library data were prepared by sequencing amplicons with the MiSeq v3 platform (Illumina®). Data sets were cleaned and analyzed using QIIME and Ezbiocloud 16S database.
Results: Sequence results indicate significant differences in gut bacterial community between healthy and asthma group. Comparing the bacterial richness and diversity, general microbiome composition was not significantly altered between two groups. In phylum level, the abundance of *Actinobacteria* was decreased, and that of *Saccharibacteria* was increased in asthma group compared to healthy group (P-value<0.05 by Kruskal-Wallis test). The abundance of 7 genera – *Eubacterium*, *Bifidobacterium*, *Subdoligranulum*, *Alloprevotella*, *Coprococcus*, *Holdemanella*, and *Sutterella* – showed statistically significant difference between asthma group and healthy controls. In the asthma group, all seven genera were decreased compared to healthy controls. Interestingly, *Eubacterium*, a bacterium associated with pectin fermentation in the colon, was significantly reduced in asthmatics compared to control group (2.7% vs. 3.8%, P-value=0.017 by K-W test).
Conclusion: In our study, significant difference in gut microbiota was observed between healthy controls and asthma group. It suggests that gut dysbiosis may contribute to pathophysiology of adult asthma.

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Key Words: adult asthma; gut microbiota; microbiome

P-47

Transforming Growth Factor-Beta1 and Eosinophil-Derived Neurotoxin as Biomarkers for Baker's Asthma

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Background: Previous studies suggest that adaptive and innate immune responses are involved in the development of work-related respiratory symptoms (WRS) in bakery workers.
Objective: We aimed to investigate human airway epithelial cells (HAECs) as major effector cells to induce airway inflammation.
Materials & Methods: We recruited 385 wheat-exposed subjects with WRS (WRS+)/without WRS (WRS-) working in a single industry and 243 unexposed controls from Ajou Medical Center (Suwon, South Korea). ELISA was used to measure levels of epithelial cell-derived cytokines (IL-8, TGF-β1, eotaxin-2) and eosinophil-derived neurotoxins (EDN) in sera or cell-free supernatants. HAECs were stimulated by wheat flour extracts and co-cultured with peripheral blood neutrophils (PBN) isolated from 4 asthmatic patients.
Results: Serum TGF-β1 levels were significantly lower in exposed subjects than in unexposed controls, in the WRS+ group than in the WRS-group ($P<0.001$ for each). The WRS+ group had significantly a higher level of serum EDN than the WRS-group ($P<0.001$). Serum TGF-β1/EDN levels predicted the development of WRS in exposed subjects (AUC=0.719, 72.4% sensitivity/70% specificity; AUC=0.759, 78.6% sensitivity/60% specificity). From wheat-stimulated HAECs, TGF-β1 release peaked at 6 h after wheat exposure and decreased, while eotaxin-2 peaked at 12 h. Co-culture of HAECs with PBN did not affect TGF-β1/eotaxin-2 release.
Conclusion: Decreased production of TGF-β1 in HECs in wheat-exposed workers may derive type-2 airway inflammation/eosinophil degranulation, contributing to the development of WRS. Serum TGF-β1/EDN are potential biomarkers for predicting WRS development in bakery workers.

Key Words: Baker's asthma, Epithelial cells, Transforming growth factor β1, Eosinophil-derived neurotoxin

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Endoplasmic Reticulum Stress Modulates Airway Remodeling in Allergic Asthma

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The hallmark pathological features of asthma include airway eosinophilic inflammation and structural changes, called as airway remodeling characterized by increased thickness of the subepithelial reticular basement membrane (RBM), increased airway smooth muscle (ASM) mass, angiogenesis and goblet cell hyperplasia which are associated with an irreversible loss in lung function. Given the importance of both inflammation and remodeling in asthma pathogenesis, most studies, both clinical and mechanistic, focus on inflammatory parameters alone. Furthermore, little is known concerning the role of endoplasmic reticulum (ER) stress in the asthmatic airway remodeling. We used a long-term exposure murine model of allergic asthma to evaluate the effect of 4-PBA, an ER stress regulator, on airway inflammation and remodeling. The chronic model of allergic asthma showed the typical pathophysiological features of asthmatic inflammation as well as remodeling including thickening of the peribronchial smooth muscle layer, subepithelial collagen deposition, and increased airway mucus production. Administration of 4-PBA reduced the pathophysiological symptoms of asthma including airway remodeling, plasma exudation, Th2 cytokines, TGF-β1, and VEGF in lungs as well as the increased expression of ER stress markers and the protein levels of UPR-related markers after OVA inhalation. These results indicate that inhibition of ER stress may attenuate chronic antigen-induced airway inflammation, hyperresponsiveness, and airway remodeling through the regulation of VEGF.

Key Words: Asthma, Airway remodeling, ER stress

P-49

PI3K-δ Signaling Induces Neutrophilic Inflammation through the Regulation of Airway Epithelial VEGFR-MHC II Expression and Epithelial Integrity in Mice

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Epithelial cells (ECs) may have primary immune functions that affect the balance between tolerance and inflammation, as evidenced by the expression of MHC class II on the EC surface. Moreover, phosphatidylinositol-3-kinase (PI3K)-δ is highly expressed in leukocytes and plays a critical role in antigen receptor and cytokine-mediated B and T cell development, differentiation, and function. In this study, we aimed to evaluate the changes of respiratory epithelium including the ultrastructure and MHC II expression and the effects of PI3K-δ signaling on MHC II expression at respiratory epithelium and the neutrophilic pulmonary inflammations. Our results showed that LPS-instilled mice showed typical features of severe lung inflammation; pulmonary neutrophilia with increases IL-17 production, vascular leakage, and nuclear translocation of nuclear factor-κB (NF-κB) and PI3K-δ activation. In addition, SEM images revealed that the respiratory epithelium was damaged severely after LPS instillation exhibiting loss of cilia, the disarrangement of epithelial lining, and the massive amount of thick mucus layer with the irregular surface. N-elastase levels were increased in the lung by LPS instillation. Interestingly, we found that the expressions of PI3K-δ, PI3K receptor 1, VEGF, VEGFR2, and MHC II were substantially increased in LPS-stimulated lung including airway epithelial cells. The treatment with PI3K-δ inhibitor restored the damaged structure of respiratory epithelium with cilia as well as the all exaggerated parameters such as MHC II and VEGFR. Besides, PI3K-δ inhibitor substantially improved the LPS-induced pulmonary neutrophilic inflammation compared to the mice treated with vehicle only. These findings suggest that PI3K-δ signaling activation can be a pathogenic contributor to LPS-induced pulmonary neutrophilic inflammation, at least in part, through the induction of VEGFR-MHC II epithelial expression and the destruction of respiratory epithelium.

Key Words: Respiratory epithelium, MHC II, Neutrophilic inflammation

P-50

Vitamin D Supplementation Attenuates Obesity-Induced Airway Hyper-Responsiveness and Lung and Liver Fibrosis

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Background: Obesity induces airway hyper-responsiveness (AHR) and lung/liver fibrosis. Vitamin D has known to modulate the immune system inducing an anti-inflammatory and anti-fibrogenic effects.
Objective: We aimed to determine whether vitamin D supplementation can affect obesity induced AHR and lung/liver fibrosis.
Methods: We fed C57BL/6J male mice a high-fat diet for 3 months with and without Vitamin D treatment (vitD; 7μg/kg, 3 days per week during 8 weeks, IP). We assigned mice to three groups: control; normal diet with vitamin D (Con); high fat diet-induced obesity (HFD); and HFD with vitamin D (HFD/VitD).
Results: VitD attenuated AHR in the HFD mouse without body weight loss. Lung and liver fibrosis resulting from HFD also improved in the HFD/VitD group compared with the HFD group. Cytokine and mRNA level of TGF-β, TNF-α, IL-6, and IL-1β in HFD was increased compared with control group and these were decreased in HFD/VitD group compared with the HFD group in lung homogenate. mRNA level of TGF-β1, Collagen-α1 which are related with fibrosis as significantly decreased after HFD with Vitamin D treatment compared with the HFD group.
Conclusion: Vitamin D alleviates HFD-induced AHR and lung/liver fibrosis. Vitamin D can be a promising therapeutic option for obesity induced asthma and non-alcoholic fatty liver disease (NAFLD).

Key Words: Obesity, Lung/liver fibrosis, Vitamin D

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Dupilumab for Adolescents with Moderate-to-Severe Atopic Dermatitis: Results from a Phase 3 Trial

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Purpose: To report the efficacy and safety of dupilumab (DPL) monotherapy in a phase 3, double-blinded, placebo (PBO)-controlled trial in adolescent patients (pts) with moderate-to-severe AD inadequately controlled with topical therapies (NCT03054428).
Methods: Pts (≥12 to <18 years) received 16-week (Wk) subcutaneous DPL every 2 weeks (q2w; 200 mg baseline [BL] weight <60 kg, 300 mg if ≥60 kg), every 4 weeks (q4w; 300 mg) or PBO q2w.
Results: 251 pts were randomized (85 PBO, 84 q4w, 82 q2w). At Wk16, DPL treatment (q2w/q4w/PBO) resulted in higher proportions of pts with Investigator's Global Assessment scores of 0 or 1 (24.4%/17.9%/2.4%; P<0.0001/P=0.0007) and ≥75% improvement in Eczema Area and Severity Index score (EASI-75; 41.5%/38.1%/8.2%; all P<0.0001). DPL improved least squares mean % changes (BL to Wk16) in EASI (-65.9%/-64.8%/-23.6%), peak pruritus Numerical Rating Scale (NRS) (-47.9%/-45.5%/-19.0%), body surface area affected by AD (-30.11%/-33.41%/-11.66%), and SCORing AD (all P<0.0001). At Wk16, more DPL- vs PBO-treated pts had ≥ 3- or ≥4-point improvement in pruritus NRS score, EASI-50, or EASI-90 (all P<0.0005). DPL also improved (BL to Wk16) Children's Dermatology Life Quality Index and Patient-Oriented Eczema Measure (all P<0.0001). Numerically higher proportions of pts used rescue medications in the PBO vs q4w vs q2w groups. Non-herpetic skin infections (11.0%/13.3%/20.0%) were more common with PBO; conjunctivitis (9.8%/10.8%/4.7%) and injection-site reactions (8.5%/6.0%/3.5%) were more frequent with DPL. There was 1 serious adverse event (AE) and 1 AE leading to treatment discontinuation (PBO only).
Conclusions: DPL treatment resulted in clinically relevant and statistically significant improvements in AD signs, symptoms and QoL in adolescents with moderate-to-severe AD, with acceptable safety. DPL q2w was numerically superior to DPL q4w in most clinical endpoints. PBO-corrected efficacy and safety of DPL in adolescent pts were similar to adults.

Key Words: Dupilumab, Atopic dermatitis, Adolescent

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The Effects of an Integrated Intervention Program for Children with Atopic Dermatitis

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Background: Atopic dermatitis (AD) is the most common chronic inflammatory skin diseases in children. It is important to control of environment, diet and skin care for preventing aggravation of symptoms and quality of life. We aimed to perform an intergrated intervention program under a single metropolitan city for AD children.
Methods: We enrolled children aged 6-12 years with AD having high severity of disease, low levels of attention about AD management, or low socioeconomic status from June 2017 to December 2018 in Busan, Korea. Total 105 children received the program consisted of teaching how to manage children with AD for their teachers and parents, counseling parents stress, visiting the allergist regularly and providing the medical payments. The changes of disease management behavior of 95 children were analyzed by data based on examination of the doctors and questionnaire. The changes of quality of life in 42 patients were analyzed by Children's Dermatology Life Quality Index (CDLQI) which has 10 categories.
Results: At time of enrollment, the rate of having regular examination, taking regular medicines, and applying moisturizers over 3 times per day were 12%, 9.5%, and 9.8%, respectively. The rate of having regular examination and applying moisturizer over 3 times per day at the end of study were 25% and 41.8%, respectively, and they were significantly increased when compared with those at enrollment (P=0.03). The change percent in total score of CDLQI was 7.1 % between before and after study. Of these, itching sense, embarrassment and school performance were improved by 14%(P=0.018), 8.7%(P=0.038) and 6.4%(P=0.06), respectively.
Conclusion: The intervention program leaded by a local government for children with AD improved the behavior of AD management and quality of life. It might have positive effects on patients' study ability.

