592 Asthma In The Elderly: The Role Of Vitamin D
Dr. Michele Columbo, MD, FAAAAI1, Dr. Reynold A. Panettieri, Jr, MD2, Dr. Albert S. Rohr, MD, FAAAAI3; 1Asthma, Allergy and Immunology Specialists, Bryn Mawr, PA, 2University of Pennsylvania, Philadelphia, PA, 3Rohr and Columbo Asthma, Allergy and Immunology Specialists, Bryn Mawr, PA.

RATIONALE: Asthma in the elderly is poorly understood and vitamin D deficiency/insufficiency are very common in older individuals. We studied the role of vitamin D in stable elderly asthmatics.

METHODS: Thirty asthmatics, age 72.6±5.6 (mean±SD) were followed every 4 weeks for 12 weeks in the period November 1, 2012-March 31, 2013. During the study period they took 2,000 I.U. vitamin D daily. Serum 25-Hydroxyvitamin D and calcium were measured at baseline and study end. 18 were female, 26 atomic, Body Mass Index was 25.1±3.2, disease duration 36.4±21.1 years. At baseline 27 subjects were on inhaled steroids (414±306 mcg/day), 21 on long-acting bronchodilators. 13 on leukotriene antagonists. Data were analyzed by the unpaired, two-tailed Student’s t-test and Pearson correlation coefficient.

RESULTS: 27% of subjects were deficient and 47% insufficient in vitamin D at baseline. Vitamin D increased from 24.8±9.1 I.U. at baseline to 34.4±7.1 I.U. at study end (p<0.001). Calcium did not change significantly during the same period (9.59±0.3 and 9.55±0.4 mg/dl, respectively). The Asthma Control Test (ACT) score at baseline was 22.5±3.1, FEV1% was 69.9±16.3%, and neither changed at the end of the study (p>0.92), similar to the other spirometric values (p>0.53). No correlation was found between vitamin D and demographics (p>0.08), comorbidities (p>0.49), inhaled steroid dose (p>0.22), spirometric values (p>0.11), or ACT (p>0.24).

CONCLUSIONS: Stable elderly asthmatics very commonly have vitamin D deficiency/insufficiency. Vitamin D supplementation did not induce changes in spirometric values or ACT scores. Serum vitamin D levels were not associated with subjects’ demographics, comorbidities, treatment, symptoms, or spirometric values.

593 A Preliminary Randomized Controlled Trial:Educational Intervention For Treatment Of Hispanic and African American Adults With Asthma: Allergen Triggers, Peak Flow, and Spirometry
Reenal Patel, MD1, Josh Fogel, PhD2, Marianne Frieri, MD, PhD, FAAAAI3; 1UMDNJ, Newark, NJ, 2Nassau University Medical Center, East Meadow, NY, 3State University of NY @ Stony brook, Stony Brook, NY.

RATIONALE: Asthma can be better managed with an understanding of allergen triggers, peak flow, and spirometry. We compare allergen triggers, baseline and follow-up peak flow, and spirometry FEV1 and FEV25-75.

METHODS: Data were obtained from a preliminary randomized controlled trial of adult patients with asthma who received either targeted education (evidence-based educational pamphlets and tailored learning style; n=7) or standard education (medication review; n=7) or no education (n=7). Peak flow was measured both at baseline and at follow-up. Allergen triggers were measured with either skin prick or allergen-specific immunoglobulin E. Spirometry and FEV1 were compared with paired t-tests and allergens with the Fisher’s exact test.

RESULTS: FEV1 (M=75.1, SD=19.43) had significantly greater mean scores (p=0.001) than FEV25-75 (M=61.7, SD=22.25). Mean peak flow did not significantly differ between baseline and follow-up. Allergens did not significantly differ between the treatment and control groups. For the 6 perennial allergies, 4 had more than 25% (cockroach, D-farinae, D-pteronyssinus, and dog-dander). For the 11 seasonal allergens, 10 had allergy presence with allergy percentages ranging as high as 42.9% for mugwort and as high as 37.5% for June grass, maple, oak, and timothy grass.

CONCLUSIONS: Clinicians should consider use of educational interventions, identification of allergen triggers, and explanation of spirometry for their Hispanic and African American asthma patients to encourage greater adherence to treatment.
Comparison of Pre-and Post-Pubertal Gender Differences in Markers of Angiogenesis and Asthma Outcomes
Dr. Amy Thomas, MD1, Mark DeVries2, Mr. Christopher J. Tisler, MT3, Ms. Victoria Rajanamikkam4, Dr. James E. Gern, MD, FAAAAI5, Dr. Robert F. Lemanske, Jr, MD, FAAAAI5, Dr. Daniel J. Jackson, MD5, 1University of Wisconsin Hospitals and Clinics, Madison, WI, 2University of Wisconsin School of Medicine and Public Health, Madison, WI, 3University of Wisconsin Hospitals and Clinics, 4Pediatics, University of Wisconsin School of Medicine and Public Health, Madison, WI.

RATIONALE: Previous studies have demonstrated increased numbers of circulating endothelial progenitor cells (EPCs), defined as peripheral blood mononuclear cells (PBMCs) co-expressing CD34 and CD133, in adults with asthma. However, it is unknown whether EPCs are differentially expressed developmentally based upon gender, puberty, and/or asthma diagnosis.

METHODS: A subset (n=42) of children in the Childhood Origins of Asthma (COAST) study were selected for this pilot study based upon pubertal status, defined as Tanner stage 4 for males, and menarche for females. Pre- and post-pubertal PBMC samples from 26 females, and 16 males fulfilling these criteria were assessed using flow cytometry to identify the percentage of EPCs (CD34+/CD133+). Relationships among EPC numbers, gender, puberty, and asthma diagnosis were assessed.

RESULTS: Both pre- and post-puberty, females had significantly higher percentages of circulating EPCs (CD34+/CD133+) compared to males (pre-puberty: 0.060% vs 0.041%, p = 0.01; post-puberty: 0.062% vs. 0.031%, p = 0.0001). EPC percentages were not significantly higher in children with asthma vs. no asthma (pre-pubertal: 0.060% vs. 0.049%, p = 0.13; post-pubertal: 0.052% vs. 0.048%, p = 0.63). The percentage of circulating EPCs did not differ by asthma severity or the presence of aeroallergen sensitization.

CONCLUSIONS: Circulating EPCs were increased in females compared to males both pre- and post-puberty. In contrast to prior studies in adults, no differences in EPCs were seen in children with asthma. Prospective pubertal follow up in the COAST cohort will help determine if these differences persist or change with the expression and remission of asthma, as well as changes in severity of asthma based on gender and age.

Asthma Exacerbation In U.S. Adults: Who Are The Frequent Utilizers Of The Emergency Department?
Dr. Kohei Hasegawa, MD, MPH1, 2, Ashley Sullivan, MPH, MS3, Stuart Turner, BPharm, MPH1, Susan Masaros, PharmD, MPH1, Dr. Carlos Camargo, Jr, MD, DrPH1, 2, 1Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, 2Harvard Medical School, Boston, MA, 3Novartis Pharmaceuticals Corporation, East Hanover, NJ.

RATIONALE: Little is known about adults who frequently visit the emergency department (ED) for acute asthma. We aimed to characterize asthma patients according to frequency of ED visits in the past year.

METHODS: Multicenter chart review study of adults, age 18-54 years, presenting with acute asthma to 9 EDs across US in 2012. We classified subjects into 3 ED utilization groups based on the number of ED visits for asthma in the past year: no prior use, 1 ED visit, and 2+ ED visits.

RESULTS: The 229 patients were classified into three groups: 111 had no ED visits in the past year (48%), 60 with 1 visit (27%), and 58 with 2+ visits (25%). Frequent ED visits were associated with several markers of chronic asthma severity (history of systemic corticosteroid use, history of intubation for asthma, hospitalization for asthma in past year), and current asthma medications (inhaled corticosteroid, leukotriene modifiers) (all P<0.001). In a multivariable model, independent predictors for 2+ ED visits were older age, history of systemic corticosteroid use, and hospitalization for asthma in past year. Patients with 2+ ED visits accounted for 84% (95%CI, 80%-88%) of all ED visits for acute asthma in the past year.

CONCLUSIONS: In this multicenter study, patients with 2+ ED visits accounted for 25% of ED patients with acute asthma, but 84% of all ED visits in the past year. Frequent utilizers of the ED for acute asthma had several markers of worse chronic asthma severity. Integrated strategies aimed at reducing potentially-preventable asthma ED visits are warranted.

The Relationship Of The Serum Vitamin D Levels With Asthmatic Severity Responses In Asthmatic Children
Dr. Julio Orellana1, Dr. Telma Varela2, Dr. Ana Romero Boni3, Dr. Ofelia Miño4, Dr. Estela Pautasso5, Dr. Susana Rivolta5, Dr. Ramón Pogonza5, Dr. Juan Carlos Muino, MD, PhD, FAAAAI7, 1Nuevo Hospital de Niños de la Santísima Trinidad Córdoba Argentina, Córdoba, Argentina, 2Nuevo Hospital de Niños de la Santísima Trinidad Córdoba Argentina, Córdoba, Argentina, 3Nuevo Hospital de Niños de la Santísima Trinidad Córdoba Argentina - CIU, Córdoba, Argentina, 4FAC CS MED UNC, Cordoba, Argentina.

RATIONALE: Vitamin D has been found to have anti-inflammatory and immune-modulating effects, and it play a role in preventing asthmatic response. However, rigorous studies are needed before a conclusion can be made. The objective of this study was to determine the relationship between the serum Vitamin D levels and clinical asthmatic types.

METHODS: We studied 74 asthmatic children, aged from 5 to 15 who were admitted to the Children’s Hospital of Córdoba, Argentina. The group was divided into severe asthmatic responses (n: 51) (a) and mild to moderate asthmatic responses (n: 23) (b) in agreement with GINA and compared with healthy children (n: 21), sex and age matched, (controls) (c). We measured vitamin D levels by Roche electrochemiluminescence. Vitamin D levels were separated in: normal level ≥ 30 ng/ml, insufficient from ≥ 30 to ≥ 20 ng/ml and deficit < 19.9 ng/ml and in addition we determined the total serum IgE levels by ELISA.

RESULTS: Vitamin D levels were: in (a) 29±8.13 ng/ml, in (b) 31.32±10.4 ng/ml and in (c) 38.4±5.45 ng/ml p=0.0071. The patients (a) with normal level were 23, insufficient: 21, and deficient: 7; in group (b) normal 12, insufficient: 9 and deficient: 2 and the control group 21/21 presented normal level, p = 0.0007. The IgE levels were in (a) 508±361 kU/L, in (b) 319±300 kU/L p = 0.0346 and when compared with (c) 38±25 p<0.0001.

CONCLUSIONS: Insufficient and deficient vitamin D levels are present in asthmatics with and without hospitalization but low levels are predominant in severe asthmatic patients.
Newly Diagnosed Asthma In The Elderly: Is It Really Different?

Prof. Bilum Gemicioglu, MD, PhD1, Prof. Oznum Abadoglu, MD2, Dr. Levent Akylidiz, MD3, Prof. Hasan Bayram, MD, PhD4, Prof. Aysit Cilli, MD5, Prof. Arif Cinrin, MD6, Prof. Hakan Gunen, MD7, Prof. Zeynep Misirigil, MD8, Prof. Tevfik Oztu, MD9, Prof. Mecit Suerdem, MD10, Prof. Esra Uzaslan, MD11, 1Istanbul Univ. Cerrahpaşa Faculty of Medicine, Istanbul, Turkey, 2Cumhuriyet Univ. Faculty of Medicine, Sivas, Turkey, 3Mardin Medical Park Hospital, Mardin, Turkey, 4University of Gaziantep, Gaziantep, Turkey, 5Akdeniz Univ. Faculty of Medicine, Antalya, Turkey, 6Dokuz Eylul Univ. Faculty of Medicine, Izmir, Turkey, 7Sürekayapasa Pulmonary Diseases Hospital and Research Center, Istanbul, Turkey, 8Ankara Univ. Faculty of Medicine, Ankara, Turkey, 9Karadeniz Teknik Univ. Faculty of Medicine, Trabzon, Turkey, 10Selcuk Univ. Faculty of Medicine, Konya, Turkey, 11Bursa Univ. Faculty of Medicine, Bursa, Turkey.

RATIONALE: The objective of this study is to investigate the differences between elderly asthmatic patients (EA) and young asthmatics (YA) living in different areas of Turkey.

METHODS: A total of 1235 newly diagnosed adult asthmatic patients from 136 secondary or tertiary centers of different geographic locations took part in this study, and a standard questionnaire was applied from July 2012 to March 2013. Patients were divided in two groups as YA (age: 18-59) and EA (≥60). The differences in biometric parameters, pulmonary functions, allergic status, comorbidities, first given therapies were analyzed.

RESULTS: New onset asthma in the elderly is found 12%. Body mass index was found as 27.8 for YA and 29.4 for EA (p<0.01). Family asthma history was significantly higher in YA (36.8%) as compared to EA (18.7%) (p<0.001). FEV1% values were significantly lower in EA than YA (p<0.01). Atopy rate was found to be higher in YA than EA (49.1% vs 39.2%; p=0.059). The presence of any comorbidity was 63.2% and 51.3% in EA and YA, respectively (p<0.01). Hypertension, coronary disease, diabetes mellitus and gastritis coexisted in EA more frequently than YA (53.3%, 10%, 15.3% for EA and 8.4%, 1.8%, 4.3%, 5.2% forYA; p<0.001, <0.001, <0.001, p<0.02, respectively). High percentages of combined inhaled steroids with long acting bronchodilator and Fraction of Exhaled Nitric Oxide (FeNO) measurements were also analyzed.

CONCLUSIONS: High percentages of combined inhaled steroids with long acting beta2 agonists were used more frequently than YA (33.3%, 10%, 15.3%, 10% for EA and 8.4%, 1.8%, 5.2%, 10% for YA), (p<0.001). The presence of any comorbidity was 63.2% and 51.3% in EA and YA, respectively (p<0.01). There was vitamin D deficiency in more than half of the patients (between the serum vitamin D levels of 5-15 ng/ml) and 19 (23.5%) had insufficiency (between the serum vitamin D levels of 15-20 ng/ml). There was no significant relationship between vitamin D levels and serum total IgE, vitamin D deficiency (between 12.4ppb and 12.4ppb, p=0.196).

Serum Vitamin D Levels and Clinical Features Of The Disease In Children With Asthma Aged 5 –To 18 Years Old

Dr. Zeynep Tamay, MD1, Dr. Nurhan Ozcan2, Prof. Firdevs Bas3, Prof. Umit Turkoglu4, Prof. Nermin Guler, MD5, 1Associate Professor of Pediatrics, Istanbul University, Istanbul School of Medicine, Department of Pediatrics, Division of Pediatric Allergy, Istanbul, Turkey, 2Ege Medical Faculty, Department of Pediatrics, 3Istanbul University, Istanbul School of Medicine, Department of Pediatrics, 4Division of Pediatric Allergy, 5Istanbul University, Istanbul School of Medicine, Department of Pediatrics, Division of Biochemistry, 6Istanbul University, Istanbul School of Medicine, Department of Pediatrics, Division of Pediatric Allergy, Turkey.

RATIONALE: We aimed to investigate the relationship between 25(OH) vitamin D and clinical features of the disease in children with asthma.

METHODS: Eighty-one asthmatic children (35 female, 46 male), aged between 5-18 years were enrolled into the study. Clinical findings of asthma, family history of atopy, allergy skin prick tests (SPT), pulmonary function tests, serum total IgE levels, peripheral blood eosinophil percentage were recorded and, asthma control level was assessed both by physician and by patient/patient’s family. Blood samples were taken from all children for determination of vitamin D levels.

RESULTS: The mean of 25(OH) vitamin D serum levels was 17.9 ± 8.3 ng/ml. Of the patients, only one (1.2%) had severe vitamin D deficiency (<5 ng/ml), 32 (39.5%) had deficiency (between the serum vitamin D levels of 5-15 ng/ml) and 19 (23.5%) had insufficiency (between the serum vitamin D levels of 15-20 ng/ml). There was no significant relationship between vitamin D levels and serum total IgE, peripheral blood eosinophil percentage, SPT, patient’s treatment regimen and asthma control level. The risk of having more than one exacerbation was found to be significantly increased in patients with vitamin D deficiency (p=0.05).

CONCLUSIONS: There was vitamin D deficiency in more than half of the asthmatic children. While there was no significant relationship between vitamin D levels and asthma control level, the risk of having more than one asthma attack was significantly increased in asthmatics with low vitamin D levels. Asthmatic children with frequent attacks may be evaluated for vitamin D deficiency.
602 Effectiveness Of Specific Immunotherapy Against Alternaria Alternata In Patients With Asthma and Allergic Rhinitis

Dr. Silvia Martinez Blanco, MD1, Dr. Ana Antón-Laíseca, MD1, Dr. R. Mielgo Ballesteros, MD1, Dr. Consuelo Fernández Rodríguez, MD, PhD1, Dr. Ruth Barranco Jiménez, MD1, Dr. R. Vives Conesa, MD2, Hospital Universitario 12 de Octubre, Spain, Hospital Universitario 12 de Octubre, Madrid, Spain.

RATIONALE: To evaluate the clinical improvement of asthma and allergic rhinitis in patients receiving specific immunotherapy against Alternaria alternata in the period 2004-2011 in the Hospital Universitario 12 de Octubre.

METHODS: Clinical improvement of asthma and rhinitis in patients sensitized to A. alternata treated with specific immunotherapy (IT) was evaluated in a retrospective study. Thirty-six patients older than 15 years with asthma and/or rhinitis, positive SPT and specific IgE to A. alternata and who had received IT for at least 1 year were included. Effectiveness was evaluated by clinical parameters including number of exacerbations, hospitalizations and variation of medication.

RESULTS: The diagnoses reported were: asthma (13, 8%); occupational rhinitis (2.7%); and rhinitis associated with asthma (83.3%). Moderate persistent asthma was the most frequent diagnosis (91.4%). Before initiation of IT, 30.6% of patients were treated with LABA, inhaled corticosteroids and antileukotriens; 61.1% LABA and inhaled corticosteroids. One patient carried only inhaled corticosteroids only, and another nasal corticosteroids alone. After the start of the IT, 34/35 patients (97.1%) remained clinically stable without requiring emergency care or hospitalization, 32/34 (94.1%) managed to reduce their medication and 7/35 (20%) of them could remove. A patient with occupational rhinitis became asymptomatic after one year of IT.

CONCLUSIONS: Only one patient had bronchospasm that forced to stop IT. In the rest of the patients no adverse reaction was documented.

603 Vitamin D Levels As Related To Severity and Ethnicity In Asthmatics

Dr. Patricia H. Stewart, MD1, Dr. Thomas Pressley, PharmD2, Dr. Deborah Minor, PharmD2, Prof. Gailen D. Marshall, Jr, MD, PhD, FAAA1; 1University of Mississippi Medical Center, 2University of Mississippi Medical Center, Jackson, MS.

RATIONALE: Associations between Vitamin D (vD) levels, asthma severity and disease control have been reported. This study explored differences in vD levels between gender, age, race, and BMI matched asthma and hypertension (HTN) patients.

METHODS: A retrospective chart review yielded 69 asthma patients and 102 HTN patients from 2010 – 2013 with recorded 25-OH Vitamin D levels. Sixteen asthma patients were matched with HTN patients, after exclusion for inability to classify severity based on the documentation, presence of COPD, pregnancy, and current vD supplementation. Both severity and control of asthma were defined by NHBAL guidelines.

RESULTS: Mean ages: 50.9 yrs (asthma), 52.8 yrs (HTN); gender: 14 female (both); race: 50% African American (AA), 50% Caucasian (both). Mean 25-OH vD: 27.9 ng/mL (asthma), 35.1 ng/mL (HTN); p = 0.0498. AA asthma patients had significantly lower 25-OH vD levels than Caucasians (21.6 vs 34.4ng/dL, p = 0.0384) not seen in HTN patients (29.2 vs 41.1 ng/dL, p = 0.0607). Most importantly, asthma severity tended to correlate with vD levels (r = -0.4159, p = 0.1091) while HTN severity did not (r = 0.2486, p = 0.3531).

CONCLUSIONS: As previously reported AA patients have lower vD levels. Also asthma patients have lower vD levels than HTN patients. The racial differences in vD were greater in asthma compared to HTN. vD levels tended to inversely correlate with severity of asthma but not HTN. The role of vD deficiency in the AA community may be more of a direct concern in chronic diseases with an inflammatory component such as asthma.

604 Real Life Study Of Safety and Efficacy Of Subcutaneous Immunotherapy With Cat and Dog Extracts

Ms. Silvia Uriarte, Prof. Joaquin Sastre, MD, PhD, FAAAAI; Fundación Jiménez Díaz, Madrid, Spain.

RATIONALE: Direct or indirect contact with cat or dog can trigger symptoms of rhinitis or asthma in allergic patients, which could be improved with specific subcutaneous immunotherapy (SCIT).

METHODS: 16 patients with allergic rhinitis and/or asthma sensitized to cat or dog were included. SCIT with Alutard SQ®(ALK-abelló) extracts of cat or dog, in up-dosing phase using a pump infusion (MediInfus51®, Italy) followed by monthly injections, was administered. Molecular diagnosis and monitoring of adverse reactions to SCIT were performed. Validated questionnaires (ESPRINT-15, AQLQ, ACT) and respiratory function tests were done at 6 and 12 months.

RESULTS: Molecular diagnosis showed 82% sensitized to Fel d1, 9% Fel d2, 55% Fel d4, 18% none measured allergen, 27% were monosensitized to Fel d1 in the cat allergy patients; dog allergic patients 60% were sensitized to Can f 1, 40% Can f2, 20% Can f3, 60% Can f5, 40% were monosensitized to Can f5. 68 doses were administered in the up-dosing phase, 8.8% had late local reactions and 5.8% immediate systemic reactions. The spirometric values showed improvement at 6 and 12 months. FENO remained high in most of patients at 12 months in spite of clinical improvement. Analysis of the validated questionnaires of rhinitis and asthma showed significant clinical improvement at 6 and 12 months (ESPRINT-15 p <0.01, AQLQ p <0.01, ACT p <0.001), 5 patients were asymptomatic and 12 did not use medication at 12 months.

CONCLUSIONS: SCIT with Alutard SQ®(ALK-Abelló) from cat or dog has demonstrated clinical efficacy and can be considered safe.

605 Improvement In Quality Of Life In Parents Of Asthmatic Children Aged < 4 Years Receiving Subcutaneous Allergy Immunotherapy

Yurydia Jorge1, Yikania Pichardo1, Paola Polanco, MD2, Xin Zheng, PhD2, Jose Adames, BS1, Dr. Andrew A. Wiznia, MD2, Dr. David L. Rosenstrech, MD, FAAAAI1, Dr. Gabriele De Vos, MD2,1Jacobi Medical Center, New York, NY, 3Jacobi Medical Center, 1Albert Einstein College of Medicine, 2Albert Einstein/Montefiore Medical Center, Bronx, NY, 3Albert Einstein College of Medicine, Bronx, NY.

RATIONALE: Subcutaneous allergy immunotherapy (SCIT) can improve quality of life (QOL). However, its effect on young children and the QOL of their caretakers is unknown. The aim of this study was to compare the QOL of parents of inner-city children aged < 4 years receiving SCIT versus parents of children receiving standard asthma care.

METHODS: A preliminary analysis of an ongoing clinical trial of SCIT efficacy in children < 4 years of age was conducted. Inner-city children with recurrent wheeze, atopy and eczema and/or parental history of asthma were randomized to receive SCIT (n = 26) or standard asthma care (n = 22). The Pediatric asthma caregiver’s quality of life questionnaire (PACQOL) was administered at each 2-monthly study visit. The results were analyzed using linear mixed effect models.

RESULTS: A total of 400 PACQOL questionnaires during a study period of 2 years were analyzed. The median age at study entry was 36 months (IQR 26. 44 months). After adjusting for age, sex and number of asthma related ER visits prior to enrollment, parents of children receiving SCIT indicated significant improvement in their overall QOL score. Both, activity related domains (p = 0.05) and emotional impact (p = 0.08) was rated with greater improvement in the treatment group compared to the control group.

CONCLUSIONS: Parents of atopic, asthmatic inner city children aged < 4 years receiving SCIT experience subjective improvement in QOL compared to parents of children not receiving SCIT. It has yet to be determined if this effect is related to an objective treatment effect on the children’s asthma severity.

All abstracts are strictly embargoed until the date of presentation at the 2014 Annual Meeting.
606
Ashmi Suppresses Neutrophil Pulmonary Inflammation In A Ragweed Allergic Asthma Model That Is Associated With Modulation Of Innate and Adaptive Immune Responses
Dr. Kamal D. Srivastava, PhD1, Dr. David Dunkin, MD2, Dr. Nan Yang, PhD, MS1, Dr. Changda Liu, PhD1, Dr. Rachel L. Miller, MD, FAxAA1, Dr. Xiu-Min Li, MD3, 1Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, 2Icahn School of Medicine at Mount Sinai, New York, NY. 3Division of Pulmonary, Allergy and Critical Care Medicine, Columbia University, New York, NY.

RATIONALE: Asthma is a heterogeneous inflammatory disease. Unlike for eosinophilic airway inflammation, there is no effective treatment for neutrophil dominant airway inflammation in which TNF-α, the key mediator is up-regulated by NF-kB. Histone deacetylase 2 (HDAC2) negatively regulates NF-kB activation. ASHMI abrogates eosinophilic inflammation in murine allergic asthma models, but its effect on neutrophil predominant airway inflammation is unknown. We sought to determine the effects of standard ASHMI and refined ASHMI on a ragweed allergy neutrophil predominant murine model of asthma and explore the pharmacoeutical mechanisms.

METHODS: Systemically sensitized BALB/c mice were intranasally challenged with RW, then treated with ASHMI, ASHMI or sham treatment and re-challenged 4 weeks later. Airway hyperreactivity (AHR), total and differential bronchoalveolar lavage fluid (BALF) cell counts, lung histology, BALF cytokine and chemokine levels were assessed. Effects of ganoderic acid C1, isolated from Ganoderma lucidum, an ASHMI constituent that inhibits TNF-α synthesis, on ragweed stimulated murine macrophage phosphorylated IkB (pIkB) and HDAC2 expression were also determined.

RESULTS: Both forms of ASHMI markedly reduced AHR (P<0.01), neutrophil as well as eosinophil inflammation, mucus production, BALF IL-4, IL-5, IL-13 and eotaxin (P<0.05-0.001), TNF-α, IL-8 and IL-17 levels (P<0.01-0.001) levels. Ganoderic acid C1, inhibited ragweed induced TNF-α production and pIkB expression, but increased HDAC2 expression.

CONCLUSIONS: This is the first demonstration that ASHMI therapy is effective in neutrophil dominant pulmonary inflammation in asthma model, and modulates the NF-kB activation pathway, suggesting that it may be a valuable option for treating neutrophil dominant asthma.

607
Longitudinal Characteristics Of Viral and Non-Viral Exacerbations Of Childhood Asthma
Dr. Amaziah Coleman, MD1, Dr. Daniel J. Jackson, MD2, Dr. Ronald E. Gangnon, PhD1, Mr. Michael D. Evans, MS1, Dr. Robert F. Lemanske, Jr, MD, FAxAA1, Dr. James E. Gern, MD, FAxAA1, 1University of Wisconsin School of Medicine and Public Health, Madison, WI, 2Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI.

RATIONALE: Asthma exacerbations secondary to viral illnesses are a known cause of morbidity among children with asthma. Longitudinal characteristics of viral and non-viral exacerbations among children with asthma have not been completely defined.

METHODS: Of the 259 children followed prospectively from birth to adolescence in the Childhood Origins of ASThma (COAST) study, 102 met criteria for asthma at age 6 or 11 years. Nasal samples were analyzed for respiratory viruses during exacerbations and for longitudinal patterns and risk factors for viral versus non-viral exacerbations.

RESULTS: Among the children with asthma, 62 (60%) reported at least one exacerbation; 47 (76%) had <3 exacerbations, and 15 (26%) had ≥3. The number of exacerbations was positively associated with total IgE at age 6 (p=0.009 and 0.02 respectively) and aeroallergen sensitization at age 11 (p=0.008). Virology was available for 192 of 219 exacerbations, and viruses were identified in 132/192 (69%) exacerbations. Of the 55 children who provided at least one nasal sample during an exacerbation, 42 (76%) had at least one viral exacerbation. When etiology was considered, viral exacerbations were positively associated with higher total IgE at age 6 (p=0.04) and aeroallergen sensitization at age 11 (p=0.03), and non-viral exacerbations were positively associated with higher total IgE at age 6 (p=0.04) and sensitization at age 11 (trend, p=0.11).

CONCLUSIONS: In this five-year longitudinal analysis of children with asthma, most children who had exacerbations were susceptible to viral respiratory infections. Indicators of atopy were important risk factors for both viral and non-viral exacerbations.

608
Bronchial Epithelial Cell Gene Expression In Relation To Exhaled Nitric Oxide Identifies New Molecular Asthma Phenotypes
Dr. Brian D. Modena, MD1, Dr. John Tedrow, MD3, Dr. Jadranka Milosevic, PhD1, Dr. Nafitali Kamiinski, MD3, Sally E. Wenzel, MD, FAxAA1, 1University of Pittsburgh Medical Center NW, Pittsburgh, PA, 2Yale-New Haven Hospital, New Haven, CT.

RATIONALE: Studies suggest exhaled nitric oxide (FeNO) associates with airway inflammation and inhaled corticosteroid responsiveness in some asthmatics. Yet, elevation in FeNO associates with a large range of clinical characteristics, limiting its use in predicting phenotypes. We hypothesized that airway epithelial gene expression in relation to FeNO would cluster asthmatics with distinct clinical characteristics and molecular phenotypes, potentially enhancing the biomarker utility of FeNO.

METHODS: RNA from epithelial brushings of 116 asthmatics and healthy controls (HC) of the Severe Asthma Research Network (SARP) identified genes that correlate with FeNO (false discovery rate <0.05). Uncentered, unsupervised hierarchical clustering clustered samples. A smaller cohort (n=41) was used to validate.

RESULTS: Five clusters (3 with high and 2 with low FeNO values) were identified with distinct clinical and genotypic characteristics. The 3 FeNO-High clusters include (1) a large, atopic, asthmatic cluster (>50% severe), (2) a much less severe cluster with less atopy, and (3) a severe cluster with blood and BAL neutrophilia. These three clusters are unique with differences in mast cell-, eosinophil-, and neutrophil-related genes, along with oxidative stress and epithelial repair pathways. The 2 FeNO-Low clusters also differ clinically, one containing 58% of HC, and the other over 40% moderate to severe, less atopic asthma. The two clusters manifest differences in innate immunity and epithelial repair genes. Similar results were found in the validation cohort.