Key Words: Atopic dermatitis, Intervention program, Child

P-53

Skin Exposure of Chloromethylisothiazolinone/Methylisothiazolinone (CMIT/MIT) Affect the Aggravation of Atopic Dermatitis in Mice Via the Modulation of T Helper 2/T Helper 17-Related Immune Response

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Background: Recently, exposure to many environmental factors such as air pollution, construction materials and harmful chemical substances has been found to cause atopic dermatitis (AD). Chloromethylisothiazolinone (CMIT) and Methylisothiazolinone (MIT) exposure has been associated with allergic contact dermatitis, occupational asthma and lung injury. Despite of the association with allergic response, there was no study to investigate the effects of exposure to CMIT/MIT on the development of AD.
Objective: We aimed to investigate the influence of skin exposure to CMIT/MIT on major symptoms of AD and a biological mechanism through an assessment of immune responses in AD mice model.
Methods: BALB/C mice were exposed to skin with CMIT/MIT for 3 weeks and then AD was developed by ovalbumin (OVA) epidermal sensitization. To assess AD symptoms, we measured transepidermal water loss (TEWL) and scored erythema, scaling, and excoriation in dorsum lesions. Total immunoglobulin (Ig) E and OVA specific IgE in serum and histopathological changes in skin were analyzed. To evaluate the immune response, the levels of T helper (Th) 2/Th17–related cytokines such as thymic stromal lymphopoietin (TSLP), interleukin (IL) –4, IL–13 and IL–17A were detected using real–time PCR. The frequency of CD4+IL–4+ and IL–17A producing cells in skin draining lymph nodes was assessed using flow cytometry.
Results: Mice exposed to CMIT/MIT in OVA challenge model had higher total serum Ig E, TSLP, IL–4 and IL–17A in skin mRNA expression and higher population of CD4+IL–4+ and IL–17A producing cells in skin draining lymph nodes than mice unexposed to that.
Conclusion: These findings demonstrated that CMIT/MIT acts as environmental antigen and enhances allergic inflammation by modulation of Th2/Th17 response in AD mice, suggesting that CMIT/MIT skin exposure might aggravate AD symptoms through dysregulation of immune response.

Key Words: Atopic dermatitis, Chloromethylisothiazolinone, Methylisothiazolinone

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Effects of Accumulated and Continuous Aerobic Exercise in Moderate Intensity on Symptoms and Inflammatory Factors of Atopic Dermatitis

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The purpose of this study is to investigate effects of accumulated and continuous aerobic exercise in a mouse model of atopic dermatitis. We used DNCB–treated ICR mouse model as atopic mouse model. The animals were treated with dinitrochlorobenzene (DNCB) to develop dermal symptom similar to that of patients with atopic dermatitis at their age of 7 weeks. The animals were given two types of exercise, accumulated aerobic exercise (AA) and continuous aerobic exercise (CA) in moderate intensity. AA group, which performed 3 short bouts of aerobic exercise (AA group: 10 min×3), and a CA group, which performed a single period of continuous aerobic exercise (AC group: 30 min×1). they were placed in a device (at 10°) during 9 days, at a speed of 16m/min. After experimental period for 9 days, the dermal symptom was ameliorated in accumulated aerobic exercise group(AA) and continuous aerobic exercise group (CA) compared to control group. There are no significant differences in Clinical skin severity test scores between AA group and CA group. AA and CA of the thickness of epidermis/dermis was reduced compared to control group and the infiltration rate of immunocytes was largely decreased compared with that of control group. Plasma levels of MCP1, IgE and TSLP in the AA and CA group were significantly reduced when compared with those in control group. However, plasma levels of MDC were only significantly reduced in AA group compared with control group. In conclusion, the accumulated aerobic exercise is may be an efficient exercise method for ameliorating symptom of atopic dermatitis by means of reduction of inflammatory factors.

Key Words: Atopic dermatitis, Aerobic exericise, Accumulated aerobic exercise

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Immunological Changes of Rituximab Treated IgG4-Related Disease Patients

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Background: Immunoglobulin G4-Related Disease (IgG4-RD) is a systemic disease characterized by the increasing infiltrated IgG4-secreting plasma cells, follicular helper T cells (Tfh). Storiform fibrosis and obliterative phlebitis are the major histological IgG4-RD phenotypes. Today, multiple studies showed that many immune cells, such as CD4 T cells and B cells, are involved in IgG4-RD pathophysiology and expression of TGFb and IL-10 are highly correlated with IgG4-RD characteristics. Rituximab (RTX) is considered that effective treatment of IgG4-RD by depleting B cells and plasma cells. Many patients are treated RTX, however RTX treated patients show occurring relapses frequently.
Objective: Identify immune cell changes in IgG4-RD patients and draw a new target for the treatment by analyzing PBMCs from RTX treated patients.
Methods: We recruited IgG4-RD patients (n=3) and healthy control subjects (n=3) with inform consent. Peripheral blood was isolated and stained for flow cytometry.
Results: As we compared the immune cell populations from IgG4-RD patients and healthy control subjects PBMCs, plasma cells (CD19+ CD20- CD38+) and follicular helper T cells (CD4+ CD45RO+ CXCR5+ PD-1+) were increased in IgG4-RD patients. Also, the frequency of CD14+ monocytes was increased and the TGFb and IL-10 production from CD14+ monocytes were dramatically augmented. By treating RTX, CD19+ cells in the patient PBMCs were depleted, and Tfh were decreased. However, the frequency and the TGFb expressions from CD14+ monocytes remained unchanged in Rituximab-treated patients PBMCs.
Conclusion: Although RTX treatment can regulate plasma cells and Tfh, TGFb productions and CD14+ monocyte frequencies still remain. These data suggested that IgG4-RD phenotypes are not completely disappeared, and it remains a possibility that IgG4-RD can relapse despite treating RTX. Therefore, it is needed to regulate CD14+ monocyte to decrease TGFb secretions for controlling IgG4-RD.

Key Words: IgG4, Monocyte, TGFb

P-56

Annual Incidence and Pattern Changes of Radiocontrast Media-Induced Immediate Hypersensitivity Reactions: Single Center 5 Year Retrospective

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Background: Radiocontrast meida (RCM)-induced hypersensitivity reactions are still important concern in current clinical practice in which large number of radiologic tests are performed. Many centers are operating their own strategies and clinical decision support systems for reducing RCM hypersensitivity reactions, but recent incidence and patterns of RCM hypersensitivity is not studied well. Here, we retrospectively investigated annual incidence and pattern changes of RCM-induced immediate hypersensitivity reactions during recent 5 years.
Methods: From January 2014 to December 2018, the number of immediate hypersensitivity was divided by the total number of CT scans using iodinated contras agents, and the annual incidence rate was calculated for each year. The severity of the reactions was classified, and the severe reaction included anaphylaxis, loss of consciousness, and desaturation. Based on this definition, we evaluated the incidence of severe immediate reaction and pattern changes of RCM hypersensitivity reactions.
Results: There were 1,450 events (0.61%) of RCM-induced hypersensitivity and 92 events (0.04%) of severe reactions among total 237,455 contrast CT scans. The incidences of both total reactions and severe reactions tend to slightly increase from 2014 to 2016 and then decrease. The overall proportion of severe reactions to total reactions was 6.41%, and tends to increase by year. Of the severe reactions, 61 events (66.30%) occurred without premedication or previous history of RCM hypersensitivity, and 31 events (33.70%) occurred even after premedication.
Conclusions: The incidence of RCM hypersensitivity reactions is decreasing after RCM hypersensitivity risk management such as premedication, but severe reactions still occur with relatively higher proportion than before. More than 30% of the severe reactions happened despite premedication. Further research is needed to find more effective preventive strategy to reduce severe immediate reaction.

Key Words: Radiocontrast media, Immediate hypersensitivity, Incidence

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Deep Vein Thrombosis and Pulmonary Thromboembolism in a DRESS Patient

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Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a serious drug-induced adverse reaction. DRESS can present various manifestations, and the major manifestations are fever, skin rash, and the involvement of several internal organs. However, thrombotic complications are not well described in DRESS.
A 63 year old male presented with fever, skin rash, cough, dyspnea and pleuritic pain visited the outpatient pulmonary clinic in our hospital. His symptoms developed after 6 weeks of treatment with diacerein, tramadol and acetaminophen for osteoarthritis. He had taken acetaminophen and tramadol for 2 years.
He stopped all medications, but his symptoms persisted. On admission day, computed tomography (CT) of chest and abdomen showed acute pulmonary thromboembolism (PTE) in both pulmonary artery and deep vein thrombosis (DVT) in both common femoral veins.
He was treated with anticoagulation, and respiratory symptom improved. However, high fever was persisted and skin rash deteriorated. Peripheral blood eosinophil and liver enzymes increased. He was suspected of DRESS and was transferred to allergy clinic on hospital day 15. DVT and PTE were not well known clinical manifestations of DRESS, but he had no risk factors of hypercoagulability. Malignant, infectious and autoimmune diseases were ruled out by various examinations including CT, bone marrow examination, serologic tests, and skin biopsy.
He was treated with prednisolone 40mg per day for 10 days. However, high fever was sustained and skin rash was aggravated. After increasing the dose of systemic corticosteroids, his clinical manifestations were improved.
We report a rare case of DRESS syndrome with DVT and PTE. However, it is unclear whether these symptoms are rare clinical manifestations of DRESS or a separate form of coagulopathy.

Key Words: DRESS syndrome, DVT, PTE

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A Case of Albendazole-Induced Alopecia

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Albendazole is an anti-parasitic drug and its common side effects include nausea, abdominal pain, and headache. However, albendazole-induced telogen effluvium has rarely been reported. Here, we report a case of alopecia caused by albendazole.
A 44-year-old woman visited our clinic for eosinophilia and pulmonary infiltrates. She was diagnosed with toxocariasis. She took albendazole 400 mg twice daily for 7 days. 9 days later, her hair began to fall off. She had been taking telmisartan 40 mg for 2 years and did not take any other medications or herbal medicine. Nearly 90% of the hair was missing after 5 days. Dermatologic examination showed that telogen was more than 70% on trichogram, indicating telogen effluvium. She was prescribed 3% minoxidil gel. One month later, alopecia was improved markedly.
In conclusion, albendazole, an over-the-counter drug that is prescribed commonly in clinical practice, can rarely induce acute diffuse and total alopecia.

Key Words: Albendazole, Alopecia

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A Case of Unusual Presentation of Interstitial Pneumonitis Induced by Sirolimus

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Background: Sirolimus have been widely used for mammalian target of rapamycin inhibitors against various malignancies. We report a case of unusual progressing interstitial lung disease (ILD) after discontinuation of sirolimus, mimicking invasive pulmonary infections.
Case Report: An 18-year girl with osteosarcoma and multiple lung metastasis was treated with sirolimus plus gemcitabine after focal radiotherapy to metastatic lung nodules. She complained of cough and dyspnea after treatment. Chest computed tomogram (CT) revealed ground-glass appearance and consolidations on the superior segment of left lower lobe. We suspected the radiation-induced pneumonitis and methyl-prednisolone (1 mg/kg/day) were started intravenously. After treatment, dyspnea was improved even though no improvement of radiologic findings. She received sirolimus therapy again as schedule and she had fever, cough and dyspnea again. The chest CT showed new interstitial lesions in right lung field. So we assumed the patient's lesion might be due to sirolimus. After confirming that the etiologies were not infection or malignancy, sirolimus was stopped and methyl-prednisolone was started again (2 mg/kg/d for 3 weeks, tapered for 2 weeks). Her symptoms and radiologic findings were improved. However, after cessation of steroid, she complained high fever and uncontrollable pain on her back and both shoulder, suspected of acute myositis. Although we started antibiotics and anti-fungal agent, her symptoms were aggrevated and the chest CT showed diffuse aggravated interstitial pneumonitis with pleural effusion. Transbronchial lung biopsy revealed mild interstitial thickening, which might possibly related to drug-induced pneumonitis. So, methyl-prednisolone was re-started, and the symptoms and radiologic findings were improved rapidly. After tapering of steroid therapy, she has no respiratory symptoms now in outpatient clinic.
Conclusion: We report a case of progressing ILD after discontinuation of sirolimus.