CONCLUSIONS: Despite similar FeNO, clinical characteristics and accompanying gene expression can identify five potential molecular phenotypes. Understanding these biologic differences should provide mechanistic insight into this heterogeneous disease.
How Common Is The Phenotype Reflected By "The Atopic March"? Results At Two Years Of Age In a General Risk Multi-Racial Birth Cohort

Dr. Christine Cole Johnson, PhD, MPH, FAAAAAI, Ms. Suzanne Havstad, MA1, Dr. Dennis Ownby, MD, FAAAAAI, Dr. Christine L. M. Joseph, PhD1, Dr. Haejin Kim, MD1, Kimberley J. Woodcroft, PhD1, Dr. Edward M. Zorati, MD, FAAAAAI1, Ganesa Wegienka, PhD1, 1Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, 2Department of Pediatrics Georgia Regents University, Augusta, GA, 3Division of Allergy and Clinical Immunology, Henry Ford Hospital, Detroit, MI, 4Henry Ford Health System, Detroit, MI.

Rationale: The "atopic march" hypothesis proposes an allergic disease phenotype that progresses from atopic dermatitis and food allergy in infancy to asthma with inhalant allergies and allergic rhinitis in childhood. We evaluated phenotype characteristics in a Detroit area general risk multi-racial birth cohort, WHEALS, at age 2 years, for early evidence supporting the atopic march theory.

Methods: Parents of children enrolled in WHEALS were interviewed and the children examined, at age 2 years, for report of a history of wheeze and for atopic dermatitis (AD), in addition to having specific IgE measured to peanut, milk, and egg. Race was reported as either African American (AA) or Caucasian (CA).

Results: Of 450 children, 301 were AA and 149 were CA. For AA, 71.8% had one or more outcomes versus 50.3% for CAs. All outcomes were more common in AA with 33.9% reporting wheeze, 28.9% atopic dermatitis and 46.5% having food-allergen specific IgE vs. 28.2%, 13.4% and 30.2% in CA. Only 6.0% of the AA children had all three outcomes; this outcome overlap was even less among CAs at 3.4%. While 227 AA had either AD or food-specific IgE, only 14.1% (32) of them had both, while 6.2% of CAs had both (4/65).

Conclusions: In the WHEALS birth cohort, overlap of AD and food sensitization, and these two outcomes with wheeze, was infrequent in both AA and CA children at age 2 years. This lack of overlap suggests that the atopic march phenotype, if it exists, is relatively uncommon and may differ by race.

Is Asthma Predictive Index Feasible For A Retrospective Study?

Dr. Chung I. Wi, MD1, Dr. Miguel A. Park, MD2, Dr. Young J. Juhn, MD, MPH1, 1Dept of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN, 2Department of Internal Medicine: Division of Allergic Diseases, Mayo Clinic, Rochester, MN.

Rationale: Asthma Predictive Index (API) has been used for predicting asthma in prospective or cross-sectional studies, not for a retrospective study. We assessed feasibility and validity of applying API to a retrospective study.

Methods: This is a cross-sectional study based on a convenience sample of children who participated in a previous cohort study. API was operationalized by 2 or more wheezing episodes in a year during the first 3 years of life PLUS one of the major or two of the minor criteria of the original API. We assessed validity of retrospective API against Predetermined Asthma Criteria which has been extensively used in clinical studies for asthma. We assessed criterion validity by measuring kappa and agreement rate between API and predetermined asthma criteria and construct validity by determining associations of API with known risk factors for asthma.

Results: Of the eligible 105 children, 55 (52.4%) were male, 90 (85.7%) Caucasians, and the mean age (±SD) was 5.8 years (±1.4). API criteria was met by 15 (14.3%), compared to 22.9% by Predetermined Asthma Criteria, respectively. The agreement rate and kappa between API and definite asthma of Predetermined Asthma Criteria were 89.5% and 0.66 (p=0.01). Atopic conditions, lower parental education, no history of breastfeeding, and family history of asthma were significantly associated with risk of asthma by retrospective API.

Conclusions: Application of API to retrospective study for ascertaining asthma status is feasible and may be suitable. Our study findings need to be replicated by future studies with a larger sample size.

Comparison Of Rates Of Prescribing Oral Corticosteroids For Asthma Exacerbations Between Step-Down Therapy Approaches Among Initiators Of Inhaled Corticosteroids and Long-Acting Beta-Agonist Combination Therapy

Ayad K. Ali, PhD1,2, Almut Winterstein, PhD2, Leslie Hendeles, PharmD2, Xiaomin Lu, PhD3, Richard Segal, PhD2, Abraham Hartzema, PhD2, 1Eli Lilly and Company, Indianapolis, IN, 2College of Pharmacy, University of Florida, Gainesville, FL, 3College of Public Health and Health Professions, College of Medicine, University of Florida, Gainesville, FL.

Rationale: The FDA recommends long-acting beta-agonists (LABA) discontinuation when asthma is controlled on inhaled corticosteroids (ICS)/LABA combination therapy, but asthma specialists disagree. This study aims to compare rates of prescribing oral corticosteroids (OCS) for asthma exacerbations as a method of evaluating the consequences of step-down therapy.

Methods: A cohort study of individuals with asthma (13-65 years) was conducted utilizing the UK Clinical Practice Research Datalink. Time-dependent Cox regression models were used to estimate the association between step-down therapy approaches and prescribing OCS. Initiators of ICS/LABA were followed for ≥3 months until ICS dose reduction while on combination therapy (50% of original dose), LABA discontinuation (maintaining original ICS dose), or continuing combination therapy with original ICS dose. Prescribing OCS was measured over 12 months following step-down start date.

Results: Among 3,226 patients who initiated ICS/LABA, 78% were on single-dosage form and 22% were on separate-dosage forms. 14% continued original-strength ICS/LABA, 27% reduced ICS dose plus LABA continuation, and 59% discontinued LABA and continued original-strength ICS monotherapy. Compared to continuing original-dose ICS/LABA combination therapy, reducing ICS/LABA dose was associated with less likelihood of prescribing OCS (HR=0.71; 95%CI=0.60-0.90) and discontinuing LABA and maintaining original ICS dose was not associated with prescribing OCS (HR=0.32; 95%CI=0.06-0.50). Compared to reduced-strength ICS/LABA combination therapy, discontinuing LABA and continuing original-dose ICS monotherapy was associated with 65% reduced risk of prescribing OCS (HR=0.35; 95% CI=0.06-0.51).

Conclusions: Step-down therapy approaches by LABA discontinuation or ICS dose reduction while on ICS/LABA combination therapy are associated with significant reduction in prescribing OCS for asthma exacerbations.
**Rationale:** We surveyed physician's attitudes towards the EPR3 guidelines regarding their adherence when managing patients and physician opinions on what aspects of the guidelines need to be improved.

**Methods:** The AAAAI-Asthma Diagnosis and Treatment committee conducted the survey. It was distributed to 6000 members of the AAAAI. We received 812 responses (769 allergists and 43 physicians from other specialties). The average years in practice for all physicians including all specialties were 19 +/- 12 years. The physicians were in private practice and were in practice longer compared to academic physicians.

**Results:** 40.7% of physicians from all specialties state they always follow the guidelines. 45.9% of allergists in academic practice follow the guidelines compared to 37.1% of allergists in private practice and there was no significant difference between new vs established physicians. Academic allergists believe that the guidelines are more practical then private physicians. More than 50% of allergists agreed guidelines should be changed and were physicians that were in practice longer than 5 years.

**Conclusions:** The emerging themes for changes to the guidelines need to reflect current evidence-based practices and need to be more concise. The addition of different patterns of ICS use and the use of LABAs in earlier steps to establish control should be addressed. More objective evidence including addition of biomarkers and personalize treatment according to different phenotypes. There needs to be changes in the step paradigm to include seasonal or intermittent symptom treatment. By addressing these issues more exhaustive approaches to improve guidelines can be done to improve care and outcomes.

**Fibrin Complexes From The Sputum Of Human Asthmatics Contain Viable Fungi**

**Rationale:** A link between severe asthma and fungi has long been known, but the fundamental basis of this relationship remains unclear. We have shown that fungal proteases induce asthma-like disease in mice by cleaving fibrinogen to create fibrinogen cleavage products that signal through Toll-like receptor 4. Fibrinogen cleavage in asthma is also seen, suggesting that fibrinogen is essential to the asthmatic response. To further define the importance of fibrinogen cleavage in asthma, we investigated the sputum of patients with severe asthma to determine if fibrin is present, and its physiological significance.

**Methods:** Spontaneously produced sputum samples were obtained from 41 severe asthmatic patients. Insoluble material from sputum was cultured for fungi. Four samples were also treated with the fibrin-degrading protease plasmin. Western blot analysis for the D-dimer antigen was then performed.

**Results:** 92.7% of sputa were positive for fungal growth. All samples contained insoluble matter which was solubilized following treatment with plasmin. All samples were positive for the D-dimer antigen.

**Conclusions:**
- Using our new culture technique, fungi can be reliably cultured from the vast majority of sputum samples from asthmatics.
- Fibrin may universally exist in the sputum of severe asthmatics as insoluble aggregates.
- Fibrin complexes produced in the airways may trap fungi to facilitate their clearance as part of an elaborate antifungal defense mechanism.
- Our findings add to the growing body of literature that supports airway surface mycotic infection as a contributing factor in severe asthma.
- We also provide further evidence of activation of the coagulation cascade in asthma.

**Proteomic Identification Of S100A8 As A Potential Effector Protein Of Acupuncture In Asthma Treatment**

**Rationale:** The beneficial effects of acupuncture for asthma have been well documented. A proteomic study based on the effectiveness of acupuncture could reveal the molecular basis of acupuncture and identify new therapeutic targets for asthma.

**Methods:** Asthmatic rats (AS group, n = 12) were sensitized and challenged with ovalbumin. Manual acupuncture was performed on asthmatic rats (AC group, n = 12) with acupoints GV14, BL12 and BL13 once every other day for two weeks. Respiratory function measurement was done to assess the effectiveness of acupuncture. Proteomic profile of rat lung tissue was examined using two-dimensional electrophoresis and mass spectrometry. The differentially expressed protein S100A8 was subsequently cloned to obtain purified recombinant protein. The effects of S100A8 on proliferation and migration of rat airway smooth muscle cells (ASMCs) were detected using WST-1 assay and Boyden chamber assay.

**Results:** Pulmonary resistance was significantly decreased 2 to 5 min after ovalbumin challenge in AC group comparing with AS group (P < 0.05). 2DE gels revealed 32 acupuncture-specific differentially expressed protein spots after treatment. MALDI-TOF-MS identified S100A8 as one of the most prominently regulated proteins in acupuncture-treated rats. Its expression pattern was confirmed by western blotting and RTPCR. In rat ASMCs, recombinant S100A8 protein promoted cell proliferation and migration in dose-dependent (0.05, 0.1, 0.5, 1, 5, 10, 50 μg/ml) and time-dependent (12, 24, 48 h) manner.

**Conclusions:** The proteomic profile of asthma could be significantly regulated by acupuncture. S100A8 was considered to be one of potential effector proteins of acupuncture, which may be a new therapeutic target for asthma.

**Are Asthma Specialists and Non-Specialists Familiar With Inhaled Corticosteroid (ICS) Dosing Recommendations and Side Effects In Children With Asthma?**

**Rationale:** ICS are routinely recommended and used to treat asthma in children and dosing recommendations and side effects are well-documented in FDA-approved package labels and NHLBI asthma guidelines.

**Methods:** A case of suspected asthma in a 6 year-old child and didactic lectures were presented to attendees of the 2012 Nemacolin Asthma Conference (NAC, n = 46, 62% asthma specialists) and the 2013 Pittsburgh Asthma Summit (PAS, n = 101, 4% asthma specialists). Responses to the same questions were gathered using anonymous audience response devices.

**Results:** Most respondents were not confident in their ability to detect growth and adrenal suppression (71% NAC, 94% PAS). Although fluticasone was identified as the ICS most-commonly used to treat asthma in children (60% NAC, 39% PAS), most were unfamiliar with the FDA-approved dose for children (66% NAC, 78% PAS) and the NHLBI guideline-recommended medium-dose range for children (93% NAC, 73% PAS). Wide variation in making the diagnosis of asthma in a child was also evident. There was evidence that education about growth and adrenal suppression was effective for both audiences.

**Conclusions:** These findings illustrate the lack of familiarity of both asthma specialists and non-specialists with FDA and NHLBI guideline dosing recommendations and side effects of the ICS they use the most and highlight the need for education and dissemination of these sources of valuable information.
616 Medication Remaining In Discarded Metered Dose Inhalers Of Asthmatic Children

Dr. Wantida Damparnrat, MD1, Dr. Pasurree Sangsupawanich, MD2, Dr. Araya Yuengyongviwat, MD1, 1Prince Of Songkla University, Hatyai, Thailand, 2Prince Songkla University, Songkla, Thailand.

RATIONALE: Currently available metered dose inhalers (MDIs) do not track the remaining number of doses. Therefore, we assume that asthmatic children use their controller MDIs regularly and we estimate the time that MDIs should be discarded is the discard point labeled on the canister and box to prevent the use of empty MDIs. However, we hypothesized that some medication remained in the discarded MDIs.

METHODS: Fluticasone propionate and budesonide were the controller MDIs used in this study. Children with asthma symptoms had a regular schedule to replace controller MDIs according to the discard point labeled on the canister. We asked asthmatic children attending our clinic from September 2012 to June 2013 to collect their discarded controller MDIs. The remaining medication in each discarded MDI was calculated from the canister weight.

RESULTS: Forty discarded MDIs were collected from 22 asthmatic children. Twenty one discarded MDIs belonged to controlled asthmatic children and all of them were used until nearly empty (>95% of labeled dose). Eight discarded MDIs(42%) which belonged to uncontrolled asthmatic children had remaining medication more than 30% of the labeled doses. Medication remaining in discarded MDIs of uncontrolled asthmatic children was unpredictable (median 15%, labeled dose range 0%–74%).

CONCLUSIONS: Nearly half of discarded MDIs of uncontrolled asthmatic children had remaining medication more than 30% of the labeled doses. Canister weight is a useful and reliable method to track a patient’s medication supply. This procedure should be implemented into the health care system to prevent discard of unused medication.

617 Defining Severe Asthma In Childhood: A Descriptive Multicenter Study In Turkey

Bulent Enis Sekerel1, Dr. Ozge Soyier2, Fatih Celmeli3, Yakup Canitez3, Ozlem Keskin1, Demet Can1, Ferhat Catal1, Mehtap Kiliar1, Burcin Nalbantoglu1, Nail Yolgoz1, Suleyman T. Yilmaz2, Belgin Gic3, Fadil Ozturk1, Gulbin Karakoc1, Suna Asliso1, Mehmet Kiliar3, Cem Razi3, Dost Zeyrek3, Semanur Kuyucu3, Hasan Yuksel3, Omer Cevit3, Ayse Bingol3, Mehtap G. Yazicioglu3, Ayse Yenigun3, 1Hacettepe University, Pediatric Allergy Unit, Ankara, Turkey, 2Hacettepe University School of Medicine, Ankara, Turkey, 3TURPESAS, Turkey.