Key Words: Sirolimus, Interstitial pneumonitis

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Impact of Electronic Management System on Iodinated Contrast Media Hypersensitivity Reactions

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Background: Iodinated contrast media (ICM) hypersensitivity reactions has become a medical problem with an increase of imaging tests. Pusan National University Hospital improved the electronic medical record system to record ICM hypersensitivity reactions in 2014. In addition, an automatic warning for the treatment of premedication was generated at the time of prescription of tests using ICM in the patient with a previous adverse reaction history.
Methods: We analyzed the patterns of ICM hypersensitivity reaction from January 2015 to September 2018.
Results: The overall prevalence of ICM hypersensitivity reactions was 0.739%, the mean age was 55.7±14.8 years, and female 57.2%. In the classification according to the degree of severity, 4.9% was very mild cases in which symptoms were self-resolved, 85.6% in mild cases, 8.9% in moderate cases and 0.6% in severe cases. The most common ICM was iomeprol (7.732%), followed by iohexol (1.375%), iobitridol (0.654%), ioversol (0.576%), iopamidol (0.441%), iopromide (0.385%), and iodixanol (0.093%). The delayed hypersensitivity reaction was found in 3.6% and the most frequent agent was iopamidol (37.5%) and Iobitridol (34.4%). The reported adverse reactions are decreasing every year since 2016 (0.423% in 2015, 1.030% in 2016, 0.809% in 2017, and 0.632% in 2018). 23.7% of the patients with ADR had at least two hypersensitivity reactions, and 34.7% of them were treated with premedication.
Conclusion: ICM hypersensitivity reactions are continuously reported. However, after establishing the management system, we confirmed the decrease in the annual report. ICM hypersensitivity reactions often occurred even after premedication, thus managing the adverse reaction through an electronic management system will be helpful.

Key Words: Iodinated contrast media, Hypersensitivity, Electronic management system

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Drug Eruption by Antihistamine Mistaken for Chronic Urticaria in a Child

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Although rare, antihistamines can cause adverse effects, including drug-induced eruptions or anaphylaxis. A 4-year-old child visited the pediatric department of a hospital for skin eruptions after administration of antihistamines, (e.g., ucerax® (hydroxyzine) or leptizine® (levocetirizine), for cholinergic rashes; he did not have pruritus. Skin prick, intradermal, and drug provocation tests were performed to determine the relationship between the antihistamines and eruptions. Levocetirizine induced wheals in the skin prick test and a rash in the oral drug provocation test. In contrast, ketotifen induced no reaction in the skin prick test but showed a positive reaction in the oral provocation test. Our case report highlights that children can experience the same types of adverse reactions as seen in adults, and cross-reactivity between various antihistamines can occur.

Key Words: Histamine antagonists, Drug eruptions, Chronic urticaria

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Genetic Variants of Adenosine Deaminase and Adenosine A2A Receptor are Associated with Antituberculosis Drugs-Induced Liver Injury

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Backgrounds: Antituberculosis drugs (ATD) are one of the common causes of drug-induced liver injury, leading to serious morbidity and mortality. Adenosine plays various immunomodulatory effects by interaction with adenosine A2A receptor in immune cells. In this study, we examined whether genetic variants in adenosine deaminase (ADA) and adenosine A2A receptor (ADORA2A) are associated with the risk of development of ATD-induced liver injury.
Methods: ATD-induced liver injury was determined based on liver function test after initiation of the first line ATD, including isoniazid, rifampin, ethambutol, and pyrazinamide. Cases were defined as an increase of alanine aminotransferase higher than 5 times of upper normal limit. We enrolled 35 patients with ATD-induced liver injury and 77 ATD-tolerant subjects. Genetic variants in exons of ADA and ADORA2A were genotyped and compared between case and ATD-tolerant controls.
Results: In ADA gene, rs73598374 (G22A) was significantly associated with ATD-induced liver injury (OR=8.88, 95% confidence interval 1.74-45.35, P<0.05). Among 5 variants in ADORA2A, rs5751876 showed significant association with ATD-induced liver injury (OR=3.47, 95% confidence interval 1.49-8.10, P <0.05), while the frequencies of the other variants were similar between case and controls.
Conclusions: These findings indicate that genetic polymorphisms of adenosine deaminase and adenosine A2A receptor are associated with the development of ATD-induced liver injury, and suggest that adenosine pathway might play important roles in the pathogenesis of ATD-induced liver injury.

Key Words: Adenosine deaminase, Adenosine receptor, Antituberculosis drugs-induced liver injury

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Comparison of 1-Bag and Multi-Bag Desensitization Protocol for Rituximab Hypersensitivity

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Background: Rituximab is prone to infusion-related reaction which requires desensitization to maintain its administration. Desensitization protocol conventionally uses a multi-step infusion by diluting solutions. However, the process of diluting drugs and delivery needs considerable time and effort.
Objective: To investigate the safety and efficacy of a non-diluting, one-bag protocol of rituximab desensitization by comparing the results with a conventional, multi-bag protocol.
Methods: A retrospective study was performed by using the electronic medical record of patients who underwent rituximab desensitization between 2009 and 2018. The completion rate, occurrence and severity of breakthrough reactions (BTR), and time required to complete the therapy were compared between the two methods.
Results: Total 190 cases of desensitization therapy were done in 49 patients; 183 cases (96.32%) were completed its infusion. Comparing the one-bag with the multi-bag protocol, the completion rate (97.28% vs. 93.02%, p=0.193) and the incidence of BTR (14.97% vs. 20.93%, p=0.352) were not different. The proportion of BTRs grade 3 or higher based on the Common Terminology Criteria for Adverse Events was smaller in the one-bag protocol, but this difference was not statistically significant (45.5% vs. 77.8%, p=0.101). Majority of the BTRs appeared at the first cycle of the desensitization process (one-bag 54.55% vs. multi-bag 50%) and tended to decrease afterwards. As for the steps in each cycle, BTR in the one-bag protocol tended to occur even through entire steps, whereas most of the BTR in the multi-bag protocol occurred at later steps of the process. The average time spent in the desensitization was 60 minutes shorter in the one-bag than the multi-bag protocol (263.35 min vs. 323.68 min, p=0.0001).
Conclusion: The one-bag desensitization protocol is not inferior to conventional multi-bag protocol in safety and showed more efficiency by shortening the time required to complete.

Key Words: Rituximab, Desensitization, Dilution, One solution

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Clinical Characteristics of Vancomycin-Induced Severe Cutaneous Adverse Reactions

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Background: Although vancomycin is the one of the frequently reported culprit drugs of severe cutaneous adverse reactions (SCARs), its clinical features have not been studied thoroughly. The purpose of this study is to assess the clinical characteristics of SCARs related with vancomycin by comparing SCARs induced by other drugs.
Methods: The data of Korean SCARs Registry for the cases occurred from 2010 to 2018 were assessed retrospectively to evaluate the clinical characteristics of vancomycin-related SCARs.
Results: Among the total number of 1,084 SCARs cases, 53 cases (4.9%) were related with vancomycin. More patients with vancomycin-induced SCARs needed treatment in intensive care unit than other-drugs related SCAR patients (19.6% vs. 8.6%, p=0.008) although the durations of ICU care or overall stay of hospital admission were not different. Fever (73.1% vs. 57.1%, p=0.023) and leukocytosis (defined as WBC >10000/mm3) (88.13% vs. 22.8%, p=0.025) were more frequently observed. In vancomycin-induced SCARs patients compared to those related with other drugs, eosinophil counts was significantly higher (2,540±4,158/mm^3 vs. 1,611±2,777/mm^3, p=0.035) but liver enzyme elevation were much milder (104.6 ±107.7 IU/L vs. 229.9±383.2 IU/L, p<0.001). If confined to 40 patients with drug reaction with eosinophilia and systemic symptoms (DRESS), vancomycin-induced DRESS presented much longer duration of ICU care (6.1±18.9 days vs. 0.7±4.7 days, p<0.001) and higher mortality rate (10.0% vs. 3.8%, p=0.084) compared to other causative drugs-related DRESS.
Conclusions: Vancomycin-induced SCARs present more severe inflammatory feature and higher rate of ICU. In DRESS cases, vancomycin-related cases showed more grave prognosis compared with DRESS cases related with other drugs.

Key Words: Vancomycin, Severe cutaneous adverse reaction, Drug reactions with eosinophilia and systemic symptom

P-65

Lysophosphatidylserine is a Potent Inducer of Eosinophil Extracellular Trap Cell Death

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Background: Recent evidence demonstrates that activated eosinophils undergo distinct pathway of cytolysis, eosinophil extracellular trap cell death (EETosis), accompanied by degranulation. EETosis is postulated to be implicated in local immune response and tissue damage in allergic conditions. We have previously showed that lysophosphatidylserine (LysoPS) induces eosinophil degranulation and triggers eosinophil cell death. Accordingly, this study aimed to examine whether and how LysoPS induces EETosis.
Methods: Human blood eosinophils were purified to more than 95%. Cells were stimulated by LysoPS in the absence or presence of signaling pathway inhibitors. Cells were stained with Sytox green for EET formation. EET-forming cells whose nuclei underwent a series of sequential changes were assigned to 4 stages, bilobed, delobulated nucleus, chromatolysis, and DNA trap. The culture supernatants were collected for cell death using LDH or MTT assays.
Results: LysoPS induced EET and cell death in dose- and time-dependent manners. EET-forming cells exhibited extensive nuclear DNA fiber network with entrapped histones and granule proteins, MBP and EPX. LysoPS-induced EET was independent of ROS production, as opposed to A23187-induced EET. Treatment with pharmacological inhibitors that block pyroptosis, necroptosis, or inflammasomal pathways showed that LysoPS-mediated EET was abrogated completely by BAY11-7082, a newly re-evaluated pyroptosis inhibitor, and partially by necroptosis inhibitors blocking RIP3 and MMKL. However, the pyroptosis inhibitor failed to inhibit the LysoPS-mediated cell death, suggesting that EET is a mechanistically separate event from cell death.
Conclusions: Our data suggest that LysoPS induces EETosis by the mechanisms involving pyroptosis and necroptosis and that LysoPS and its receptors are therapeutic targets to dampen eosinophil-associated allergic diseases.

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Key Words: Eosinophil, Lysophosphatidyl serine (LysoPS), Eosinophil extracellular DNA trap cell death (EETosis)

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In vitro Comparison of 6 Different Species Total Fish Allergen Extracts from 4 Companies

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Background: Fish is a frequent cause of allergic reaction. However, imported fish allergen extracts may not reflect the regional differences, especially for consumed species and way of cooking. In this study, we compare the fish allergen extracts which are commonly consumed in Korea.
Methods: Six different species fish allergen extracts (mackerel, codfish, common eel, flat fish, cutlass, and catfish) were purchased from 4 companies (Allergopharma-Germany, Lofarma-Italy, Hollister-Stier-USA, Prolagen-Korea), and compared by Bradford assay, SDS-PAGE, and immunoblotting.
Results: Protein concentrations (0.241 to 1.808 mg/mL) and protein compositions were observed to be variable among companies. A 12 kDa component, a parvalbumin, was shown to be the strongest allergen in all fish extracts tested. Cutlass and catfish extracts were available only from Prolagen, and cutlass parvalbumin displayed the highest allergenicity not by IgE immunoblotting but also by anti-parvalbumin antibodies.
Conclusions: Cutlass seems to be an important cause of fish allergy at least in Korea, and this newly developed allergen extract in local company could be useful for the development of allergy diagnostics and therapeutics.

Key Words: Fish allergen, Parvalbumin, Allergenicity

P-67

Causes of Food Allergy from Infants to the Elderly: A Recent 10-Year Data from a Single Tertiary Hospital in Korea

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Purpose: Recent studies of food allergy (FA) covering all ages in Korea are rare. We performed this study to identify causes and characteristics of FA from infants to the elderly in a single tertiary hospital in Korea, for better understanding of major items for food allergen labeling and regulation.
Methods: A retrospective medical record review was performed on patients of all ages diagnosed with immediate-type FA between March 2008 and February 2018 in Ajou University Hospital.
Results: A total of 4,680 cases of FA among 2,733 patients were reported, of which 54.3% were male. The distribution of onset ages of the first FA symptom was as follows: 45.3% below 2 years, 16.2% in 2–6 years, 5.5% in 7–12 years, 4.0% in 13–18 years, 16.9% in 19–40 years, 10.4% in 41–65 years, and 1.8% above 65 years of age. The major 10 causative foods were hen's eggs (17.2%), followed by cow's milk (16.7%), wheat (8.6%), crustaceans (8.5%), fish (4.6%), walnuts (4.4%), pork (3.2%), peanuts (3.2%), shellfish (3.0%), and peach (2.2%). The causative foods ranked from 11th to 20th were as follows: soybean, apple, chicken, buckwheat, beef, kiwi, almonds, perilla seeds, tomato, and squid. The distribution of major causative foods was rather distinct between subgroups according to ages among children, whereas similar patterns were observed in adults. The top 3 causative foods in children were hen's eggs, cow's milk, and wheat, and the top 3 causative foods in adults were crustaceans, wheat, and fish. Food-induced anaphylaxis was reported in 29.2% of all cases, with cow's milk, hen's eggs, wheat, crustaceans, fish, walnuts, pork, shellfish, buckwheat, and peanuts being the major 10 causes.
Conclusion: This study is meaningful in that it is a recent study that has thoroughly examined the causes and characteristics of 4,680 FA cases covering all ages. [This research was supported by a grant from Korea Ministry of Food and Drug Safety in 2018.]

Key Words: Food allergy, Anaphylaxis, All age

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Safety of Ultra-Rush Schedule of Subcutaneous Allergen Immunotherapy with House Dust Mite Extract Conducted for 8 Hours in an Outpatient Clinic in Patients with Allergic Rhinitis

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Background: Ultra-rush schedule of subcutaneous allergen immunotherapy (UR-SCIT) administering a maximum maintenance dose of allergen extract within one day can save time and effort in patients with allergic diseases. However, UR-SCIT is associated with an increased risk of systemic reaction (SR) compared to conventional subcutaneous allergen immunotherapy and is usually conducted in a hospital admission setting. To overcome these limitations of UR-SCIT, we evaluated the safety of UR-SCIT conducted in an outpatient clinic in patients with allergic rhinitis.
Method: UR-SCIT was performed in 26 patients with allergic rhinitis and hypersensitivity to house dust mites (HDM). A maximum maintenance dose of tyrosine-adsorbed HDM extract (1mL of maintenance concentration) was divided into 4 increasing doses (0.1, 0.2, 0.3, and 0.4 mL) and administered to the patients by subcutaneous injections at 2-hour interval for 8 hours in an outpatient clinic. SR associated with UR-SCIT was classified according to the World Allergy Organization grading system.
Results: SR was observed in 3 of 26 patients (11.5%) during UR-SCIT. Observed SR was grade 1 in one patient (3.8%), grade 2 in one patient (3.8%), and grade 3 in one patient (3.8%). Grade 4 SR or grade 5 SR was not observed. Prescheduled 4 increasing doses of HDM extract could be administered in 24 of 26 patients (92.3%) except two patients who developed grade 2 SR at 15 minutes after the second dose (0.2 mL) injection and grade 3 SR at 120 minutes after the third dose (0.3 mL) injection. SR observed within 2 hours in all three patients who experienced an SR after administration of the last dose of HDM extract.
Conclusion: UR-SCIT conducted in an outpatient clinic was safe and well-tolerated in patients with allergic rhinitis sensitized to HDM. UR-SCIT can be a safe and useful option to start subcutaneous allergen immunotherapy for allergic rhinitis.

Key Words: Allergens, Desensitization, Allergic rhinitis

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Safety and Utility of Rush Immunotherapy with Aqueous Allergen Extracts for the Treatment of Respiratory Allergies

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Background: Allergen immunotherapy (AIT) needs treatment duration of 3 to 5 years. Rush immunotherapy (RIT) shortens the duration of build-up phase and improves convenience compared with conventional immunotherapy (CIT). However, RIT has been usually performed with modified allergens such as depot adjuvants. This study aimed to investigate the safety and utility of RIT with aqueous allergen extracts.
Methods: We reviewed medical records of patients who have taken AIT with aqueous allergen or aluminum hydroxide adsorbed depot allergen for allergic rhinitis and/or asthma. They were divided into 3 groups: group A (n=36) received RIT with aqueous allergen; group B (n=25) received RIT with depot allergen; group C (n=22) received CIT with aqueous allergen. Patients treated with AIT targeting only house dust mite were excluded.
Results: Mean allergen numbers mixed in AIT was 3.7±1.0, 3.1±1.1 and 3.4±1.1, in group A, B and C, respectively. Mean injection numbers during build-up phase was 14.1±1.1, 17.0±0.2 and, 14.2±1.4 in group A, B and C, respectively (P<0.001). Number of outpatient clinic visit decreased to 2.1±1.4 and 1.0±0.2 in group A and B, respectively, compared with 13.3±2.9 in group C (P<0.001). Build-up phase decreased to 25.0±11.3 days and 17.4±1.8 days, in group A and B, respectively, compared with 88.2±17.8 days in group C (P<0.001). Proportion of patient experienced systemic reaction increased to 77.8% and 80.0% in group A and B, respectively, compared with 31.8% in group C (P<0.001). Mean number of systemic reaction per patient increased to 2.0±1.9, 1.4±1.0 in group A and B, respectively, compared with 0.5±0.8 in group C (P=0.001).
Conclusion: RIT with aqueous allergen was found to reduce frequent hospital visit and duration of build-up phase as well as to offer comparable safety with aluminum hydroxide adsorbed allergen. AIT with aqueous allergen can be widely applied to patients with respiratory allergies.

Key Words: Rush, Immunotherapy, Aqueous allergen

P-70

Role of IgE-VH in FcεRIα and Superantigen Binding in Allergy and Immunotherapy

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Background: VH family frameworks have been reported to affect antibody receptor and superantigen binding, however such effects in IgE remains largely unknown. Given that VH family biases have been previously reported in IgE of certain allergies, there is a need to investigate this phenomenon and how it may contribute to allergy pathogenesis.
Objective: We sought to investigate the effects of VH families on IgE interaction with FcεRIα, anti-IgE Omalizumab, antigen, and superantigen spA using the Pertuzumab and Trastuzumab IgE models.
Methods: Pertuzumab VH1-VH7 family variants of IgE with the same CDRs were analyzed with regards to their binding interactions to FcεRIα, Her2, Omalizumab, and spA. Notable FcεRIα -IgE observations were cross-checked against appropriate Trastuzumab IgE VH variants. Computational structural modeling and simulations were also performed for insights into the mechanism of interactions with various VH FWRs.
Results: The Pertuzumab VH5 IgE variant but not the Trastuzumab VH5 IgE was found to interact with FcεRIα significantly higher than the respective VH family variants within each model antibody. No significant differences in interaction were found between IgE and Omalizumab for the Pertuzumab VH variants. Although Trastuzumab VH3 interacted with spA, all our Pertuzumab VH variants including VH3 did not associate with spA.
Conclusion: We found unexpected varying allosteric communications caused by the VH family frameworks to the FcεRIα, Her2, and spA binding regions of Pertuzumab IgE, with implications on the use of IgE/anti-IgE therapeutics to treat allergy and IgE therapeutics in allergooncology.
Clinical Implications: IgE-VH family effects were found for FcεRIα but not Omalizumab interactions, with a possible role in allergy. On allergoncology therapeutics, designing non-spA binding IgEs may be necessary for clinical safety.

P-71

Altered Sphingolipid Metabolites in an Ovalbumin-Induced Asthma Mouse Model

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Background: Recent studies revealed dysregulation of sphingolipid (SL) profiles in patients with asthma, which are important in modulating allergic responses and inflammation. Therapies to recover SL pathway should be considered.
Objective: We aimed to investigate the inhibitory effect of dexamethasone on the altered SL metabolites using an asthma mouse model.
Materials & Methods: BALB/c mice were used to induce allergic asthma by intraperitoneally injection of ovalbumin (OVA) on days 0, 14, followed by challenge with OVA 1% on days 28–30. Some mice were received dexamethasone (1mg/kg) for 30 minutes prior to nebulization. On days 31, mice were assayed to measure airway hyperresponsiveness (AHR) to methacholine. Levels of interleukin (IL)–4, 5, 13 in bronchoalveolar lavage fluid (BALF) were measured by ELISA, while SL metabolites were analyzed by chromatography–tandem mass spectrometry. The expression of sphingosine kinase 1 (SPHK1) in lung tissues were estimated by immunohistochemistry.
Results: The OVA mice showed higher levels of IL–4, IL–5, IL–13, SPHK1 expression, increased recycling pathway compared to NC. Levels of BALF S1P and C1P were increased significantly in OVA mice compared to NC ($P<0.05$ for all). Levels of sphingomyelins and ceramides were increased in OVA mice compared to NC ($P<0.05$ for all). BALF S1P correlated positively with IL–4 ($r=0.659$, $P=0.009$) and IL–13 ($r=0.589$, $P=0.023$). Dexamethasone attenuated AHR, BALF levels of IL–5, IL–13, S1P and SPHK1 expression significantly, while there was no effect on C1P. Dexamethasone also downregulated sphingomyelins and ceramides significantly ($P<0.05$ for all).
Conclusions: Dexamethasone suppress the airway inflammation and hyperrepsonsiveness through recovering the disturbance of SL metabolites in asthma.

Funding Sources: This work was supported by Basic Science Research Program of the National Research Foundation (NRF) grant funded by the Korea government (NRF–2018R1A2B6004905)

Key Words: Asthma, Dexamethasone, Sphingolipid metabolites

P-72

Clinical Features of Pneumonia due to Mycoplasma Pneumoniae Infection in Children of Different Ages

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Purpose: We aimed to investigate possible age–dependent clinical features of pneumonia due to Mycoplasma pneumoniae (MP) in children and also evaluated if there is any difference in relation to patients' atopic status and viral co–infection.
Methods: Two hundred and ninety–two patients who were admitted with MP pneumonia were enrolled. MP infection was confirmed by real–time PCR in nasopharyngeal secretions and/or by serological examination. The patients were divided into 3 age groups: group 1: <3 years (infants/young children, N=43), group 2: 3–6 years (pre–school children, N=126), group 3: >6 years (school children, N=123). Medical reports were reviewed retrospectively and analyzed for demographics, clinical presentation, atopic status, viral co–infection, radiological and laboratory findings.
Results: The number of patients with high IgE levels and/or atopic sensitization was significantly higher in group 2 & 3 compared with group 1. Viral co–infection was significantly higher in group 1 than in group 2 & 3. Frequency and duration of fever were significantly increased in group 2 & 3 compared to group 1. Lobar pneumonia, pleural effusion and breathing difficulties were more frequently observed in group 3. However, development of acute wheezing, recurrent wheezing after discharge and post–infectious bronchiolitis obliterans (PIBO) during follow–up were more frequent in group 1 compared to group 2 & 3. No significant difference was observed in clinical presentation in relation to patients' atopic status or viral co–infection in each patient group.
Conclusions: Our study showed age–dependent difference in clinical features of MP pneumonia in children. Later development of recurrent wheezing and PIBO after MP pneumonia was more frequent in infants/young children than in school children, and it suggests that follow–up evaluation is needed especially in those young patients after discharge from hospital.