RATIONALE: Severe asthma causes significant burden in terms of morbidity and healthcare resource use. Moreover, it is a heterogeneous disease creating difficulty in discrimination/classification.

METHODS: In order to define characteristics of children having high level of asthma treatment and burden, 23 asthma centers of the country recorded patients during one year period. 372 children with asthma were allocated and from those who fit either Severe Asthma Research Program (SARP) or Problematic Severe Asthma (PSA) criteria were defined as severe asthma and the remainder served as controls.

RESULTS: According to the criteria of PSA and SARP, 135 and 77 were classified as severe asthma, respectively and majority of the latter group appeared to be a subgroup of PSA. Compared to control group (n=232, moderate asthma), patients in severe asthma group had higher school absenteeism, unscheduled healthcare resource use, admission to an emergency unit, hospitalizations and systemic corticosteroid use within last year and had lower scores for ACT/C-Act and FEV1 (p<0.05). Patients classified as both PSA/SARP were younger than the patients classified only as PSA and had higher unscheduled healthcare resource use of Songkla University, Songkla, Thailand.

CONCLUSIONS: Children with severe asthma have significantly higher burden compared those with moderate asthma. The use of criteria of PSA for severe asthma causes inclusion of more patients compared the definition of SARP indicating the employment of a wider spectrum for the definition. The utility and value of definitions for severe asthma need to be further determined prospectively.
620 Safety and Efficacy Of Biweekly Hizentra® Administration in Patients With Primary Immunodeficiency Diseases: A Retrospective Single-Center Study

Clare Malcolmon, Dr. Alison Jones; Great Ormond Street Hospital, London, United Kingdom.

RATIONALE: Patients with primary immunodeficiency diseases (PID) require life-long immunoglobulin replacement therapy. Conveniently, subcutaneous IgG (SCIG) can be self-administered at home. This study retrospectively evaluated the safety and efficacy of biweekly (Q2W) administration of a 20% SCIG (Hizentra®) in clinical practice.

METHODS: Children and adults with PID received their first one or two doses of Hizentra® in hospital, and subsequent doses at home. Safety and efficacy data were based on measurements made during clinic visits and retrospectively collected feedback, and analyzed using descriptive statistics.

RESULTS: 54 patients (75.9% male, median age [range] 7.8 [1–18.8] years) received Hizentra® weekly (n=30), biweekly (n=22) or once every 10 days (n=2). Total monthly Hizentra® doses were similar in the biweekly and weekly groups (mean [SD] 674.8 [166.9] versus 662.7 [174.8] mg/kg, respectively). Despite baseline age differences between biweekly and weekly groups (median age [range] 3.2 [1–10.9] versus 12.3 [3.5–18.8] years, respectively), on-treatment trough serum IgG levels were similar (mean [SD]: 10.5 [2.8] versus 12.2 [3.4] g/L, respectively). Among 37 patients analyzed for safety, treatment-related adverse events were rare: 7/14 [50%]; 2/21 were rare, with no serious adverse events. Median observation periods were 9.5 and 10 months (biweekly and weekly groups, respectively).

CONCLUSIONS: In this population, the efficacy and safety profile of biweekly Hizentra® administration was comparable to that of weekly administration. Flexibility offered by weekly or biweekly Hizentra® administration schedules allows patients to adapt therapy to their lifestyle; these alternatives should be considered by physicians. Young children, who require smaller doses, could particularly benefit from less frequent biweekly injections.

621 Long-Term Tolerance and Safety Of Facilitated-Subcutaneous Infusion Of Human Immune Globulin G (IgG), 10%, and Recombinant Human Hyaluronidase (rHuPH20) (IGHy): A Phase 3 Extension Study In Patients With Primary Immunodeficiencies (PIs)

Dr. Isaac Reuven Melamed, MD1, Dr. Richard L. Wasserman, MD, PhD, FAAAAI2, Dr. Mark Stein, MD, FAAAAI3, Dr. Arye Rubinstein, MD, FAAAAI4, Dr. Jennifer M. Puck, MD5, Sudhir Gupta, MD, PhD, FAAAAI6, Werner Engl1, Dr. Heinz Leibl, PhD7, Dr. Leman Yel, MD, FAAAAI8, Dr. Richard I. Schif, MD, PhD9; IMMUNOHeath Centers, Centennial, CO, 2Dallas/AllergyImmunology, Dallas, TX, 3Allergy Associates of the Palm Beaches, North Palm Beach, FL, 4Albert Einstein College of Medicine, Bronx, NY, 5Department of Pediatrics, University of California San Francisco and UCSF Benioff Children’s Hospital, San Francisco, CA, 6University of California, Irvine, Irvine, CA, 7Baxter BioScience, Vienna, Austria, 8Baxter BioScience, Westlake Village, CA.

RATIONALE: In a phase 3 trial of IgHy in PI patients, rHuPH20 permitted mostly single-site infusion (every 3-4 week IgG dosing) with bioavailability/infusion rates comparable to intravenously administered IgG. We will report the final analysis of the long-term extension of the phase 3 study, with a duration of up to 3 years of treatment plus follow-up.

METHODS: Sixty-six patients completing the phase 3 study enrolled in the extension study. Patients continued their pre-study IGHy dose/ frequency every 3-4 weeks. After 3 months, some patients switched to 2-week dosing to evaluate effects of shorter IGHy interval on trough IgG levels. From an interim analysis in April 2012, tolerability/safety after up to 3 years of treatment were evaluated. The IGHy study was followed by a 24-48 week observation period.

RESULTS: Forty-nine patients completed the study. No patients withdrew due to drug-related reactions (ADRs). At interim analysis, no serious ADRs were reported. Systemic ADRs/infusion rate=0.10. Local adverse events/infusion rate=0.17. Annual infection rate=3.10. Of 2501 IGHy infusions, 97.6% had no administration changes (rate reduction/interruption/discontinuation) due to tolerability concerns/adverse events. Reducing the dosing interval from 4 to 2 weeks (same monthly dose) resulted in a 12% increase in trough IgG levels. Fifteen patients had binding anti-rHuPH20 antibodies with no associated AEs; no patients had neutralizing anti-rHuPH20 antibodies. No safety issues were observed during follow-up after IGHy discontinuation.

CONCLUSIONS: IGHy was well tolerated and effective, with no serious ADRs for treatment periods up to 3 years plus 24-48-week follow-up after discontinuation of rHuPH20 exposure. The final analysis will be presented.

622 Health-Related Quality Of Life Of Japanese Patients With Primary Immunodeficiency Diseases Receiving IgPro20, a 20% Liquid Subcutaneous Immunoglobulin (Hizentra®)

Prof. Hirokazu Kanegane, MD, PhD1, Prof. Kohsuke Imai, MD, PhD2, Prof. Masafumi Yamada, MD, PhD3, Prof. Hidetsoshi Takada, MD, PhD4, Prof. Tadashi Ariga, MD, PhD5, Prof. Ataru Igarashi, PhD6, Prof. Kiichiro Tsutani, MD, PhD7, Dr. Martin Bexon, MD8, Dr. Mikhail Rojavin, PhD9, Ms. Midori Kobayashi, BPSPharm, MBA10, Dr. John-Philip Lawo, PhD11, Mr. At Zbrozek, RPh, MSc, MBA12, Prof. Shigeaki Nonoymada, MD, PhD13, Prof. Toshiro Hara, MD, PhD14, Prof. Toshio Miyawaki, MD15, 1Department of Pediatrics, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan, 2Department of Community Pediatrics, Perinatal and Maternal Medicine, Tokyo Medical and Dental University, Tokyo, Japan, 3Department of Pediatrics, Hokkaido University Graduate School of Medicine, Sapporo, Japan, 4Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, 5Department of Drug Policy and Management, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan, 6Clinical Research and Development, CSL Behring AG, Bern, Switzerland, 7Clinical Research and Development, CSL Behring LLC, King of Prussia, PA, 8Research and Development, CSL Behring K.K., Tokyo, Japan, 9CSL Behring GmbH, Marburg, Germany, 10CSL Behring LLC, King of Prussia, PA, 11Department of Pediatrics, National Defense Medical College, Tokorozawa, Japan.

RATIONALE: This study aimed at evaluating health-related quality of life (HRQL) of Japanese patients with primary immunodeficiencies (PID) receiving a 20% liquid immunoglobulin (Hizentra®) administered subcutaneously (SCIG) compared to preceding intravenous IgG (IVIG) treatment.

METHODS: Twenty-four patients with PID treated with IVIG at 3–4-week intervals, received 3 further IVIG doses before they were switched to a dose-equivalent weekly SCIG for 24 weeks. Questionnaires on HRQL (“Life Quality Index” [LQI] and Treatment Satisfaction) were completed by the patient/patient representative at baseline after IVIG therapy (Week 1), at the end of the wash-in/wash-out period (Week 12) and at the end of the SCIG efficacy period (Week 24).

RESULTS: As per study design, after training period, all patients received all but every fourth infusion at home. At Week 24, 58.3% of patients were self-administering Hizentra®, the rest (mostly children) received infusions from their relatives. Mean (SD) scores of treatment satisfaction (0, worst; 100, best) increased from 66.7 (22.52) at baseline to 73.9 (21.22) at Week 24. Mean (SD) LQI scores were 53.7 (19.53) at baseline and 71.5 (15.14) at Week 24 and showed an improvement in all subcategories, with the largest change observed in “Costs and Therapy Setting”.

CONCLUSIONS: Hizentra® demonstrated a positive effect on HRQL in Japanese PID patients. In addition to the known benefits of SCIG therapy such as home-based self-administration, dosing flexibility, good tolerability, absence of the “wear-off” effects typical of IVIG dosing cycles, and following its use in Europe and the US, Hizentra® administration resulted in high treatment satisfaction in Japanese patients.
223 Efficacy and Tolerability Of Privigen® In Clinical Practice
Dr. Morna J. Dorsey, MD, MMSc, FAAAAI1, Viet Ho2, Dr. Mohns I. Mabudian, MD3, Pere Soler-Palacin4, Nerea Dominguez-Pinilla5, Dr. Robert W. Hellmers, MD, FAAAAI5, Dr. Radha Gandhi Rishi, MD, FAAAAI6, Rahul Rishi1, Dr. Duane W. Wong, MD6, Dr. Mikhail Rojavin, PhD6, Dr. Alphonse Hubsch6, Dr. Melvin Berger, MD, PhD, FAAAAI7; 1Department of Pediatrics, University of California, San Francisco, San Francisco, California, 2Moffitt Cancer Hospital, FL, 3Beaver Medical Group, Inc., Department of Allergy and Clinical Immunology, Redlands, CA, 4Pediatric Infectious Diseases and Immunodeficiencies Unit, Hospital Universitari Vall d’Hebron, Barcelona, Spain, 5Department of Pediatrics, Hospital 12 de Octubre, Madrid, Spain, 6Arizona Allergy Associates, Chandler, AZ, 7Arizona Allergy Associates, Phoenix, AZ, 8Clinical Research and Development, CSL Behring LLC, King of Prussia, PA, 9CSL Behring AG, Berne, Switzerland.

RATIONALE: This retrospective chart review evaluated the efficacy and tolerability of Privigen® in patients with primary (PfD) or secondary immunodeficiencies in clinical practice.

METHODS: Patients who had received Privigen® for ≥3 months in six clinical practices in Europe and the US were treated with individually determined regimens. Efficacy, serum IgG levels, and safety endpoints were assessed.

RESULTS: Seventy-two patients (52.8% male, median age 30.5 years [range: 0.1–90.0 years]) were included. Sixty patients (83.3%) had PID, 12 (16.7%) had immunodeficiency secondary to cancer. Three patients with severe combined immunodeficiency were analyzed separately due to continuous hospitalization and/or exceptionally high Privigen® doses (≥2700 mg/kg/month). In the remaining 69 patients, with a mean (±SD) Privigen® dose of 520±182 mg/kg/month, median trough serum IgG level was 954 mg/dl (range: 407–1581 mg/dL). Only 2 patients (2.9%) had documented IgG levels ≤500 mg/dL. Nine patients (13.0%) experienced 10 serious bacterial infections over a mean of 22.3 ± 15.3 months of treatment (0.080 events/patient/year), the most common being pneumonia (n=7; 10.1%). The rates for any infections and hospitalization were 1.072 events/patient/year and 3.68 days/patient/year, respectively. However, two patients accounted for 303 hospital days. Thirteen patients (18.8%) experienced adverse events (AEs); 10 (14.5%) had AEs at least possibly related to study medication. The most common related AEs were headache after infusion (n=5), fever, and chills (n=2; 2.9% each), which are characteristic of IVIG. No related serious AEs were reported.

CONCLUSIONS: Despite a more heterogeneous population, efficacy and tolerability of Privigen® in clinical practice were similar to those in clinical trials.

224 Safety and Tolerability Of An Intravenously Administered Alpha1-Proteinase Inhibitor (A1PI) At An Increased Infusion Rate: A Randomized, Rate Control, Placebo-Masked, Crossover Study In Healthy Adults

RATIONALE: A1PI (GLASSIA; Kamada Ltd) is indicated for chronic augmentation therapy in adults with emphysema due to congenital deficiency of alpha1-antitrypsin at an intravenous infusion rate of 0.04mg/L/kg/min. This study assessed the safety and tolerability of A1PI when administer intravenously at a faster rate (0.2mL/kg/min).

METHODS: This is a prospective, randomized, rate-control, placebo-masked, crossover study in healthy subjects aged 18-65 years. Day 1 (D1): Subjects received intravenous A1PI 0.04mg/kg/min + placebo 0.2mg/kg/min [A1PI/0.04] or A1PI 0.2mg/kg/min + placebo 0.04mg/kg/min [A1PI/0.2] simultaneously through a Y-connector into 1 infusion site. D15: Treatments were switched in the same subjects. Safety, tolerability, and infusion changes were assessed on D1 and D15. Subject diaries (adverse events [AEs]; concomitant medications) were collected on D29. Laboratory assessments were performed at screening, D1, D15, D29, and D105. Because of simultaneous A1PI and placebo administration, any AE assessed as related to an infusion was conservatively attributed to A1PI.

RESULTS: Thirty subjects were randomized (15/cohort) and completed the study. The mean age was 28 years (range, 19-61), 77% were male, and mean BMI was 25.3kg/m² (range, 19.5-31.5). All AEs (reported in 43.3% [A1PI/0.04] and 26.7% [A1PI/0.2] of subjects) were nonserious and mild. Adverse reactions (most commonly headache; dizziness) occurred in 23.3% (A1PI/0.04) and 16.7% (A1PI/0.2) of subjects. There were no viral seroconversions after dosing. There were no reductions in infusion rate, and no infusion interruptions or discontinuations due to AE.

CONCLUSIONS: A1PI 0.2mL/kg/min was safe and well tolerated; faster administration with decreased infusion duration did not lead to an increased rate in adverse reactions.

225 Pharmacokinetic Modeling Predicts Different IgG Exposures Using Different IVIG-SCIG Dose Conversion Factors In Patients With Primary Immune Deficiency
Dr. Jagdev S. Sidhu, PhD1, Dr. Mikhail Rojavin, PhD2, Dr. Melvin Berger, MD, PhD, FAAAAI3, Dr. Martin Bexton3, Dr. Jonathan M. Edelman, MD4, 1Clinical Pharmacology & Early Development, CSL Ltd, Parkville, Australia, 2Clinical Research and Development, CSL Behring LLC, King of Prussia, PA, 3CSL Behring AG, Berne, Switzerland.

RATIONALE: Currently, US Food and Drug Administration and European Medicines Agency recommendations suggest different methods of calculating dosing when switching from intravenous (IVIG) to subcutaneous IgG (SCIG). The recommendations are based on results from small clinical trials. To predict changes in drug exposure metrics more precisely, we built a population pharmacokinetic (PPK) model based on a large number of data points and simulated switching from 4-weekly IVIG (Q4W-IVIG) to weekly SCIG using different IVIG-SCIG dose conversion factors (DCFs).

METHODS: A PPK model based on four trials of Hizentra® and Privigen® (including switch trials with DCFs 1.0 or 1.53) was used to estimate exposure (steady-state area under the IgG concentration-time curve [AUC], and IgG trough concentration [Cmin] geometric mean ratios for IVIG/SCIG switch) using DCFs 1.30, 1.37, and 1.53. The endogenous IgG concentration was set to 4 g/L, although setting it to 1.5 g/L gave similar results. 300 trials of 25 patients each were simulated.

RESULTS: Increasing DCFs applied to SCIG increased exposure metrics with an approximately linear dose-response. For the DCFs 1.30, 1.37, and 1.53, but all AUCs fell within the bioequivalence range of 0.80 to 1.25.
Flexible Dosing For Hizentra®: Pharmacokinetic Simulations Of Various Subcutaneous Dosing Regimens and Compliance In Patients With Primary Immunodeficiency

Dr. Mikhail Rojavin, PhD1, Dr. Jagdev S. Sidhu, PhD2, Dr. Martin Bexon, MD3, Dr. Jonathan M. Edelman, MD1, 1Clinical Research and Development, CSL Behring LLC, King of Prussia, PA, 2Clinical Pharmacology & Early Development, CSL Ltd, Parkville, Australia, 3Clinical Research and Development, CSL Behring AG, Berne, Switzerland.

RATIONALE: Pharmacokinetic modeling and simulation analyses were performed to evaluate whether the same monthly dose of subcutaneous immunoglobulin (SCIG) can be administered in patients with primary immunodeficiency at various dosing intervals (allowing treatment flexibility) and to assess the effect of non-compliance.

METHODS: Simulations of SCIG dosing used a population pharmacokinetic model developed previously, based on four studies of Privigen® and Hizentra® (data from 151 unique patients). IgG concentration-time profiles and exposure metrics (steady-state area under the IgG concentration-time curve [AUC], IgG peak concentration [Cmax], and IgG trough concentration [Cmin]) were simulated for various infusion intervals or missed doses.

RESULTS: The equivalent of the weekly SCIG maintenance dose administered 1, 2, 3, 5, or 7 times/week, or biweekly (every second week) produced overlapping steady-state concentration-time profiles and similar AUC, Cmax, and Cmin ratios (95% CI were 0.98–1.03, 0.95–1.09, and 0.92–1.08, respectively). Three- and 4-weekly administration resulted in higher peaks and lower troughs; the 95% CI of the AUC, Cmax, and Cmin ratios were 0.97–1.04, 1.02–1.26, and 0.86–0.98, respectively. The reduction in median exposure due to treatment non-adherence was minimal: three consecutive missed doses, replaced at the following infusion, resulted in a drop of only 4% in the median concentration relative to consistent daily dosing (recovered within 2–3 days following resumed daily dosing).

CONCLUSIONS: The same total monthly SCIG dose can be administered at different intervals, from daily to biweekly, with minimal impact on serum IgG levels. Lowering of trough (Cmin) with 3- and 4-weekly administrations may be clinically relevant.

Effect Of Synthetic Steroids and Hydroxychloroquine On B-Cell IgE Production

Dr. Ahila Subramanian, MD, MPH, Yingchun Han, Dr. Fred H. Hsieh, MD; Cleveland Clinic Foundation, Cleveland, OH.

RATIONALE: Previous studies have suggested that hydrocortisone may potentiate IgE synthesis by B-lymphocytes. With various synthetic glucocorticoids used widely in the treatment of allergic disorders we aimed to determine if other synthetic glucocorticoids or drugs interacting with the glucocorticoid receptor may have an effect on in vitro IgE production.

METHODS: U266, human IgE-producing myeloma B-cells, were treated with the glucocorticoid receptor may have an effect on in vitro IgE production. Hydrocortisone suppressed IgE production by 32% (p<0.005, n=8), 0.1uM Dexamethasone suppressed IgE production by 35% (p=0.003, n=6), 10uM Budesonide suppressed IgE production by 47% (p=0.0004, n=8), 1uM Methylprednisone suppressed IgE production by 34% (p=0.005, n=5), and 100uM Hydroxychloroquine suppressed IgE production by 27% (p=0.02, n=8). There was no difference in IgE production of U266 cells treated with 0.1uM, 1uM, or 50uM Beclamethasone at 72 hours.

RESULTS: Drug treatment suppressed IgE production by U266 cells in the absence of cell apoptosis. At 72 hours, treatment with 1uM Hydrocortisone suppressed IgE production by 32% (p=0.005, n=8), 0.1uM Dexamethasone suppressed IgE production by 35% (p=0.003, n=6), 10uM Budesonide suppressed IgE production by 47% (p=0.0004, n=8), 1uM Methylprednisone suppressed IgE production by 34% (p=0.005, n=5), and 100uM Hydroxychloroquine suppressed IgE production by 27% (p=0.02, n=8). There was no difference in IgE production of U266 cells treated with 0.1uM, 1uM, or 50uM Beclamethasone at 72 hours.

CONCLUSIONS: Selected glucocorticoids and Hydroxychloroquine appear to have a suppressive effect on IgE production by U266 cells. No compound tested in these experiments up-regulated IgE production by U266 cells.
629 In Vitro Effect Of Intravenous Immunoglobulin (IVIG) On Natural Antibody Producing Human B1 Cells
Kevin A. Cook, MD1, Sudhanshu Agrawal, MS1, Sudhir Gupta, MD, PhD, FAAAAI2, 1University of California, Irvine, 2University of California, Irvine, CA.

RATIONALE: B1 cells are the major source of natural IgM antibodies important in immune homeostasis, immune tolerance, and microbial defense. Since IVIG has an immunomodulatory role, it is likely that IVIG regulates the expression of FcγR and directly interacts with the FcγRb inhibitory receptor thus regulating the function of B1 cells.

METHODS: Human PBMC was sorted by flow cytometry on a BD FACs Calibur 4 channel analyzer after immunofluorescent staining as follows: CD19-PerCP, CD27-FITC, and CD43-APC in combination with either Fcγ-R-PE, CD70-PE, or CD32-PE. Separately, enriched B cells were incubated in varying concentrations of IVIG. IgM natural antibody production was measured using ELISA.

RESULTS: B1 cells represented by the CD19+, CD27+, CD43+ subset expressed elevated levels of FcγR compared to B2 cells (MFI = 78.2±21.0 vs. MFI = 39.0±10.5, 95% CI). B1 cells expressed low levels of CD32 compared to B2 cell (MFI = 207±171 vs. MFI = 840±395, 95% CI). CD32 represents FcγRIIB in the CD19+ subset. Enriched B cells incubated in IVIG demonstrated elevated levels of secreted IgM by ELISA, though no measurable difference was observed when compared to controls containing only IVIG and growth media. Two samples demonstrated measurable spontaneous IgM in the absence of IVIG.

CONCLUSIONS: Modulation of B1 cell activity and function is likely primarily through FcγR given its high expression in the B1 cell subsets. IVIG may act on B1 cells by regulating FcγR. The effect of IVIG on spontaneous IgM production was not observable by ELISA secondary to high background from IgM contaminates in IVIG.

630 Effect Of A Novel, Oral Histamine H4R Antagonist On Histamine-Induced Pruritus In Healthy Subjects
Dr. Alexa F. Kollmeier, MD1, Paul Dunford, MSc1, Xie Xu, PhD1, Andrew Greenspan, MD1, Yichuan Xia, PhD2, Bei Zhou, PhD2, Klaus Francke, MD, PhD1, Dr. Robin L. Thurmond, PhD1, 1Janssen Research & Development, LLC, La Jolla, CA, 2Janssen Research & Development, LLC, Spring House, PA, 3Parexel International, London, United Kingdom.

RATIONALE: Histamine H4 receptor (H4R) antagonists are potential promising treatments for pruritus, with superiority over H1R antagonists in preclinical pruritus models. This study evaluates the efficacy of an H3R antagonist, JNJ-39758979, on histamine-induced pruritus in healthy males.

METHODS: A single oral dose of 600mg JNJ-39758979, 10mg cetirizine, or placebo was administered in a randomized, double-blind, double dummy, 3 way cross over study. An intra-dermal histamine challenge was administered on day -1 and at 2 and 6 hours post-dose on day 1 of each treatment period. Pruritus was assessed using a 0-10 numerical scale over 10 minutes in 30-60 second intervals and wheal and flare areas were assessed at 10 minutes post-challenge.

RESULTS: 23 of 24 enrolled subjects completed the study. Due to a significant carryover effect of JNJ-39758979, only data from treatment period 1 were used for pruritus-related evaluations. Compared with placebo, the reduction of area under the curve (AUC) of pruritus score (primary endpoint) was significant for JNJ-39758979 at 2 hours (17.429, p=0.0248) and 6 hours (19.193, p=0.0060), and for cetirizine at 6 hours (13.572, p=0.0417). JNJ-39758979 did not have an effect on wheal or flare area (secondary endpoints) while a significant decrease was observed with cetirizine at 2 and 6 hours (p<0.0001). There were no relevant safety findings.

CONCLUSIONS: A novel histamine H4R antagonist was effective in inhibiting histamine-induced pruritus in healthy subjects. In conjunction with published anti-inflammatory effects in models of allergy, these data further suggest the utility of H4R antagonists in the treatment of allergic and pruritic indications.

631 Decreasing Risk Of Infection and Severity Of Infections Resulting In Hospitalizations In Patients With Primary Immunodeficiency Disease Changing From IVIG To Scig Therapy
Mr. Art Zbrozek, RPh, MSc, MBA1, Ms. Sonam Mehta1, Dr. Dipen A. Patel2, Mr. Marc Botteman, MSc2, 1CSL Behring LLC, King of Prussia, PA, 2Pharminter National, Bethesda, MD.

RATIONALE: The effect of switching from intravenous immunoglobulin (IVIG) to subcutaneous immunoglobulin (SCIG) therapy on risk of infections is currently unclear. This retrospective analysis was designed to identify outcome differences in patients with primary immunodeficiency who switched from IVIG to SCIG.

METHODS: Patients within the IMS Health claims database (2005–2012) who switched from IVIG to SCIG therapy during a 12-month period (6 months pre- and post-switch; n=251) were compared with time-of-year and propensity-score matched controls who received continuous IVIG (n=502). The main intent-to-treat (ITT) group included all patients who entered the cohort (n=251); the SCIG-ITT group included only patients receiving SCIG continuously for 6 months (n=193). Differences were tested using multivariate regression.

RESULTS: Most patients (64%) were female and aged 40 years. The percentage of patients experiencing at least one infection decreased from the pre-to post-switch period by 1.6% in the control group (71.5% to 70.5%) and by 7.6% in the IVIG to SCIG group (76.1% to 68.5%). Co-morbid asthma and infection experienced in the pre-switch period were significant (P<0.05) predictors of post-switch infections. Patients who switched had an odds ratio of developing an infection post-switch of 0.79 (95% CI: 0.54–1.31) in the main ITT group and 0.74 (95% CI: 0.49–1.13) in the SCIG-ITT group. No increase in monthly immunoglobulin dosing per patient was observed post-switch from pre-switch.

CONCLUSIONS: A trend toward a lower infection risk was observed in patients who were switched to SCIG therapy.

632 A Multicenter Non-Interventional Study On The Efficacy and Tolerability Of The Polypotent Intravenous Immunoglobulin Privigen
Dr. Rainer Hoffmann, MD1, Dr. Peer Lotichius, PhD2, Dr. Dietmar Pfreunder, MD2, 1Praxis für Neurologie und Psychiatrie, Berlin, Germany, 2CSL Behring, Hattersheim, Germany.

RATIONALE: Privigen® (IgPro10) is a 10% polyclonal human IgG preparation for intravenous administration (IVIG) using L-proline as stabiliser. An ongoing observational study in Germany investigates the efficacy and tolerability of Privigen® in a large sample of patients with various diagnoses.

METHODS: This is an interim analysis of an observational study on the efficacy and tolerability of Privigen® in 159 German centers (protocol number: Ig Pro10_5001; cut-off date: July 09, 2013).

RESULTS: 1,865 patients (895 males, 970 females) with a mean age of 61 years and a mean weight of 75 kg were included in this analysis. They received a total of 19,691 Privigen® infusions. The most frequent indications were primary immunodeficiency (n=196), secondary immunodeficiency (n=1,165), immune thrombocytopenia (n=204), multiple sclerosis (n=142) and chronic inflammatory demyelinating polynuropathy (n=17). In secondary immunodeficiencies, the most frequent underlying diseases were chronic lymphocytic leukemia (n=592), other leukemias (n=33), myeloma (n=195), macroglutelinemia Waldenström (n=30), other non-Hodgkin lymphomas (n=268), Hodgkin lymphoma (n=13) and solid tumors (n=16). Efficacy was judged as very good or good in 90.9%, moderate in 6.2% and insufficient in 2.9% of evaluable cases (n=1756). Tolerability was judged as very good or good in 92.6%, moderate in 4.5% and insufficient in 2.0% of all cases (0.9% missing data). Adverse events possibly or probably related to Privigen® were reported for 227 of the 19,691 infusions (1.2%); 14 events were considered serious (0.07%).

CONCLUSIONS: These results demonstrate very good or good efficacy and tolerability of Privigen® in the majority of patients across several different indications.
633 The Immunoglobulin Diagnosis, Evaluation, and Key Learnings (IDeA) Patient Registry: Analysis Of Ig Dosing, Infection Control, and Quality-Of-Life Assessments In Our Primary Immunodeficiency Population
Sean Kearns, PhD1, Keith Crawford1, Loretta Kristofek, RN1, Robbyn Kurylo1, Dr. Lauman Seidu, MD2, Coram Clinical Trials, Denver, CO, 2Allergy and Asthma of Atlanta LLC, Atlanta, GA.
RATIONALE: The IDeA Patient Registry collects longitudinal information on patients receiving immunoglobulin (Ig) replacement therapy from Coram Specialty Infusion Services in an alternate care setting. This poster is focused on Ig dosing, infection control, and quality-of-life assessments in the primary immune deficiency (PID) population.
METHODS: Patients of our 138 investigators are eligible for the Registry. With patient consent acquired, patient information from July 2010 onward that had been collected by Coram providers was entered into the IDeA database. Additionally, patients were asked to complete an SF-36 questionnaire and an LQIQ survey every six months.
RESULTS: As of August 2013, 235 PID patients were enrolled. The average dose for SCIG was 135 mg/kg per week, and for IVlg, 409 mg/kg per month. The overall annual number of infections was three, with no significant difference between SCIG and IVlg. Side effect incidence rates for IVlg and SCIG were almost identical, though there were significant differences in the incidence rates of specific side effects. Patient-quality-of-life surveys showed that most patients felt positive about their infusions, though differences in perceptions of baseline effectiveness and infusion pain by route were noted.
CONCLUSIONS: Overall, patients reported good infection control, low side-effect rates, and positive quality-of-life assessments on Ig therapy. The IDeA Patient Registry provides a real-world population of PID patients with a heterogeneous baseline presentation. Outcomes data on this population provides important feedback on Ig therapy, and may offer insights into patients’ baseline status and their treatment optimization.