Key Words: Mycoplasma

P-73

Prospective Study on Macrolide Response and Efficiency of Diagnostic Method to Mycoplasma Pneumoniae Penumonia in Children between MSMP and MRMP

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Mycoplasma pneumoniae(MP) is a most common cause of community acquired pneumonia. But during previous epidemics, resistance to macrolide was reported to be increased. Many studies discussed about this phenomenon, but there has been no prospective study including previous antibiotic history. This study was conducted to evaluate the response to macrolide and efficiency of diagnostic method of Mycoplasma pneumonia and investigated the clinical difference between MSMP and MRMP prospectively.
We prospectively got the precise antibiotic history and observed the response to macrolide from patients who was diagnosed as radiological pneumonia from January 2017 to march 2019. If the fever resolved within 72 hours after macrolide, we defined it to macrolide sensitive(MSMP). We changed macroide to doxycycline (macrolide unresponsive patients: MURMP) and observe the respnse for another 72 hours. If there was no defeverescence, we used steroid. Diagnostic method, clinical information, laboratory data and radiological findings were analysed. And we'll compare the clinical results according to the macrolide resistance PCR.
Macrolide sensitive Mycoplasma pneumoniae (MSMP) was 69.4%(n=25) and Macrolide unresponsive Mycoplasma pneumonia (MURMP) was 30.6%(n=11) and steroid responsive MP was 11.1%(n=4). 69.4%(n=25) was diagnosed with MP PCR from nasopharyngeal swab. 30.6%(n=11) was MP PCR negative and diagnosed with serologic marker. Mean fever day was 5.9(day) in MSMP patients and 8.4(day) in MURMP patients. Lactate dehydrogenase (LDH) and C-reactive proetin(CRP) levels were significantly higher in MURMP patients than MSMP patients. Lobar type pneumonia was more related to MURMP compared to MSMP.
Sensitivity of Mycoplasma PCR was about 70% and serology supported the diagnosis in 30%. Clinical MSMP was about 70%, higher than previous epidemics. And correlation with MP PCR resistance to clinical response will be discussed

Key Words: Mycoplasma pneumoniae, Macrolide, Resistance

P-74

Glucagon-Like Peptide 1 Receptor (GLP-1R) Agonist Improved Asthmatic Airway Inflammation in High Fat Diet Induced Obese Asthma Mice Model

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Background: Obesity is a correctable factor for uncontrolled bronchial asthma. However, the effects of weight loss by GLP-1R agonist, recently approved antiobestic drug, on airway hyperreactivity (AHR) and immune responses are not known.
Methods: Mice were fed with high fat diet (HFD, 60% fat) to induce obesity for 8 weeks and ovalbumin (OVA) sensitization and challenges were performed for 7 weeks. Intraperitoneal GLP-1R agonist (Liraglutide) injection was done 5 times a week for 4 weeks. AHR were measured by flexivent system, blood as well as bronchoalveolar lavage fluid (BALF) were collected. Lung tissues were examined to evaluate the changes of bronchial inflammation by obesity and GLP-1R agonist in asthma mice. Expression level of Th2, Th17 cytokines and IL-33 were also analyzed.
Results: HFD induced significant weight change (142% of the average weight) in the obese mice group. HFD-OVA mice showed increased AHR compared to control mice. Treatment of GLP-1R agonist made significant weight loss and suppression of AHR in obese OVA mice. The expression of IL-4,5,13 and 33 were increased in HFD-OVA mice compared to lean OVA mice and decreased with GLP-1R agonist treatment. Leptin and adiponectin ratio was elevated in HFD-OVA mice, decreased in GLP-1R agonist administered group. Lung tissue H&E stain revealed that peribronchial inflammation induced by obesity and OVA was effectively suppressed by GLP-1R agonist treatment.
Conclusions: Weight loss induced by GLP-1R agonist effectively suppressed bronchial airway inflammation and AHR. Changes of immune responses mediated by GLP-1 pathway could be involved in anti-asthmatic effects in obese asthma.

Key Words: Asthma. Obesity, GLP-1

P-75

Therapeutic Potential of an Indole Derivative on Murine Models of Environmental Compound-Associated Lung Disease

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Various environmental compounds are implicated in fatal lung injury. Mitochondria are crucial organelles for normal lung function that can be impacted by many lung diseases. Recently, we developed an antioxidant indole-derived NecroX compound (NecroX), which preserves mitochondrial functionalities. In this study, we investigated therapeutic effects of NecroX on lung injury associated with polyhexamethylene guanidine (PHMG), a well-known chemical compound implicated in humidifier disinfectant-associated fatal lung injury in human, and bleomycin, a widely used chemical for inducing experimental lung fibrosis in mice, focusing on functionalities of mitochondria. Respiratory exposure to PHMG and bleomycin led to lung injury manifesting inflammation (increases of inflammatory cell infiltrations, TNF-α, IL-1β, IL-17, and KC) followed by fibrosis (elevated total collagen amount and TGF-β1) in the lung parenchyma, which was further verified by histopathologic and radiologic measurements. Exposure to these compounds impacted on mitochondria in regard to biogenesis, mitochondrial DNA (mtDNA) integrity, and generation of mitochondrial reactive oxygen species (mtROS) in various cells of the lung. Notably, NecroX significantly improved these pathobiologic features of the PHMG- and bleomycin-induced lung injury and ameliorated mitochondrial functionalities. These findings imply that NecroX has therapeutic potential in the treatment of environmental compound-induced lung injury.

Key Words: Environmental compound, Lung injury, NecroX

P-76

Implication of the Cross-Talk between Endoplasmic Reticulum Stress and Mitochondria in Environmental Compound-Induced Lung Disease

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Endoplasmic reticulum (ER) is important cellular protein-folding factory and highly susceptible to cellular stresses leading to accumulation of misfolded and/or unfolded proteins in the ER, ER stress. ER stress is a pivotal player in pulmonary fibrosis and cross-talk between mitochondria-ER has been suggested to be implicated in pulmonary fibrosis. We investigated whether this cellular cross-talk may be implicated in the experimental environmental compound-associated lung injury/fibrosis induced by polyhexamethylene guanidine (PHMG) and bleomycin. Respiratory exposure to PHMG and bleomycin into mice led to lung injury/fibrosis. Various ER stress markers were increased in the lung of PHMG- and bleomycin-exposed mice. A potent ER stress inhibitor reduced the ER stress markers in the lung PHMG- and bleomycin-exposed mice and attenuated inflammatory/fibrotic features. Interestingly, increases of the immunofluorescence intensity of an ER-resident chaperone in bronchoalveolar lavage cells from PHMG-exposed mice were markedly lowered by a potent mitochondrial ROS scavenger, NecroX. NecroX improved pathobiologic features of the PHMG- and bleomycin-induced lung injury and ameliorated mitochondrial functionalities. Lastly, intensity of immunoreactive CHOP, an ER stress marker, was significantly increased in environmental compound-associated lung injury patients compared to control subjects. These data highlight the therapeutic potential of cellular cross-talk between ER and mitochondrial for treating fatal fibrosing type of interstitial lung disease in humans.

Key Words: Environmental compound, Lung injury, ER-mitochondrial crosstalk

P-77

Laboratory Animal Allergy among Korean Laboratory Animal Researchers: A Cross-Sectional Questionnaire Survey

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Background: This study aimed to investigate the prevalence rates of laboratory animal allergy (LAA) and evaluate the current status of prevention of allergen exposure in Korea.
Methods: We conducted questionnaire survey for Korean laboratory researchers who attended 2018 annual symposium of Korean Association of Laboratory Animal Science. Self-reported questionnaires included the characteristics of LAA, exposure control, prevention, medication, and health care service utilization related to LAA.
Results: A total of 223 subjects were responded. They are mostly female aging 20-29 years and duration of occupation and laboratory animal exposure were mostly less than 5 years. In them, 76% were directly exposed to laboratory animals, and mouse and rat were most common animals they were recently exposed to. Allergic symptoms were reported in 29.1% of subjects exposed to mice compared to 13.0% in those to rats, and skin itchiness and symptoms of rhinitis were the most frequent symptoms. In terms of both personnel and affiliated organizations, the most common mandatory control before laboratory works was wearing glove, followed by wearing mask, washing hands, wearing clothing cover and hair-covering caps, whereas wearing respirator and wet preparation before shaving showed low rates. Individuals with LAA were likely to take more efforts to prevent LAA by restricting time and frequency of laboratory animal contact compared to individuals without LAA. Only 16% of subjects with LLA visited medical institutions and 42% remained untreated.
Conclusion: About one third of laboratory animal researchers had LAA. However, measures and strategies to control LAA seemed to be insufficient. Further efforts are mandatory to provide medical surveillance for LAA raising awareness of LAA and as well as prevention programs and proper treatments against LAA.

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Key Words: Questionnaire survey, Laboratory animal allergy, Prevention

P-78

Up-Regulation of Periostin Production in Tears of Allergic Ocular Disease Patients

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Purpose: We focused on periostin, an established mediator and biomarker of Th2 immune response and fibrogenesis, and investigated whether it is associated with the pathogenesis of severe allergic ocular diseases, such as atopic keratoconjunctivitis (AKC) and vernal keratoconjunctivitis (VKC). We also examined whether periostin could serve as a biomarker for these diseases.
Methods: Patients with allergic ocular diseases (AKC, VKC or seasonal allergic conjunctivitis (SAC)) and age-matched control subjects were enrolled, and tear samples were collected. Tear periostin levels were measured by ELISA, and IL-13 were measured by milliplex assay. To examine the expression of periostin in diseased conjunctival tissues, immunofluorescence staining was performed. We also established primary cultures of conjunctival fibroblasts derived from giant papillae tissues of AKC patients (AF) and normal conjunctival tissues (NF), and we analyzed the expression of periostin levels by qPCR and ELISA.
Results: Tears from allergic ocular disease patients contained significantly higher periostin levels compared to tears from control subjects. Especially, tear periostin levels in AKC patients were associated with serious comorbidities such as giant papilla formation and corneal damage. Immunofluorescence staining revealed that more intense periostin expressions were found in AKC tissues than normal tissues. Moreover, higher periostin expressions were also observed in the AFs than NFs despite prolonged cell cultures. Although tear periostin levels were positively associated with tear IL-13, tear periostin levels appeared to enable the most accurate discrimination of allergic ocular diseases.
Conclusion: Periostin produced mainly in fibroblasts in the conjunctival tissues, presumably enhanced expression by IL-13, may contribute to the pathogenesis of allergic ocular diseases. Furthermore, tear periostin levels seem to be potentially useful as a biomarker for distinguishing allergic ocular diseases from other conditions.

P-79

Therapeutic Effects of Recombinant Salmonella Typhimurium Harboring CCL17 miRNA in Mouse Model of Ashtma

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Asthma is result from multifactorial inheritance, with interaction between genetic and environmental factors. In particular, the chemokine CCL17 is considered as a key regulator of Th2-mediated inflammation in allergic asthma and its levels are significantly elevated in serum and correlated with disease severity in asthma. We tested the suppression of the CCL17 gene by microRNA (miRNA) and observed the effects in mice with inflammation similar to asthma. We used Salmonella as a vector to deliver miRNA. The recombinant strain of Salmonella typhimurium expressing CCL17 miRNA (ST-miRCCL17) was prepared for in vivo knockdown of CCL17. ST-miRCCL17 was orally inoculated into mice and the CCL17 gene suppressed with CCL17 miRNA in the activated lymphocytes. IgE were inhibited and interferon-γ was induced after treatments with ST-miRCCL17 and CCL17 was suppressed. Further, Th17 cells were suppressed in the asthmatic mice treated with ST-miRCCL17. These results suggest that ST-miRCCL17 may be an effective genetic agent for treating allergic asthma.

Key Words: Biological therapy, Chemokine CCL17, Asthma, Immunotherapy, RNA interference

P-80

Factors Affecting Depression in Adolescents with Allergic Diseases

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Background: Depression is common in adolescents with allergic diseases and has a negative impact on adolescent development. Considering the large number of adolescents suffering from allergic diseases, it is important to identify the contributing factors so that appropriate interventions can be developed.
Purpose: This study is to identify the affecting factors of depression in adolescents with allergic diseases in order to develop the intervention programs.
Methods: The study used raw data from the Korean Children and Youth Panel Survey conducted in 2016, included first-grade high school students with allergic diseases (including asthma, allergic rhinitis, and atopic dermatitis).Data was analyzed using SPSS 21.0 for descriptive statistics, t-test, Chi-square t-test, Pearson's correlation coefficients, and multiple regression analysis.
Results: The multiple regression analysis revealed that the affecting factors to depression were as follows: the explanatory power was 59% (F=181.236, p<.001), gender (β=-.09, p<.001), social withdrawal (β=.28, p<.001), subjective health status (β=-.07, p=.004), self-esteem (β=-.45, p<.001), and smart phone addiction(β=.12, p<.001) had significant effects on depression.
Conclusion: Thus, depression in adolescents with allergic diseases seems to be close linked to social and physical health problems. In order to help adaptation of adolescents with allergic diseases, it is necessary to have an interest in overall mental health problems including depression, and to develop various interventions by building family, school and community teams will be effective in improving the quality of life.