634 Retrospective Analysis Of The Clinical Utility Of Biweekly Dosing With High-Concentration Subcutaneous Immunoglobulin In 10 Patients With Primary Immunodeficiency
Dr. Richard L. Wasserman, MD, PhD, FAAAAI1, Dr. Shahnaaz Fatteh1, Dr. Javid M. Khan, DO2, Dr. Elie Haddad, MD3, 1Medical City Children’s Hospital, Dallas, TX, 2Larkin Community Hospital, South Miami, FL, 3CHU Sainte-Justine, Montreal, QC, Canada.
RATIONALE: Limited data are available to assess if biweekly (every 2 weeks) administration of subcutaneous immunoglobulin (SCIG) is effective in preventing serious bacterial infections (SBIs) while increasing treatment flexibility.
METHODS: A retrospective record review of patients with primary immunodeficiency disease (PIDD) who were administered 20% SCIG at biweekly intervals assessed the occurrence of SBIs, general overall patient health, and serum immunoglobulin (Ig) levels at 3 centers.
RESULTS: Ten patients (8 females, 2 males) aged 9–46 years (4 were ≥18 years) with common variable immunodeficiency (n=6) or specific antibody deficiency (n=4) were treated with 20% SCIG every 14 days. Total monthly doses ranged from 231–744 mg/kg using 2–8 infusion sites. The duration of infusions ranged from 50 to 180 min. The most recent serum Ig concentrations ranged from 720–1828 mg/dL. To date, total therapy duration has ranged from <1 to >35 months (median approximately 21.5 months). Only 1 patient was hospitalized for pneumonia during her >28 months of biweekly treatment; 9 patients experienced no acute SBIs and did not require hospitalization. Most patients were subjectively evaluated to be in “fair,” “good,” or “excellent” general health during biweekly SCIG therapy. All patients have continued the biweekly dosing regimen.
CONCLUSIONS: Biweekly administration of 20% SCIG maintained effective prevention of SBIs and allowed patients with PIDD to experience good general health. Increasing the options for dosing flexibility and individualization with SCIG could improve patient adherence and quality of life.

635 Concomitant FMF and TRAPS Mutation In a Periodic Fever Patient
Dr. Adrianne C. Nettterville, MD1, Dr. Victoria Dimitriadis, MD1, Dr. Paul D. Nieto, MD2, 1Louisiana State University Department of Pediatrics, New Orleans, LA, 2Allergy Asthma and Immunology, Ocean Springs, MS.
RATIONALE: Familial Mediterranean Fever (FMF) and TNF-Receptor Associated Periodic Syndrome (TRAPS) are two autoinflammatory disorders characterized by unprovoked inflammatory events without high titer autoantibodies. We report a case of recurrent fevers consistent with periodic fever syndrome. On genetic analysis she was found to be heterozygous for two different variants: one each in the MEFV (FMF) and TNFRSF1A (TRAPS) genes.
METHODS: DNA PCR and sequencing of periodic fever syndrome panel performed by GeneDx.
RESULTS: This is a 2 year old female with recurrent fevers every 3-4 weeks for over one year with bouts lasting 3 days. These episodes varied in nature, and included pharyngitis, mouth ulcers, intermittent diaper rash, leg pain, and abdominal distension. Additionally, not in conjunction with fevers, she experienced erysipelas like rashes. Initial lab work including inflammatory markers and immunity workup were normal. With her clinical history and absence of infection, malignancy, or autoimmune disease, a periodic fever syndrome panel was sent. Genetic analysis revealed that she was heterozygous for two gene variants, I591T mutation in the MEFV (FMF) and R92Q mutation in the TNFRSF1A (TRAPS). Given the above findings it was believed that she was suffering from a mild form of Familial Mediterranean Fever (FMF). She was placed on a trial of colchicine, and has not had any recurrent fevers to date.
CONCLUSIONS: This case illustrates that different mutations in the periodic fever syndrome panel can coexist together. Although FMF and TRAPS are treated differently, our patient clinically manifested as FMF and therefore was treated with colchicine.

636 Association Of Interleukin-23 Receptor Single Nucleotide Polymorphisms With Ulcerative Colitis
Dr. Mona Hedayat, MD1, Dr. Naser Ebrahimi Daryani2, Dr. Farnaz Najmi Varzaneh3, Dr. Nima Rezaei, MD, PhD4, 1Boston Children’s Hospital, Boston, MA, 2Department of Gastroenterology and Hepatology, Tehran University of Medical Sciences, 3Molecular Immunology Research Center, Department of Immunology, Tehran University of Medical Sciences, 4Research Center for Immunodeficiencies, Children’s Medical Center, Tehran University of Medical Sciences, Tehran, Iran.
RATIONALE: Over the past decade, considerable progress has been made in understanding the role of mucosal immunity and host genetics in the pathogenesis of Crohn’s disease (CD) and ulcerative colitis (UC). Genome wide association studies have showed a highly significant association between interleukin 23 receptor (IL23R) single nucleotide polymorphisms (SNPs) and CD; however, there are contrary results regarding the disease-modifying effects of IL23R variants in UC. This study was performed in a group of patients with UC to test the possible role of IL23R SNPs in conferring susceptibility (or protection) to the disease.
METHODS: The study was performed on 77 Iranian adult patients with UC and 78 healthy controls. Eight IL23R SNPs were genotyped, using Real-Time polymerase chain reaction (RT-PCR). The frequencies of alleles and genotypes at each position were determined and compared between two groups of patients and controls.
RESULTS: The frequency of the T allele at position rs1343151 was significantly higher in the patient group, compared to the controls (p=0.018). The TT genotype at the same position was also significantly overrepresented in the patient group (p=0.02). There was no significant difference in alleles and genotypes frequencies of other SNPs between patients and controls.
CONCLUSIONS: This study identified a new susceptibility locus associated with UC. Our findings provide further insight into the genetics of UC, which might be amenable to future therapeutic intervention.
637 A Novel Immunoablative Regimen Utilized In The Successful Remission Of Pulmonary Hemorrhage In An Adolescent Female With Systemic Lupus Erythematosus

RATIONALE: Standardized immunosuppressive regimens with cyclophos-phamide, rituximab, high dose steroids, mycophenolate and plasmapheresis failed to suppress pulmonary vasculitis and nephritis complicating SLE in an adolescent girl. Planned management focused on the successes identified with Hemopagocytic Lymphophiotyosis (HLH) after being treated with Alectzumab. The shared central role of immune dysregulation in HLH and SLE made an immunoablative protocol likely to achieve disease control.

METHODS: Literature review utilizing key words: autoimmune disease, immune ablation, systemic lupus erythematosus, hemophagocytic lymphophiotyosis and Alectzumab

RESULTS: A 17-year-old female with four year history of SLE, pulmonary hypertension, class IV nephritis, hypertension, cutaneous lupus, ANA 1:640, anti-dsDNAab positive, C3 (18 mg/dl) and C4 (5 mg/dl) presented with acute pulmonary hemorrhage, respiratory failure, and declining kidney function. The patient initially failed high dose steroid pulses, plasma exchange, rituximab and intrapulmonary installation of rFVIIa. The patient subsequently received an immunoablative regimen consisting of rituximab 375mg /m2 (Days 1, 7), Thymoglobulin 3mg/kg/day (Days 4-6) and Etoposide (75mg/m2 D4, 56mg/m2 D8). The patient’s pulmonary bleed gradually improved and she was extubated two weeks later. Four months later, she remained asymptomatic on mycophenolate maintenance therapy.

CONCLUSIONS: Successful outcome was achieved utilizing an immunoa-blative protocol modeled after treatment for HLH. Beneficial outcomes were measured by improved levels of C3 and normalization of C4. Repeat HR chest CT demonstrated complete resolution of interstitial thickening suggestive of pulmonary hemorrhage while remaining free from bronchiectasis and intersti-tial lung disease. This novel immunoablative regime may provide insight into a new approach in treating other patients with refractory autoimmune disorders.

638 Haptoglobin Deficiency and Autoimmune Manifestations: A Case Series
Dr. Anna Kochin, MD1. Dr. Jenny Shliozberg, MD, FAAAAI2. Dr. Ayre Rubinstein, MD, FAAAAI2. Montefiore Medical Center, Bronx, NY. 3. Albert Einstein College of Medicine, Bronx, NY.

RATIONALE: Haptoglobin is an acute-phase reactant with clinical utility in defining conditions of hemolysis. Haptoglobin also has important anti-inflammatory properties; haptoglobin reduces tissue damage in initial events of inflammation. Mechanisms by which haptoglobin has effect on adaptive and innate immunity are multifactorial. Haptoglobin receptors have been identified on macrophages, dendritic cells and bind to CD22 B cells.

METHODS: We reviewed charts of haptoglobin deficient patients diagnosed with autoimmune disorders.

RESULTS: Patient #1 is a 26 year old woman with chronic, unexplained inflammatory and autoimmune manifestations found to have a haptoglobin deficiency. The patient suffered from chronic and progressive fatigue, headaches, myalgias and Raynaud-like symptoms. She was also found to be hypothyroid and suffer from adrenal insufficiency. Patient #2 is a 39 year old female diagnosed with Multiple Sclerosis, hypogammaglobulinemia and found to have haptoglobin deficiency with negative thyroglobulin and thyroid peroxidase antibodies. Patient #3 is a 42 year old female who presented with fatigue, anxiety, weight changes and joint pains and found to have strongly positive thyroglobulin antibodies and haptoglobin deficiency. Patient #4 is a 56 year old female who complained of fatigue, persistent cough, and found to have haptoglobin deficiency with positive thyroglobulin antibodies and thyroid peroxidase antibodies.

CONCLUSIONS: Taken together it appears that mild immune aberrations and extensive autoimmune manifestations in our patients were related to the absence of haptoglobin with its associated regulatory and anti-inflammatory effects.

639 Immunogenicity Analysis Of Two Anti-TNF (Infliximab vs Etanercept) Therapies In Rheumatologic Patients
Dr. Yvelise Barrios, MD, PhD1. Dr. Victor Matheu, MD2. Dr. Andres Franco, MD3. Dr. Esmeralda Delgado, MD3. Dr. Sagrario Bustabad, MD4. Immunology, Hospital Universitario de Canarias, LA LAGUNA, Spain. 2. Allergy Section, Hospital Ofra, Tenerife, Spain. 3. Rheumatology, Hospital Universitario de Canarias, LA LAGUNA, Spain.

RATIONALE: The aim of this study was to investigate the immunogenicity and the drug-level of two anti-TNF therapies (Infliximab-IFX vs Etanercept-ETN) in the serum of patients attending the Rheumatology Area and included in this treatment option.

METHODS: Serum from 15 ETN and 13 IFX-treated patients were sent to the Immunology Laboratory. The IFX and ETN serum level and anti-IFX and anti-ETN antibodies were measured in all samples at the same time using PROMONITOR® IFX and ETN following manufacturer’s instructions. Samples were collected the day before next dose of drug was infused and remained frozen until analysis.

RESULTS: 7/15 (46%) ETN-treated patients and 5/13 (38%) IFX-treated patients have level of ETN/IFX >= 1.5 ug/ml (therapeutic level for AR). 5/13 (33%) ETN and 5/13 (38%) IFX have levels between 0.1 and 1.5 (sub-therapeutic level). 3/15 ETN-treated (20%) and 3/13 (23%) IFX-treated patients were below the level of detection of the method. All patients below the level of detection in the IFX-group (3/13) have high level of Anti-IFX antibodies whereaspatients in the ETN group (3/13) were negative for Anti-ETN antibodies.

CONCLUSIONS: Anti-TNF therapies are widely used for the treatment of patients with several rheumatologic conditions. Nowadays, these biological treatments represent a high proportion of the budget of the health care system. The possibility of a routine monitoring of levels of each drug and also the immunological response of patients against the different lines of treatment should be mandatory in order to choose the best cost-effectiveness strategy and to benefit the patients from a tailored therapy.

640 Circulating Endothelial and Platelet Microparticles for Diagnosis and Monitoring Vasculitis
Prof. El-Desouki E. Fouda, MD, FAAAAI1. Dr. Marwa Ahmed2. Prof. Mona Afraay3. 1-Al-Azhar university Allergy & Immunology Cr., Cairo, Egypt. 2-Al-azhar Allergy&Immunology Cr., Cairo, Egypt. 3-Al-Az-har Allergy& Immunology Cr., Cairo, Egypt.

RATIONALE: Microparticles (MPs) have received increased attention as universal markers of activation in eukaryotic cells. Endothelial microparticles (EMPs) are increased in many autoimmune diseases characterized by vascular damage, which may serve as circulating markers for vascular dysfunction. Platelet microparticles (PMPs) are the most abundant circulating MPs. We hypothesized that the use of EMPs and PMPs as a non-invasive, easily measured tool would be valuable for diagnosis and monitoring vasculitis activity and response to therapy.

METHODS: This study included; 45 patients with vasculitis secondary to autoimmune diseases, 15 rheumatoid arthritis (RA) without vasculitis as a comparative group and 15 healthy volunteers as a control group. Platelet-free plasma was ultra centrifuged. EMPs (CD105) and PMPs (CD42a) were enumerated by flow cytometry during activity and after remission. Similarly, ANCA test was done.

RESULTS: EMPs and PMPs were elevated in active vasculitis (15563±8465 & 24682±77815 /ml respectively) at 6 months follow up compared with controls (P = 0.001). There was significant reduction of EMPs and PMPs (3871±2585 & 193215±12561/ml respectively) at remission (p=0.001). EMPs and PMPs were elevated in both ANCA positive and ANCA negative vasculitis with no significant difference. No significant correlation between EMPs and PMPs was found. PMPs ≥ 204673.5/ml and EMPs ≥ 4050/ml revealed (100% sensitivity for both and 100% & 96.7% for specificity respectively).

CONCLUSIONS: EMPs and PMPs are independent factors seem to be correlated to the vascular insult. Both are highly sensitive and specific for diagnosis and monitoring vasculitis and might substitute ANCA test especially in ANCA negative vasculitis.
AB186 Abstracts

642 Th-17 Cytokines In Oral Lichen Planus
Prof. G. N. Drannik1, Prof. A. I. Kurchenko1, Dr. R. A. Rehuretska1, Dr. A. G. Drannik2, Prof. Lawrence M. DuBuske, MD, FAAAAA3, 1National Medical University, Kiev, Ukraine, 2National medical University, Kiev, Ukraine, 3George Washington University School of Medicine, DC.

RATIONALE: Oral Lichen planus is a chronic inflammatory mucocutaneous disease. The impact of T-helper cell subtype Th17 cytokines interleukin-17, 21, 22, (IL-17, IL-21, IL-22) on progression and frequent relapses erosive oral lichen planus is assessed in this study.

METHODS: 97 persons age 18 to 60 years were studied including 35 patients with erosive oral lichen planus, 32 patients with typical non-erosive forms of oral lichen planus and 30 healthy control subjects of similar age. The levels of serum cytokines (IL-17, IL-21, IL-22) were determined by ELISA (“Immunotech” ; France).

RESULTS: In patients with lichen planus of the oral mucosa in relapse an increase in serum IL-17 was seen. In erosive lichen planus patients there was a 1.5 fold increase in serum IL-17 compared with controls. Disease remission was associated with reduced concentrations of serum IL-17, IL-21, IL-22. Remission of erosive lichen planus showed a significant 1.4 fold reduction in the concentrations of IL-17 compared with healthy persons, but also reduced serum levels of IL-21, IL-22 by 1.2 fold in comparison to patients with recurrent disease

CONCLUSIONS: Acute relapses of lichen planus of the oral mucosa are characterized by increases in Th17-associated cytokine concentration (IL-17), while the chronic stage is characterized by immunologic abnormalities in which serum Th17 cytokines influence the chronic inflammatory process. In patients with lichen planus of the oral mucosa increased levels of IL-17, both in relapse and in remission, can serve as a marker for the appearance of increased chronic inflammation.

643 A Study On Allergy Sensitization Of Dense Urban Dwellers To Dog and Cat Allergens Using The Skin Prick Test
Dr. Racquel Joy Y. So, Dr. Florencia Padua, Dr. Shirley Kwong; Fe Del Mundo Medical Center, Quezon City.

RATIONALE: Pet allergen exposure has been a long debate amongst experts. Studies in different countries have produced rather conflicting results.

METHODS: This is a cross-sectional study that aims to demonstrate cutaneous allergy sensitization to cats and dogs of Filipinos living in a dense urban area where pets and strays are commonly seen. One hundred fifteen subjects (n=115) were tested for cutaneous skin prick test reactivity to dog and cat allergens. There were 73 female and 42 males with 31 pediatric subjects. Among the subjects (n=115), 54.8% (n=63) were pet owners while 45.2% (n=52) have no pets.

RESULTS: Using chi-square, skin prick test reactivity to dog and cat allergens were compared to patient demographic data and patient pet ownership profile. Our results show that neither gender nor age correlates to skin prick test reactivity to both allergens. Comparing skin test reactivity to dog allergen, there was no significant difference between those who are dog owners versus those who do not own dogs (p-value 0.183). Cat owners have significant increase in cat allergen skin reactivity (p-value 0.031).

CONCLUSIONS: In conclusion, this study shows that regardless if you owned a dog or a cat, the event of having a positive dog skin prick is the same. In contrast, if one owns a cat, there is a higher event of having cat allergen sensitization compared to not owning cats at all. Lastly, those without pets in general do not have a significantly lower incidence of skin test reactivity showing that animal allergens cannot be fully avoided.

644 Rhinix™ Nasal Filters For The Treatment Of Allergic Rhinitis: A Randomized, Double-Blinded Placebo-Controlled Crossover Clinical Trial
Peter Kenney, BSc1, Ole Hilberg, MD, DMSc2, Henrik Pedersen, PhD3, Ole Berggaard Nielsen, PhD4, Torben Sigsgaard, MD, PhD5, 1Department of Public Health, Aarhus University, Aarhus, Denmark, 2Department of Respiratory Diseases and Allergology, Aarhus University Hospital, Aarhus, Denmark, 3Department of Engineering - Signal Processing, Aarhus University, Aarhus, Denmark, 4Department of Biomedicine, Aarhus University, Aarhus.

RATIONALE: Nasal filters might be useful as an alternative to current treatments for seasonal allergic rhinitis. The aim of this study was to evaluate the efficacy, safety and usability of Rhinix™ nasal filters in the treatment of seasonal allergic rhinitis.

METHODS: The trial was a single-centre, randomized (1:1), double-blind placebo-controlled crossover clinical trial (NCT01699165) conducted out of season in an Environmental Exposure Unit (EEU) in Aarhus, Denmark on 24 subjects with proven grass allergy. A total nasal symptom score (TNSS) consisting of nasal congestion, nasal discharge, nasal itching and sneezing was used as the primary outcome measure. TNSS was rated 9 times during each study day and evaluated based on the difference in daily TNSS (the sum of all 9 ratings) and maximum TNSS (the highest score of the 9).

RESULTS: Rhinix™ reduced daily TNSS by 21% (P=0.049), daily sneezing by 45% (P=0.01), maximum itching by 46% (P=0.004) and maximum sneezing by 38% (P=0.001) when compared to placebo. Rhinix™ failed to show a significant reduction in the primary efficacy endpoint of difference in maximum TNSS (P=0.14) with a mean reduction of 14% and median reduction of 33% when compared to placebo. The nasal filters were well tolerated and no serious adverse events were recorded.

CONCLUSIONS: Although maximum TNSS showed no statistically significant difference, statistically significant and clinically relevant reductions were achieved with Rhinix™ nasal filters in daily TNSS as well as in a subset of individual symptoms for patients with seasonal allergic rhinitis.
**ABSTRACTS**

**645** Airborne Allergen Exposure As a Quantum Phenomenon

**Dr. Gert Doekes, PhD**
**Dr. Peter S. Thorne, PhD**
**Dr. Ingrid Sander, PhD**
**Dr. Inge Wouters, PhD**
**Dr. Wijnand Eduard, PhD**
**Dr. Dick Heederik, PhD**
**Institute for Risk Assessment Sciences, University Utrecht, NL, Utrecht, Netherlands, University of Iowa, Iowa City, IA.**

**RATIONALE:** IgE sensitization to potent allergens may occur at average airborne concentrations <0.1-1 ng/m³. Measured levels in parallel samples or job categories show however an often high variability that cannot be explained by sampling or assay errors. We therefore focused on characteristics of allergenic particles.

**METHODS:** Airborne dust was collected in bakeries with a low-flow (2 L/min per filter) parallel sampling unit (PSU), and allergens of wheat and fungal amylase were measured by ELISA. Total numbers of wheat flour and amylase particles were estimated, as collected on the filters or inhaled during the work day.

**RESULTS:** High CV values for amylase could be explained by a high (>90%) allergen content of the enzyme particles, of which each (diameter 10-20 nm) would contain 0.8-8 ng of allergen, and 4-8-hr monitoring, even at ‘high’ amylase exposure, would lead to Poisson-distributed numbers of <5-10 amylase particles per sample. As a consequence, sensitizing time-weighted average levels of <1 ng/m³ correspond to inhalation of <10-100 allergen particle per day. In contrast, the estimated number of wheat flour particles in the same samples was >100,000/filter, with approximately 100 pg allergen per particle.

**CONCLUSIONS:** The quantum nature of allergen exposure should be taken into account in airborne measurements and exposure-sensitization analyses. Sensitization at average levels of <1 ng/m³ may be due to incidentally inhaled ‘peaks’ of <10-100 allergen particles, followed by days or even weeks without exposure. Calculations for allergenic particles from mites, pets and pollen suggest that similar conclusions apply to exposure and sensitization to many common and work-related allergens.

**646** Computer-Aided Design Of An Allergen Challenge Theatre

**William H. Yang, MD**
**Jimmy Yang, MBA**
**Robert Perrins, PEng**
**Suzanne Kelly, PhD**
**Jacob Karsh, MD**
**Red Maple Trials Inc., Ottawa, ON, Canada.**

**RATIONALE:** Allergen challenge theatres (ACT) expose sensitive subjects to predetermined concentrations of allergen in a controlled environment to induce clinical symptoms and measure effects of medication. Computer modeling can be used to optimize the allergen delivery system.

**METHODS:** Computational Fluid Dynamics (CFD) analysis was used to govern technical development of an ACT. Extensive CFD analysis was used to optimize room ventilation and the targeted flow of allergen to each participant’s head. The analysis was used to characterize allergen concentrations between 1000 - 5000 grains/m³ and size variations from 10 to 60 μm. Modeling included simulation of 111 participants and their related heat load, in a 133m² clean room. The modelling and design will be validated in the actual facility using an array of impact samplers and laser particle counters monitoring 20 sample locations, in 4 zones controlled by a real-time control system.

**RESULTS:** The most important variables for allergen delivery were established by >40 repeated CFD simulations evaluating duct inlet and outlet configurations and air flow velocities to allow pollen to flow across the room from front to back. The model indicated that pre-determined stable allergen concentrations can be achieved within <10 minutes after start-up and maintained over the exposure duration.

**CONCLUSIONS:** CFD permits optimization of allergen delivery systems to ensure accurate and consistent allergen concentrations throughout a large chamber, to effectively manage large test groups. More consistent allergen levels have the potential to decrease the number of subjects needed to power a study.

**647** Evaluation Of a Compact Ionic Capture Device For Airborne Allergens In Inner City Schools

**Dr. Julian Gordon, PhD**
**Ms. Prasanthi Gandhi, MBA, MPH**
**Dr. Gajendra Shelkhatt, PhD**
**Ms. Ann Bailey, BA**
**Dr. Wanda Phipatanakul, MD, MS, FAAAAI**
**Inspirotec LLC, Chicago, IL.**

**RATIONALE:** We evaluated the performance of a compact ion capture device (cICD) for the sampling of a set of airborne allergens and endotoxin in school classrooms as part of a larger study of the relation of allergen exposure to asthma in an inner city school system. Since smaller particles penetrate deeper in the lungs, we determined size distribution of captured particles.

**METHODS:** Samples were collected over 4 days in 3 rooms at 3 time intervals. Multiplex assays for allergens (MARIA™) and Endotoxin were by Indoor Biotechnologies. Size distributions of particles collected were measured directly on the electrodes of the cICDs with a Bruker dimension ICON AFM system with sub-nm resolution. Imaging was done in tapping mode with super harp silicon probes.

**RESULTS:** Means and standard deviations over all locations in fg/liter of air were Feld 1 (1.7±0.17); Can f1 (0.7±0.0.5); Mus m1 (1.9±1.3) and endotoxin (28±2). Seven other allergens were undetectable. There was 100% qualitative agreement with parallel determinations made by a reference method using a full size ion capture device and measurements as μg/gram of dust. AFM measurements on the cICD showed particles captured down to less than 200nm. The particles were distributed uniformly across the surface and consistent in size.

**CONCLUSIONS:** The cICD is an extremely inexpensive, quiet, compact and simple device that can be unobtrusively deployed in critical locations without sacrificing performance. The ability to capture particles in a size range that is lower than currently used methods provides the opportunity to determine the fraction most significant for asthma provocation.

**648** Relevance Of Sensitization To Blomia Tropicalis, Dermatophagoides and Tropomyosin- Containing Antigens Among Atopics Living In a Tropical Region

**Dr. Beverly K. Di Giorgi, MD**
**Dr. Sylvette Nazario, MD, Dr. Fernando J. Lopez, MD, Dr. Javier A. Mendez, MD**
**University of Puerto Rico School of Medicine, San Juan, PR.**

**RATIONALE:** Allergens produced by dust mites are among the most common triggers of asthma. Pyroglyphids (Dermatophagoides farinae, D. pteronyssinus and Euroglyphus maynei) are the predominant species worldwide. In tropical areas, storage mite sensitization, including Blomia tropicalis (Bt) has been reported, but its role in allergic manifestation and cross reactivity with other tropomyosin-containing antigens, has been less well described.

**METHODS:** Evaluate prevalence of Bt, Dermatophagoides, cockroach, crustacean, and aspirin sensitization among atopic adults attending a community Allergy Clinic in San Juan, Puerto Rico form August 2012 to 2013; and compare with atopic manifestations including allergic rhinitis, conjunctivitis, asthma, urticaria, anaphylaxis, food allergy and atopic dermatitis.

**RESULTS:** Fifty records were reviewed. The average age was 43.3 years and 70% were female. Allergic rhinitis was the most common atopic manifestation (70%), followed by asthma and urticaria (40% and 40%, respectively). 5% of subjects were sensitized exclusively to Dermatophagoides, 6% to Blomia, 16% to neither and 70% to both. Sensitization to Dermatophagoides and Blomia, was associated to rhinitis (p=0.052), but not to asthma, anaphylaxis nor atopic dermatitis. Subjects sensitized to either mites were less likely to suffer urticaria (p=0.021, OR =0.132). Cockroach sensitization but not crustacean sensitization was significantly associated to mite sensitivity (p=0.005).

**CONCLUSIONS:** Blomia tropicalis is an important inhalant allergen among adults suffering allergic rhinitis in San Juan, Puerto Rico but not to anaphylaxis emphasizing its role as a domestic rather than storage mite.
649 **Update In The Prevalence Of Atopic Conditions, IgE Levels and Skin Test Sensitization To Aeroallergens In Northern Puerto Rico**

Dr. Rafael H. Zaragoza, MD, PhD; Doral Bank Center, San Juan, PR; University of Puerto Rico School of Medicine, San Juan, PR; Maria Cristina Pérez-Mitchell, BS; José A. Rivera, RN; José Zaragoza-Buxó, MD; San Juan, Puerto Rico.

**RATIONALE:** Puerto Ricans have one of the highest asthma prevalence rates among Hispanics and other ethnic groups in the United States. Very limited information is available on the prevalence atopic conditions, IgE levels and aeroallergens sensitivities among Puerto Ricans.

**METHODS:** We evaluated a cohort of subjects attending unadvertised Ambulatory Allergy Screen Clinics in 4 regions in the northern part of the island of Puerto Rico between August 2009 and May 2010. Subjects answered a survey on asthma, rhinitis and other atopic conditions; were skin tested to common aeroallergens and total IgE levels were measured.

**RESULTS:** 135 subjects, with a mean age of 45 years. 36% reported a lifetime history of asthma, 22% still have asthma and 46% reported rhinitis. 68% of the subjects were sensitized to at least one antigen and averaged IgE of 526.36 IU/ml. 10% reported non-allergic conditions and averaged an IgE of 61.53 IU/ml. Subjects sensitized to mites were 95% more likely to have suffered from asthma than non-mite sensitized subjects (OR=1.95, p<0.001).

**CONCLUSIONS:** Mites, pet’s dander and Outdoor Molds were the most prevalent sensitivities identified in northern Puerto Rico. We confirmed the relevance of mite sensitivity in asthma among Puerto Ricans and present data supporting the relevance of other external aeroallergens in allergic diseases in this cohort.

650 **Stability Of Immunoassay Analytes and Test Kits Used For Monitoring Environmental Allergen Exposure**

Bryan Smith, Denise Block, Stephanie Filep, Dr. Martin D. Chapman, PhD, FAAAI, Dr. Eva-Maria King, PhD; Indoor Biotechnologies, Inc., Charlottesville, VA.

**RATIONALE:** Allergen exposure assessments are routinely based on dust extracts tested in immunoassays. The stability of immunoassay test kits and allergens in dust extracts has not been fully established.

**METHODS:** Microtiter plates were coated with an antibody specific for one of eight common environmental allergens. Plates were treated with stabilizing buffer, dried, and packaged in foil pouches. The stability of pre-coated plates and assay reagents was evaluated after one, two, three, and six months. To measure the stability of allergens in dust, extracts were prepared from four sieved dust samples. The extracts were aliquoted and pre-coated plates and assay reagents was evaluated after one, two, three, and six months. Pre-coated immunoassay plates and reagents remained stable for at least six months. Allergens in dust extracts remained stable for 1-3 days at 30°C, 3 days at RT, and 1-3 weeks at 4°C. Allergens were most stable when dust extracts were stored frozen at either -20°C or -80°C.

**CONCLUSIONS:** Dust extracts may be stored at 4°C for up to one week, but should be frozen at or below -20°C for long-term storage to maintain allergen stability. This finding is particularly relevant for determining sample shipping and handling conditions. The results showed that pre-coated allergen ELISA kits are stable for six months and may be suitable for epidemiological studies involving allergen exposure assessment.