Key Words: Depression, Adolescent, Allergic diseases

P-81

Predictions of Length of Hospital Stay in Infants with Acute Bronchiolitis Using Machine-Learning Algorithms: Preliminary Study

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Purpose: Recently, several studies showed that machine learning techniques have been used for predicting the diseases prognosis and improving the prognosis. We compare six machine learning models with classical models for Predictions of length of hospital stay in infants with acute bronchiolitis

Methods: This is a retrospective study on the predictive performance of several machine learning techniques for hospital stay length prediction in infants with bronchiolitis. We used the database of infants with bronchiolitis admitted at a tertiary -care hospital from August 2014 to August 2016. We developed models for hospital stay prediction with six machine learning algorithms using fever, laboratory results, clinical severity score and past medical history. Six machine-learning algorithms were used including random forest, Gaussian Naïve Bayes, support vector machine, Extreme Gradient Boosting, lostic regression, and K-nearest neighbor.

Results: Two hundred forty three cases were categorized as training dataset and test dataset. Mean duration of hospitalization for this data was 5.24 (+-3.62) days. Mean age is 4.74 (_+-3.30) months. The machine learning models had an area under the curve (AUC) ranging from 0.64 to 0.76. The best performing machine learning algorithm, Gaussian Naïve Bayes, achieved an AUC of 0.77 (95%CI 0.75-0.78) and next is Random Forest, achieved an AUC of 0.75 (95%CI 0.73-0.76). K-nearest neighbor and linear regression are showed less accuracy, ACU 0.66 (95% CI 0.64-0.68) and 0.67 (95% CI 0.65-0.69). In Random forest, important features are the body temperature and PCO2.

Conclusions: In this study developing models for prediction of length of hospital stay in infants with acute bronchiolitis, the top performing machine learning algorithms, Gaussian Naïve Bayes and Random Forest. Future prospective validation is needed.

Key Words: Machine learning, Bronchiolitis, Hospital stay

P-82

Evaluation of Therapeutic Response of rare Pulmonary Disease through Thoracic Ultrasound

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Background: The use of thoracic US for lung examination is increasingly gaining wide acceptance in emergency and critical care medicine.

Objectives: The purpose of this study was to evaluate the diagnostic performance of thoracic US in patients with rare pulmonary disease.

Methods: Thoracic US was done before and after treatment serially, at the 4 probe points on each hemitorax. Case report 1: We present the case of an 14 month-old boy with Surfactant C deficiency, for whom lung US was very useful for directing diagnosis and for follow-up during therapy. The case is presented of a term newborn that developed respiratory distress, recurrent pulmonary diffuse interstitial infiltration, and a complicated neonatal course requiring 2 months of mechanical ventilation. Genetic studies confirmed the nonsense variant (p.Tyr195) of surfactant protein C deficiency. The lung US findings are assessed based on comet-tail artifacts (B lines) and sub-pleural thickening in the anterior and lateral 4 regions of the each thorax. The chest US performed after several steroid pulse therapy showed progressive improvement of the pleural thickening and reduction in the number of B-lines. Case report 2: 8 month-old girl, who presented of a preterm newborn with pulmonary infiltrates, chylothorax and hemothorax that developed respiratory distress was diagnosed with lymphangiomatosis on chest MRI. The thoracic US showed diffuse pleural thickening, pleural effusion and peripheral parenchymal infiltration. The thoracic US performed after corticosteroid treatment showed improvement of the pleural thickening and peripheral parenchymal infiltration. The celiac lymph node biopsy shoed proliferation of lymphatic vessels. She was diagnosed with Gorham-Stout Disease according to clinical and pathologic findings.

Conclusions: Thoracic US was useful in evaluating the response of treatment to patients with rare pulmonary disease such as Surfactant protein C deficiency and pulmonary lymphangiomatosis.

Key Words: Thoracic, Ultrasonography, Pulmonary disease

P-83

Cough-Related Laryngeal Sensations and Triggers in Adults with Chronic Cough: Symptom Profile and Impact

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Purpose: Recent evidence suggests that cough hypersensitivity may be a common feature of chronic cough in adults. However, the clinical relevance remains unclear. This study evaluated the cough-related symptom profile and the clinical relevance and impact of cough hypersensitivity in adults with chronic cough.
Methods: This cross-sectional multi-center study compared cough-related laryngeal sensations and cough triggers in patients with unexplained chronic cough patients following investigations and in newly referred patients with chronic cough. A structured questionnaire was used to assess abnormal laryngeal sensations and cough triggers. Patients with unexplained cough were also evaluated using the Leicester Cough Questionnaire (LCQ) and a cough visual analogue scale (VAS), and these scores were assessed for correlations with the number of triggers and laryngeal sensations.
Results: This study recruited 478 patients, including 62 with unexplained chronic cough and 416 with chronic cough. Most participants reported abnormal laryngeal sensations and cough triggers. Laryngeal sensations (4.4±1.5 vs. 3.9±1.9; p=0.049) and cough triggers (6.9±2.6 vs. 5.0±2.8; p<0.001) were more frequent in patients with unexplained chronic cough than in those with chronic cough. The number of triggers and laryngeal sensations score significantly correlated with LCQ (r=−0.51, p<0.001) and cough VAS score (r=0.53, p<0.001) in patients with unexplained chronic cough.
Conclusions: Cough hypersensitivity is a common feature in patients with chronic cough, especially those with unexplained chronic cough. Cough-related health status and the severity of cough was inversely associated with the number of triggers and laryngeal sensations, suggesting that they are potentially relevant in the assessment of chronic cough.

Key Words: Chronic cough, Cough hypersensitivity, Leicester Cough Questionnaire

P-84

A Prospective Observational Study to Investigate the Comparison of Clinical Differences between Elderly and Young Adults with Allergic Rhinitis (AR)

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Introduction: The prevalence of allergic rhinitis (AR) is 10%-25%, increasing over the last 30 years with environmental changes. Control of AR is critical, as it impacts on the quality of life and physical performance. Adherence and drug responses may be different in elderly AR patients compared to younger ones. The present study was aimed to compare clinical features and responses to pharmacological treatment between elderly patients with AR (over 65 years) and younger ones (aged from 19 and 40 years).
Methods: This is a prospectively designed observational study conducted for 4 weeks, 151 moderate/severe and persistent AR patients (50 in the elderly group; 101 in the young group) were enrolled. Both groups were treated following the ARIA guideline for 4 weeks. Changes of TSS6 (total symptoms score 6), RCAT (rhinitis control assessment test), RQLQ (rhinitis-specific quality of life questionnaire), VAS (visual analog scale) from the baseline scores and treatment satisfaction scores were compared between the 2 groups.
Results: There were no significant differences in baseline scores of TSS6, RCAT, and RQLQ between the 2 groups. After the 4-week treatment, no significant changes were noted between the 2 groups in aspects of RCAT (22.49±3.49 vs. 21.45±4.21, P=0.137), RQLQ (55.76±21.42 vs. 61.28±21.34, P=0.140) and VAS by patients (29.45±24.44 vs. 34.04±26.66, P=0.313) and treatment satisfaction (3.04±0.87 vs. 3.07±0.70, P=0.841). However, TSS6 answered by patients was significantly lower in the elderly group (OR −1.81, P=0.002).
Conclusion: These findings suggest that elderly AR patients under an adequate treatment can achieve symptom control and improved QoL by the extent observed in the younger patients. However, the discrepancy between RCAT on AR control and TSS6, RQLQ, VAS by physicians/patients indicates that more objective measures are needed for evaluating elderly AR patients.

Key Words: Allergic rhinitis, Elderly, TSS6

P-85

Complementary Cooperation of Genetic and Epigenetic Components in the Development of NERD

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Epigenesis is the most exciting solution for the missing heritability of GWAS in asthma. Nonsteroidal anti-inflammatory drugs are one of the important environmental factors inducing epigenetic changes. We previously reveled 490 differentially methylated CpG (DMC) in nasal polyp of NERD compared to ATA (Allergy 2011,637-44). However, genetic impact of the DMC on prostaglandin and leukotriene pathways has not been evaluated, especially in terms of interaction with SNPs. In the present study, we performed in silico analysis using the data of global CpG methylation (5 NERD vs. 4 ATA) and SNPs (100-200 NERD vs. 200-1000 ATA). Ontology classification demonstrated 259 genes on arachidonate pathways. Among them, 66 genes were differentially methylated (25.4%), which was 10 times greater than that (3%) of global DMG, indicating that genes in arachidonate pathways are much more labile to CpG methylation in NERD. Number of the genes having SNPs was 49 (18.9%) and 7 genes had DMC and SNPs on the same gene. Among them, only one (S100A9) had the CpG site-related SNPs, which can lead to gain or loss of CpG sites. Among 37 CpGs on 19 genes on the prostaglandin and leukotriene biosynthesis pathways, 14 CpGs on 11 DMG which included highly hypomethylated PGDS and ALOX5AP and hypomethylated PTGES. These methylation changes are really in good agreement with the metabolite levels in nasal polyps. Among the 14 receptor genes on prostaglandin and leukotriene pathways, 8 CpGs were significantly different on 6 genes which included LTB4R and LXA4R. In the prostaglandin pathway, synthesizing enzymes were hyper- and hypomethylated while receptors for PGE, PGD, PGI, and TBXA2R were affected by SNPs. Similar pattern of methylation and SNPs was observed in the leukotriene pathway. In conclusion, Genetic and epigenetic components are in complementary cooperation in the development of NERD. Fund source (HD14B1248) and all data were obtained from a BioBank at Soonchunhyang University Hospital.

Key Words: Asthma, Aspirin, Epigenetics

P-86

The Risk of Tetracyclines-Induced Tooth Discoloration and Fluoroquinolones-Induced Tendinopathy in Childhood Pneumonia

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Objective: The emergence of macrolide-resistant Mycoplasma pneumoniae pneumonia (MRMP) has made its treatment challenging. A few guidelines recommended tetracyclines (TCs) or fluoroquinolones (FQs) as the second-line drug of choice for treating MRMP, but concerns about potential adverse events (i.e., tooth discoloration or Achilles tendon rupture) were raised. The aim of this study was to investigate risks of TCs or FQs for adverse events, with dose, age-dependent response.
Methods: Childhood pneumonia cohort with hospitalization (total of 3,393,935 episodes) from 2002 to 2017 were enrolled utilizing a healthcare claims records of the Korean NHISS database. The independent risk of TCs or FGs for the tooth-discoloration (TD) or Achilles tendon rupture (ATR) were analyzed by Generalized Estimating Equation with adjustment for age, sex, and preexisting diseases.
Results: Among 3,393,935 episodes, 1,199 episodes (0.04%) exposed to TCs, and 7,012 (0.21%) exposed to FQs for the treatment of pneumonia. TCs-exposure group showed a 0.58% (7/1,199) incidence of TD, and 2.5-fold higher risk than non-exposures (adjusted OR; 2.5, 95% CI; 1.02-5.99). According to TCs classification, the incidence of TD was 1.9% (2/105) in tetracycline, 0.5% (5/995) in doxycycline, and 0% (0/91) in minocycline. FQs-exposure group showed a 0.17% (12/7,012) incidence of ATR, and 0.11 fold less risk than non-exposures (aOR; 0.89, 95% CI; 0.44-1.78). Among TCs-exposures, group (<8 years old) showed higher incidence of TD than older group (OR; 8.43, 95% CI; 7.89-11.58), (aOR; 1.18, 95% CI; 1.17-1.19) without dose-dependent response. In FQs-exposures, no age, dose-dependent responses were observed.
Conclusion: Tooth discoloration and Achilles tendon rupture were very rare adverse-event. However, TCs, particular in tetracycline, showed higher risk of tooth discoloration with age-dependent response.

Key Words: Tetracyclines, Fluoroquinolones

P-87

2 Cases of Pediatric Patients Aggravated by An-A-Ki

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An-A-Ki is a group that seeks alternative medicine rather than evidence-based medicine, associated with vaccine refusal, steroid phobia, etc. We reported one severe respiratory infection case and allergic case by An-A-Ki.
Case 1: A 3-month-old girl visited the hospital for 2days of fever and paroxysmal cough. Starting with rhinorrhea 2 weeks ago, cough 10days ago, paroxysmal cough 5days ago, fever 2days ago. Birth history was 3rd, vaginal delivery, 40weeks and 3,300g. There was no medical history after birth, never been vaccinated including other two siblings. At admission, Vital sign were heart rate 216/min, respiratory rate 42/min, body temperature 38.2'C, and O2 saturation 91%. She presented fever, tachypnea, tachycardia, chest retraction and rales in both lung field on auscultation. Chest X-ray diagnosed segmental pneumonia which showed right middle lobe consolidation with increased peribronchial vascular marking. On the blood test, white blood cell count was 79,490/μl (lymphocyte 59%), Hemoglobin 11.7g/dL, Hematocrit 36.1%, Platelet count 732X103/μl, C-reactive protein 0.30mg/L, which states leukocytosis with lymphocyte dominant and thrombocytosis. Respiratory PCR was positive to Bordetella pertussis. Treatment started macrolide (azithromycin) medication and O2 inhalation by humidified high-flow nasal cannula with monitoring. There was no complications such as apnea or encephalitis. We experienced a typical pertussis infection with leukocytosis by vaccine refusal.
Case 2: A 26-month-old boy firstly visited the hospital due to recurrent wheezing, dyspnea. At 6-month-old, he was diagnosed as atopic dermatitis, but refused topical steroid. Birth history was 3rd- vaginal delivery, 40weeks, and 3,200g. He has never been vaccinated at all. Around 12-month-old, recurrent wheezing with severe dyspnea made him admit the hospital twice, but refused inhaled steroid. Every chest X-ray showed recurrent right middle lobe syndrome. He also refused leukotriene receptor antagonist, because penile erection happened repeatedly which suspected adverse effects. After that wheezing everyday graded severe persistent asthma. Atopic dermatitis graded as moderate-to-severe that managed by only emollient. At 35-month-old, after intake beverage including cow's milk, complaint of urticaria, dyspnea, and severe cough diagnosed as anaphylaxis, recovered by intramuscular epinephrine. But he refused epinephrine autoinjector.
On allergic test, Eosinophil was 9%, total IgE 2,109U/ml, Df 100 kUA/L, egg white 16.2 kUA/L, cow's milk 72.6 kUA/L, wheat 20.6 kUA/L, soybean 26.9 kUA/L, walnut 54.0 kUA/L, peanut 19.4 kUA/L, shrimp 0.79 kUA/L, cod 0.13 kUA/L, and buckwheat 18.0 kUA/L. He moved to Austrailia searching for clear environment with keeping An-A-Ki mind. We experienced atopic dermatitis, bronchial asthma and anaphylaxis aggravated by steroid.

Key Words: Bordetella pertussis, Anti-vaccination movement, Treatment refusal

P-88

Development of Colorectal Cancer Risk Assessment Model through Stool Microbes Analysis

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There are approximately 500-1000 species of bacteria living in our body and the sum of their genetic material is known as the microbiome. Recently, the impact of the gut microbiome on metabolism and disease has received attention as an environmental factor influencing human health. In this study, we explored the connection between the gut microbiota and colorectal cancer (CRC) and developed diagnostic model for CRC.
We conducted 16S rDNA-based metagenomic analysis of bacteria isolated from CRC patients and healthy subject stool. Through this analysis, we determined several genera altered significantly in CRC patients including Ruminococcus, Fusobacterium, Acinetobacter, Bacteroides, Catenibacterium. Then we designed genera-specific primers and probes targeting the five selected gut microbiota-derived biomarkers and measured the abundance of these genera in stool samples using real-time PCR methodology with the primers and probes. Based on the results of real-time PCR analysis, we developed CRC risk assessment model using 3 bacterial biomarkers with age and sex as covariates. This model showed high accuracy and model strength with AUC value greater than 0.9. These results demonstrate that gut microbiota are a reliable source of biomarkers for colorectal disease and further study should validate these results in larger cohorts.

Key Words: Microbiome, Colorectal cancer

P-89

Comparison of Interferon-Gamma Release Assay and Tuberculin Skin Test for Screening of Tuberculosis among Korean Children and Adolescents

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Introduction: Despite the high Bacillus Calmette-Guerin vaccination coverage in South Korea, the tuberculin skin text (TST) is routinely recommended for tuberculosis (TB) screening among children whereas interferon-gamma release assay (IGRA) has emerged as a new screening tool. It is uncertain whether these two tests give concordant results.
Aims: The aim of this study was to evaluate the concordance between the results of the TST and the IGRA for TB screening among Korean children.
Method: Children aged less than 19 years who visited clinics for TB screening in The Catholic University of Korea, Seoul St. Mary's Hospital from April 1, 2009 until November 30, 2018 were retrospectively analyzed. The subjects underwent both the TST and the Quanti FERON-TB gold test. The exclusion criteria were: interval between tests over 120 days; unknown TST result; indeterminate IGRA result; and underlying non-TB disease. Diagnoses were made by attending physicians. TST induration greater than 10 mm was considered positive according to the Korean Guidelines for Tuberculosis.
Result: The overall agreement for the 118 included patients was 59%; 33% in under 2 years, 30% in 2-4-year-olds, 61% in 5-10-year-olds, and 65% in over 10 years. Comparing patients with and without TB-patient contact, agreement was 63% and 58%, respectively. It was 67%, 37%, and 67% in patients diagnosed as not having TB, and having latent tuberculosis infection (LTBI) and TB disease, respectively. Based on patients' TST induration, agreement was 95% at 0-9 mm, 13% at 10-14 mm, and 48% at over 15 mm.
Summary: Agreement between TST and IGRA in children was low, especially in children under 5 years, children without TB-patient contact, and those with LTBI and TST induration 10-14 mm.
Conclusion: There was poor concordance between TST and IGRA, particularly among children with LTBI and those with positive results in TST. This study indicates that TST should be interpreted with caution in these cases.

Key Words: Tuberculin test, Interferon-gamma release tests, Child

P-90

Effect of Addition of ICS with Conventional Therapy in Stable COPD with Higher Blood Eosinophil Count

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Purpose: COPD patients with increased airway eosinophilic inflammation show a favorable response to inhaled corticosteroids (ICS) in combination with a long-acting bronchodilator(LABA). Thus, this study investigated the effect of 3-months treatment with Inhaled Corticosteroid/long-acting beta2-agonist (LABA) in stable COPD patients with high blood eosinophils with an improvement in forced expiratory volume in 1 second (FEV_1) and quality of life.
Methods: It was a interventional study conducted at the OPD of National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka from which 80 stable COPD patients were selected. Baseline blood eosinophils level was measured of all patients and randomly assigned to 12-weeks treatment with Salmeterol/fluticasone proprionate inhaler (ICS/LABA) 25/250μg in group A and Salmeterol 25μg in group B. Subjects began 3-month ICS/LABA treatment after washout period. Objectives measurement of FEV_1 and subjective measurement of symptoms by COPD assessment test (CAT) score were done in initial visit and during follow up at 4^{th}, 8^{th} and 12^{th} week.
Results: In this study, mean FEV_1 change between group A (Salmeterol/fluticasone proprionate 25/250μg) and group B (Salmeterol 25μg) at 1^{st} visit was 11.9 ml, at 2^{nd} visit 13.04 ml and at final visit at 12^{th} week was 16.62 ml. All the differences were statistically significant ($p<0.001$). Mean COPD Assessment Test (CAT) score change between two group at 1^{st} visit was 1.53, at 2^{nd} visit 1.45 and at final visit was 2.06. Differences were statistically significant ($p<0.05$). So, mean FEV_1 gradually increases and CAT score decreases in consecutive 3 follow up than baseline record. Thus, COPD patients with eosinophilia, ICS-based therapy was associated with significant improvements in FEV_1 and CAT scores compared with bronchodilator (BD) therapy alone.
Conclusions: Treatment with ICS/LABA combination in stable COPD patients with high blood eosinophil count are associated with improved lung function and quality of life.

P-91

Development of COPD and Lung Cancer Diagnostic Models based on Metagenomic Analysis of Microbial Extracellular Vesicles in Serum

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Chronic obstructive pulmonary disease (COPD) is an emerging public health threat that aside from having a detrimental impact on quality of life, also increases the risk of lung cancer incidence and severity. Mounting evidence suggests that the microbiome, the total genetic content contributed by all microorganisms in our body, has tremendous influence on immune function and disease. Furthermore, recently interest in the role of microbial extracellular vesicles (EVs) in systemic microbiota activity has been rising. However, no previous studies have investigated the association of systemic microbial EV composition with COPD and lung cancer.
Here, we sought to develop predictive diagnostic models for COPD, lung cancer, and lung cancer risk in COPD patients based on serum microbial EV metagenomic analysis. We conducted 16S rDNA-based metagenomic analysis on microbial EVs isolated from the serum of 723 Korean male COPD, lung cancer, and healthy control serum samples in order to determine significantly altered taxa between groups. The COPD and lung cancer cohorts yielded a multitude of significantly altered taxa in comparison to the healthy control group as well as a variety of altered taxa between the two disease groups. We then developed COPD, lung cancer, and COPD-lung cancer diagnostic risk models utilizing 19, 32, and 22 bacterial EV biomarkers at the species and genus levels, respectively, with age as a covariate. All three models demonstrated high validity and diagnostic strength with AUC values ranging from 0.87 to 0.95.
In conclusion, the results of this study highlight the utility of microbial EVs as accurate, noninvasive markers of COPD and lung cancer risk. Further clinical study is required to determine the accuracy of the diagnostic risk models in larger cohorts at varying stages of disease progression.

Key Words: COPD, Lung cancer, Microbiome

P-92

An Association of Chronic cough with Exercise and Exposure to Mold in School-Aged Children

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Background: Chronic cough is one of the most common reasons for medical encounters in children. The aim of this study was to determine the prevalence and identify the risk and protective factors of chronic cough in school-aged children.
Methods: This cross-sectional study examined 1,259 children from the general pediatric population who were 7 to 13 years-old in Korea. The parents completed a chronic cough questionnaire that included questions regarding the characteristic, duration, and triggering factors of coughing and environment questionnaire and agreed with the skin prick test.
Results: The prevalence of chronic cough was 5.7% (n=72). The 1st and 2st grade of school children have a high prevalence than that of the 5st and 6st grade (6.8% vs 2.5%, P=0.030). There was no difference in gender, obesity, prenatal history between chronic cough and control groups (P>0.05). Children with asthma, allergic rhinitis, and sensitization to pollen were significant increased the prevalence of chronic cough (P<0.05). After adjustment for confounding factor including the asthma and aeroallergen sensitization, exposure to mold (aOR=1.988, 95% CI=1.168-3.383, P=0.011) and smoking (aOR=4.442, 95% CI=1.831-10.776, P=0.001) were associated with increased the risk of chronic cough, while exercise frequency was strongly decrease the risk of chronic cough (aOR=0.734, 95% CI=0.546-0.986, P=0.040).
Conclusion: The preventable factor of chronic cough in school-aged children is an exercise, but risk factors of it are exposure to smoking and mold and sensitization to pollen. Therefore, strategies to prevent and treat modifiable chronic cough risk and preventable factors in school-aged children should be tailored accordingly.

Key Words: Chronic cough, Mold, Exercise

P-93

The Deficiency of Vitamin D3 is Associated with Allergic Rhinitis and Sleep Problem

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Background: Sufficient sleep is essential for the physical growth, emotional stability, and maintenance of cognitive function in children. So sleep disturbance is an important disease that lowers the quality of life in children.
Objective: Sleep disturbance is well-known to be associated with allergic rhinitis (AR), but no study about an association between vitamin D3 levels and nasal volume in children.
Methods: We distributed the questionnaire, including the pediatric daytime sleepiness scale (PDSS) and questions related to sleep pattern, sleep satisfaction, and emotional state, to 615 students in grades 5-6 of elementary school. We investigated allergic sensitization with skin prick test, nasal volume with acoutic rhinometry, and the level of vitamin D3, ferritin, and Hb.
Results: There were 111 children (18.0%) with sleep disturbance. The level of vitamin D3 was associated with sleep disturbance (r=0.114, p=0.012). After adjusting gender, age, body mass, location, parental allergic history, prematurity, low birth weight, and AR, the quality of sleep was associated with increased level of vitamin D3 (aOR 0.939, 95% CI 0.895 to 0.985, p=0.009), and nasal volume (aOR 0.857, 95% CI 0.761 to 0.964, p=0.010). The quality of sleep was decreased in children with AR (aOR 1.642, 95% CI 1.023 to 2.636, p=0.040) and the level of vitamin D3 <20 ng/dL (aOR 1.776, 95% CI 1.071 to 2.945, p=0.026).
Conclusion: Vitamin D deficiency is associated with sleep disturbance in children, independent of AR and nasal volume.

Key Words: Vitamin D3, Allergic rhinitis, Sleep disturbance

P-94

Awareness of 119 (911) Rescue Team on Anaphylaxis and Asthma Exacerbations in Korea: Before and After the Education

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Background: Anaphylaxis and asthma exacerbation could be life-threatening medical emergency in allergy. 119 (911 in USA) rescue teams are at the forefront of such emergency conditions. Early recognition and proper prehospital managements by 119 rescuers is important.
We evaluated the awareness of 119 rescuers on anaphylaxis and asthma exacerbation in Korea.
Method: From May 17 to June 28, 2018, a total of 180 rescuers were recruited from Gyeonggi province, Korea. The 3-hour educational sessions on anaphylaxis and asthma exacerbation were provided by an allergy specialist including lectures and hands-on workshop on self-injectable epinephrine autoinjector. Questionnaire survey with the same content was done before and after education to assess the improvement of awareness. The questionnaire had three domains: anaphylaxis awareness, asthma awareness, and program satisfaction.
Results: After education, awareness score about anaphylaxis increased from an average of 3.1 to 5.5. Particularly, the effect of education on the use of epinephrine, the most crucial treatment for anaphylaxis, was greatest. The awareness score of asthma after education increased from an average of 21.3 to 25.1. The effect of education on treatment and management of asthma was greatest.
Conclusion: 119 rescuers could be the first persons at the forefront of anaphylaxis and asthma exacerbation. It is important to increase their awareness on anaphylaxis and asthma exacerbation. Simple educational activity can dramatically change the level of the awareness.

Key Words: Anaphylaxis, Asthma, 119 rescuers

P-95

The First Case Series of Cryopyrin-Associated Periodic Syndrome in Korea

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Cryopyrin-associated periodic syndrome (CAPS) is a hereditary autoinflammatory syndrome caused by mutations in NLRP3 (encoding cryopyrin), which presents with fever, fatigue, and arthralgia. However, thus far, there have been no reports of CAPS in Korea. Herein, we report 3 cases of CAPS for the first time in Korea. The first case, a 28-year-old man with recurrent urticaria, arthralgia, and fever induced by cold, all of which were observed in his father, showed elevated erythrocyte sedimentation rate and C-reactive protein. He exhibited a p.Gly303Asp variant of the NLPR3 gene. The second case, a 2-year-old girl who had recurrent urticaria, arthritis, and oral and genital ulcers, was positive for HLA B51 and a p.Glu569Lys mutation in exon 3 of the NLRP3 gene. Administration of anakinra greatly improved her symptoms. The third case, a 4-year-old boy who presented with recurrent urticaria, arthralgia, and fever, exhibited a p.Val72Met mutation in exon 1 of the NLRP3 gene. Administration of tocilizumab improved all of his symptoms. This small case series highlights that clinicians should consider CAPS and conduct genetic studies when arthralgia and fever are accompanied by urticaria in Korea.

Key Words: Cryopyrin-associated periodic syndromes, NLRP3 protein, Urticaria

P-96

Increased Platelet Activating Factor Levels in Chronic Spontaneous Urticaria Predicts Refractoriness to Antihistamine Treatment: An Observational Study

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Background: Platelet activating factor (PAF) is an endogenous, active phospholipid released from inflammatory cells, platelets, and endothelial cells, and is involved in the regulation of immune responses. The purpose of this study was to investigate relationships among clinical parameters, including urticaria severity and treatment responsiveness, and PAF and PAF-AH levels in sera from patients with chronic spontaneous urticaria (CSU).
Methods: Serum PAF and PAF-AH levels were measured by enzyme-linked immunosorbent assay in 283 CSU patients and 111 age- and sex-matched, healthy normal controls (NCs). Urticaria severity was evaluated by urticaria activity score over 7 days (UAS7). Within 3 months after measuring PAF levels, patients whose urticaria was not controlled by antihistamine treatment were classified as histamine receptor 1 antagonist (H1RA) non-responders.
Results: Serum PAF levels were significantly higher in CSU patients than in NCs (median 4368.9 [17.0-14768.3] vs. 3256.4 [27.1-13886.7] pg/ml, p=0.015), while serum PAF-AH levels were significantly lower in CSU patients (105.6 [2.6-296.4] vs. 125.7 [2.0-291.1] ng/ml, p=0.001). H1RA non-responders had higher levels of PAF (median 3804.5 [17.0-11716.3] vs. 5426.3 [53.1-14768.3], p<0.001) in their sera. A generalized linear model revealed that a higher UAS7 score (odds ratio 1.023, p=0.024) and a PAF level ≥ 5000 pg/ml (1.409, p<0.001) were significant predictors of a poor response to H1RA treatment.
Conclusions: Compared with NCs, CSU patients, particularly those with H1RA refractoriness, showed significant increases in serum PAF levels and decreases in PAF-AH. Therapies modulating PAF and PAF-AH levels could be effective in patients with CSU refractory to antihistamines.

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Key Words: Platelet activating factor, Platelet activating factor acetylhydrolase, Chronic spontaneous urticari

P-97

Cluster Analysis on Longitudinal Data of Patients with Chronic Urticaria

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Background: Despite increasing prevalence and impaired quality of life, little is known about the clinical course and predictors of the prognosis of chronic urticaria (CU).
Objective: We attempted to classify clusters in CU based on medication score for the initial 3 months. Finally, this study was aimed to investigate treatment duration and time to remission of CU according to the 4 clusters and to identify predictors of the remission.
Methods: In total, 4,552 patients (female 57.9% and mean age) with CU were included in this retrospective cohort study. K-medoid algorithm was used for clustering CU patients. Kaplan-Meier survival analysis with Cox regression were applied to identify predictors of CU remission.
Results: Four distinct clusters were identified: patients maintaining low disease activity (cluster 1, n=1786), those with medium-to-low disease activity (cluster 2, n=1031), with maintaining medium disease activity (cluster 3, n=1332), and with staying at the high disease activity (cluster 4, n=403). In the cluster 4, mean age, treatment duration, platelet counts, neutrophil to lymphocyte ratio, serum total IgE, and complements 3 and 4 levels were significantly increased compared with other 3 clusters. Mean time to remission was also quite different among the 4 clusters (8.81 vs 9.43 vs 11.32 vs 12.35 years, P<0.001). Together with clusters, eosinophil and sensitization of house dust mites (HDM) at least class 3 were identified as significant predictors of CU remission.
Conclusion: The present study demonstrates that 4 clusters in CU determined by the medication score during the initial 3 months, peripheral eosinophil and a strong sensitization against HDM are the major predictor of the CU remission.

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Key Words: Chronic urticaria, Cluster analysis, Natural course

P-98

Can We Expect Favorable Responses to Omalizumab in Cholinergic Urticaria?

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Background: Omalizumab, a monoclonal antibody against IgE, is a new therapeutic option of refractory chronic spontaneous urticaria. Omalizumab has been reported to be effective in various chronic inducible urticaria such as dermographism and cold urticaria. There have been few reports about the efficacy of omalizumab in patients with cholinergic urticaria.
Methods: A total of 27 patients with H1 antihistamine-refractory cholinergic urticaria who had been treated with omalizumab (8 weeks or more treatment period at doses of 150mg or 300mg) were enrolled from 3 University Hospitals. Clinical and laboratory data were reviewed retrospectively. Response to omalizumab was divided into three groups by patient global assessment; complete responder: absence of symptoms, partial responder: 50% or more improvement of symptoms; non-responder: less than 50% improvement of symptoms. Statistical analyses were performed using SPSS version 21 (SPSS Inc, Chicago, Illinois).
Results: Among 27 patients with omalizumab treatment, two patients (7.4%) were complete responders, 17 patients were partial responders (63.0%) and 8 patients were non responders (29.6%). Eight patients of 19 partial/complete responders (42.1%) were given omalizumab at dose of 300mg, while two of 8 non-responders (25.0%) was given at that dose. There were no significant differences in clinical characteristics such as sex, age, disease duration, presence of atopy, serum total IgE levels among the three groups.
Conclusion: About 70% of patients with cholinergic urticaria could respond partially or completely to omalizumab treatment, therefore, omalizumab can be a treatment option of H1 antihistamine-refractory cholinergic urticaria.

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Key Words: Cholinergic urticaria, Omalizumab

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Depression and Anxiety in Korean Patients with Chronic Urticaria

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Introduction: Chronic urticaria (CU) is a common and not life-threatening skin disease. It has been reported to have a substantial impact on psychological health. However, litter information is available about psychiatric comorbidities such as depression and anxiety in Korean CU patients. This study aimed to investigate the prevalence of depression and anxiety in Korean adult patients with CU and to explore potential impact on urticaria treatment.
Methods: The 79 patients with CU were prospectively recruited from four university hospitals in 2015 and 2017. The 29 patients with persistent asthma were used as disease controls. Psychiatric comorbidity was determined by the hospital Anxiety and Depression Scale (HADS). The level of stress by stress response inventory questionnaire and CU-specific quality of life (CU-QoL) were assessed. Demographic and clinical data such as urticaria activity score (UAC) were extracted.
Results: HADS score was 12.92±6.48 in all subjects with CU, and the prevalence of depression and anxiety based on the HADS were 48.1% and 38.0%, respectively. The prevalence of anxiety was not different when compared with asthma control (38.0% vs 41.0%), but depression was more prevalent in CU patients (48.1% vs 28.2%, P<0.039). Although depression was not associated with age, disease duration, and treatment status, it was more prevalent in female patients. Patients with depression tended to show worse CU-QOL with higher stress levels. The HADS score was significantly correlated with UAS, visual analogue score, CU-QOL, and stress level.
Conclusion: Our data confirm that CU patients frequently suffer from psychiatric comorbidities, especially depression. The parameter of depression and anxiety were associated with poor urticaria control and quality of life in Korean adult CU patients.

Key Words: Chronic urticaria, Depression, Anxiety

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Omalizumab Response in Patients with Chronic Spontaneuos Urticaria

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Purpose: Several reports have described the response of omalizumab in patients with chronic spontaneuos urticaria (CSU), however, clinical factors for the efficacy of omalizumab are not clearly known yet. We investigated determinants affecting the effect of omalizumab between the complete and incomplete response group.
Methods: We reviewed 118 CSU patients with treated omalizumab from January 2010 to December 2015 in Asan Medical Center. The median number of injections was four (mean: 6.4±5.1). One hundred eleven patients received 1 vial and 7 patients received 2 vials, each time. Thirty one patients (26%) were in complete remission (CR) group, which was defined as patients in absence of urticaria symptoms for at least four weeks without any medication. The primary outcome of this study was to find out which factors affect effect of omalizumab treatment.
Results: The mean age of overall patients was 45.6±14.8 years and median age was 45 years. There were 62 female patients (52.5%). Total IgE levels (p=0.154) and eosinophil counts in blood (p=0.449) did not differ significantly between in the CR group and in the non-CR group. The urticaria activity score (UAS, p=0.185) and rescue steroid dose (p=0.184) before omalizumab treatment did not differ significantly between the CR and non-CR group. The number of antihistamine prescribed before omalizumab treatment was significantly lower in the CR group than in the non-CR group (CR: 3.1±1.1, non-CR: 3.5±0.9, p=0.041). The mean days of response onset were 13.6±9.9 (range: 1-35) and did not differ significantly between two groups (p=0.803). The mean days of disease free interval after fourth injection was 19.9±33.2 (range: 0-144).
Conclusion: The number of antihistamine prescribed before omalizumab treatment affected response of omalizumab treatment in CIU patients. However, other factors such as total IgE, UAS and mean days of response onset had no influence on omalizumab response.

Key Words: Omalizumab, Chronic spontaneuos urticaria, Treatment response