651 **Factors Affecting Pollen Rupture and Protein Release From Allergenic Pollens**

Ms. Umaporn Siriwattanakul1, Dr. Wisuwat Songmuang2; 1Master of Science Program in Plant Science, Department of Plant Science, Faculty of Science and Department of Pharmaceutical Botany, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand, 2Department of Plant Science, Faculty of Science, Mahidol University, Bangkok, Thailand.

**RATIONALE:** Allergenic proteins located in the cytoplasm of pollen are rapidly released upon contact with wet surface, thereby inducing allergic symptoms in sensitized patients. Yet, little information is known about factors affecting pollen protein release. This study investigated the effect of pollen species, pollen age, incubating solution, and incubating time on pollen rupture and amount of proteins released from four common allergenic pollens in Thailand (Johnson grass, careless weed, sedge, and cattail).

**METHODS:** Ten milligrams of freshly collected, 3-, and 7-day old pollen grains were incubated in 1 ml of each solution (artificial tear, PBS, rainwater, distilled water, and ethanol) for 0, 15, 30, 45, 60, and 120 minutes. Ruptured pollen grains were counted using a light microscope. Concentration of proteins released from pollen was investigated with Bradford’s method. ANOVA and LSD statistical analyses were used in this study.

**RESULTS:** In all species tested, fresh pollens released more proteins than aged pollens. Seven-day old pollens released only about 30% of the amount of proteins released by fresh pollens. All tested solutions, except ethanol, caused considerable release of pollen proteins. The highest amount of released proteins was found at 15 minutes after incubation. Johnson grass had the highest percentage of pollen rupture and highest concentration of released protein, followed by sedge, careless weed, and cattail. Up to 70% of Johnson grass pollen ruptured instantaneously upon contact with solutions, releasing more than 100μg protein/mg pollen.

**CONCLUSIONS:** Pollen species, age, incubating solution, and incubating time significantly affect the amount of proteins released from allergenic pollen.
Uniformed Distribution Of Aerosolized Dust Mite Allergen In The Allergen Biocube (ABC)

Keith Lane1, Paul Gomes2, Endri Angjeli1, Dr. Anne K. Ellis, MD, MSc, FAACIA1,4, Ora Inc., CA, 5. Ora Inc., CA, Ora, Inc, Andover, MA, 6. Allergy Research Unit, Kingston General Hospital, Kingston, ON; 3. Departments of Medicine and Biomedical & Molecular Science, Queen’s University, Kingston, ON, Canada.

RATIONALE: Dust mite allergy can be difficult to study in clinical trials due to unreliable exposure patterns and poor correlations between rhinitis response and skin test response. To overcome these challenges, The Allergen Biocube was developed to deliver dust mite allergen in a uniform manner to a capacity of 25 subjects.

METHODS: Dust mite carapaces (D. pteronyssinus) were cryomilled to 5um size and were distributed using proprietary techniques. Twenty-five 25 separate subject locations were evaluated for dust mite levels using laser particle counters and active air filters. Der p1 levels were confirmed using ELISA techniques.

RESULTS: Mean dust mite levels as assessed by laser particle counter were 2065 ± 422 across the ABC. ELISA testing confirmed Der p1 concentrations of 9.4 ± 3.3 ng of Der p1/µg of dust particulate. This results in 95 µg of Der p1 per hour of exposure delivered to each subject within the Allergen Biocube.

CONCLUSIONS: The Allergen Biocube delivers dust mite allergen in a controlled and uniform manner and can be used to evaluate the efficacy of therapies designed to reduce or eliminate allergic rhinitis signs and symptoms resulting from dust mite exposure.

In Vitro Tumor Necrotic Factor Alpha Responses To Persistent Chlamydia Pneumoniae Infection From PBMC Of Asthmatic Children

Dr. Kobukki Chotikanatis, MD, 1. Dr. Diana Weaver, MD, 2. Danielle Lent, 3. Eva Estrella, 4. Dr. Margaret R. Hammerschlag, MD, 5. Dr. Rauno O. Joks, MD, FAAAIA1,4, Dr. Stephan Kohlhoff, MD2,5, SUNY Downstate Medical Center, Center for Allergy and Asthma Research, Brooklyn, NY, 2. Kings County Hospital Center, Brooklyn, NY, 3. SUNY Downstate Medical Center, Brooklyn, NY, 4. Department of Medicine, State University of New York Downstate Medical Center, Brooklyn, NY, 5. Center for Allergy and Asthma Research, State University of New York Downstate Medical Center, Brooklyn, NY, 6. Department of Pediatrics, State University of New York Downstate Medical Center, Brooklyn, NY.

RATIONALE: Infection with Chlamydia pneumoniae (Cpn) can lead to exacerbations of asthma. Cpn can also cause persistent infection, to which asthmatics are particularly susceptible. Innate immune responses might have a significant role in susceptibility to persistent infection of Cpn. There are no data on innate cytokine responses in persistent Cpn infection in asthmatics. We studied innate immune responses to persistent Cpn infection by measuring cytokine in asthmatic children and non-asthmatic healthy controls.

METHODS: Peripheral blood mononuclear cells (PBMC) from stable allergic asthmatic children (n=17) and healthy non-asthmatic children (n=9) were mock infected or infected with Cpn AR-39 at MOI of 0.1 and cultured up to 10 days. Tumor necrotic factor alpha (TNF-α) and interferon gamma (IFN-γ) were assayed in supernatant by ELISA. Cytokine levels of uninfected were subtracted from those of infected PBMC in each subject. Quantitative PCR for Cpn was performed on nasopharyngeal swabs. Suggestive evidence of persistent Cpn infection was a presence of Cpn-specific effector memory T lymphocyte response (INF-γ) in the absence of Cpn DNA as we have previously reported.

RESULTS: 62.5% of asthmatics had suggestive evidence of persistent Cpn infection, compared to 0% of healthy controls. In vitro Cpn-induced production of TNF-α was found in 30% of asthmatics with persistent Cpn infection, compare to 77.8% of healthy controls. Significantly, more healthy controls had TNF-α productions than asthmatics with persistent Cpn infection (77.8% vs 30%; p=0.037).

CONCLUSIONS: Cpn-induced TNF-α responses were diminished in asthmatics that suspected to have persistent Cpn infection. Innate immune responses may play the critical role in susceptibility to persistent Cpn infection in asthmatics.

Cytokine Profiles In Bronchoalveolar Lavage In A Mouse Model Of Bronchial Asthma During A(H1N1)pdm09 and Seasonal H1N1 Infection

Dr. Shunji Hasegawa1, Dr. Seigo Okada2, Dr. Hiroyuki Wagiguchi2, Dr. Hideki Hasegawa1, Dr. Akira Aina1, Dr. Komei Shirabe2, Dr. Shiochi Toda2, Dr. Ryo Atsuta3, Dr. Akihiro Hasegawa1, Dr. Takashi Ichiyama4, 1. Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan, 2. Department of Pediatrics, Yamaguchi University Graduate School of Medicine, 3. Department of Pathology, National Institute of Infectious Diseases, 4. Influenza Virus Research Center, National Institute of Infectious Diseases, 5. Yamaguchi Prefectural Institute of Public Health and Environment, 6. Department of Respiratory Medicine, Juntendo University School of Medicine, 7. Department of Microbiology and Immunology, Yamaguchi University Graduate School of Medicine.

RATIONALE: Many reports have shown that A(H1N1)pdm09 infection induced severe pulmonary complications. Bronchial asthma is thought to be one of the risk factors the exacerbate respiratory symptoms of A(H1N1)pdm09-infected patients. However the pathogenesis remains unclear.

METHODS: We induced mouse models of bronchial asthma using ovalbumin and infected with A(H1N1)pdm09 or seasonal H1N1 (1x105 pfu/mouse) intranasally. We analyzed cytokine profiles in bronchoalveolar lavage (BAL) in the mouse models, and compared them between asthma mice and non-asthma mice on the day 7 after infection. We also determined their virus titers on day 7 after infection.

RESULTS: The levels of interleukin (IL)-6, IL-10 and tumor necrosis factor (TNF-α) in asthma mice infected with A(H1N1)pdm09 were significantly higher than those in non-asthma mice on day 7 post-infection. On the other hand, those levels of in asthma mice infected with seasonal H1N1 were significantly lower than those in non-asthma mice after the viral infection. In addition, virus titers in BAL in asthma mice infected with A(H1N1)pdm09 were also significantly higher than those in the non-asthma mice, but not seasonal H1N1 infection.

CONCLUSIONS: Our results suggest that A(H1N1)pdm09 infection may induce more severe pulmonary inflammations and increase replications of virus in patients with bronchial asthma, compared with healthy individuals, unlike seasonal H1N1 infection.
Human Rhinoviruses/Enteroviruses Associated Wheezing In Children

Ananyat Wanitchakhon, MD1, Dr. Wiparat Manuyakorn, MD1, Wasu Kamchaisitan, MD1, Dr. Wasun Chantratra2, Kanjana Premchaiporn1, Suwat Benjaponpitak, MD1; 1Division of Pediatric Allergy/Immunology/Rheumatology, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 2Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

RATIONALE: Respiratory viruses are major causes of wheezing-associated lower respiratory tract infection (LRTI). Human rhinoviruses (HRVs) are associated with wheezing and subsequent asthma in children. This study was to determine viruses that are associated with LRTI and to identify risk factors for human rhinoviruses (HRVs)/enteroviruses (HEVs) induced wheezing in children.

METHODS: Medical records of LRTI children age 0-15 years old whose nasopharyngeal swab samples screened for respiratory viruses using Multiplex-PCR (Luminex®200™ System) during January-December 2012 were reviewed. Subjects with positive for HRVs/HEVs were classified into 2 groups: wheeze and non-wheeze. Risk factors for the HRVs/HEVs induced wheezing were analyzed.

RESULTS: Viruses were detected in 324 out of 520 samples (62%). Among difference aged groups (1-5 years,6-10 years and 11-15 years), children aged 1-5 years had the highest percentage of viral detection (71%vs60%vs37%, P<0.01). HRVs/HEVs were the major viruses identified in all age and were detected in all seasons, while RSV was found only in rainy-winter season. Comparing between wheeze and non-wheeze from HRVs/HEVs, there were no difference in age and sex. Children in wheeze group were significantly older than non-wheeze group (median age 34 months vs. 25 months, P=0.03). Underlying asthma or having fever were significantly associated with wheezing (P=0.04). There is no association of season and wheezing from HRVs/HEVs.

CONCLUSIONS: Virus plays an important role in respiratory tract infection in young children. Seasonal variation has an impact on type of respiratory viral infection. Children with asthma or having fever tend to have wheezing after HRVs/HEVs infection.

Prevalence Of Toxocara Infection In Subjects With Suspected Allergies

Dr. Rosanna M. Qualizza1, Dr. Cristofo Corvoaia2, Dr. Anna Maraschini1; 1Istituti Clinici di Perfezionamento, Milano, Italy, 2Istituti Clinici di perfezionamento, Milano, Italy, 3RCCS Fondazione Ca’ Granda Policlinico, Milano, Italy.

RATIONALE: Toxocara canis is a nematode (roundworm) that infects dogs and cats. Humans become occasional hosts by ingesting embryonated eggs. Once infected, the larvae migrate to various tissues and organs and cause many symptoms. Typical allergy symptoms, including rhinitis, asthma, angioedema, urticaria and dermatitis, may occur. This study evaluated the incidence of Toxocara antibody positivity in a population of individuals with suspected allergies.

METHODS: Since 2003, 18,237 patients with suspected respiratory or skin allergies have been referred to our Allergy unit. All patients underwent various allergy tests (prick tests for inhalants or foods, patch tests). In a subgroup of 1429 patients who suffered from chronic symptoms but showed negative results to tests or unrelated histories, we performed immunological tests including antibodies to T. canis, by ELISA and Western blot. RESULTS: In this subgroup, 385 patients (26.9%) were positive for antibodies to T. Canis; 79 of them were atopic (as defined by positive tests for allergen extracts), and 306 were non-atopic. The most frequent symptoms were: asthma (105 cases), urticaria/angioedema (84), dermatitis (51), conjunctivitis (33) and cough/rhinitis (48). Eosinophilia was present in 27 atopic patients and in 132 non-atopic patients.

CONCLUSIONS: Infestation from Toxocara canis is more frequent than thought, especially in suspected allergy patients with negative test results or unrelated histories. The prevalence of Toxocara infection was around 27% compared to 3.9% reported for the general population in Italy. The present study suggests we should bear in mind the possible role of Toxocara canis in inducing allergy-like symptoms.

Viral-Induced Wheezing

Sirirak Kanchanateeraphong, MD, Gun Phongsamart, MD, Tassalapa Dangsuwan, MD, Mukda Vangveeravong, MD; Queen Sirikit National Institute of Child Health (Children Hospital), Bangkok, Thailand.

RATIONALE: Viral-induced wheezing is one of major causes of recurrent-wheezing in young children. Recent evidence suggests increasing risk of asthma by persistent-wheezing. Cysteiny1-leukotrienes are found in viral-induced wheezing pathway therefore Leukotriene-receptor antagonist has a role in the management. The aims of this study are the effectiveness and optimum-duration of Montelukast in the treatment of acute and post viral-induced wheezing.

METHODS: A randomized-control study of 201children, aged 6-36months who admitted with viral-induced wheezing, were enrolled between July2012 to June2013. The patients were divided in 2groups, with conventional-therapy(n=50) and the other(n=151), Montelukast 5mg was given for 7days. LRI-score and LOS were recorded. Three and six-months follow up for all patients, which are divided in 3 Montelukast-regimens: prn 7days for RTIs(n=46), continued for 1month(n=40), 3months(n=39) and control-group(n=39) were compared.

RESULTS: LRI-score(<3) in Mk-group was 41.48±18.98hrs compared with 50.72±20.74hrs in control-group(p=0.031) and LOS were 3.39±1.29 vs 4.19±1.4days(p=0.001). At 3-month follow up, %total-SFD were increased in intermittent-group 73.02±5.23 vs 68.93±4.98(p<0.001) and in 3month-group 72.06±5.28 vs 68.93±4.98(p=0.006). But only intermittent-group was significantly decreased of recurrent-wheezing(p=0.010).

CONCLUSIONS: Montelukast is effective in acute and post viral-induced wheezing. Optimum-duration in post viral-induced wheezing is suggested in intermittent 7days for RTIs. Long-term follow up is needed to conclude this finding.
659 The Effects of Dexamethasone On Community-Acquired Pneumonia In Children

Prof. Yoon Ho Shin1, Dr. Jun Hwan Kim2, Dr. Jung Won Youn3, Prof. Sun-Hee Choi, MD, PhD4, Dr. Hyeung Yoon Kim, Hye Mi Jee, MD5, Prof. Man-Yong Han, MD, PhD6, Dr. Jin-Tack Kim, MD, PhD7, 1Department of Pediatrics, CHA Medical Center, CHA University School of Medicine, Seoul, South Korea, 2Department of Pediatrics, CHA University School of Medicine, South Korea, 3Department of Pediatrics, Myoungji Hospital, Gyeonggi-do, South Korea, 4Gangdong Kyung Hee University Hospital, Seoul, South Korea, 5Department of Pediatrics, Bundang Jaesaeng Hospital, Seongnam, South Korea, 6Department of Pediatrics, CHA University School of Medicine, Seongnam, Korea, South Korea, 7Department of Pediatrics, CHA University School of Medicine, Seongnam, South Korea, 8Department of Pediatrics, Uijeongbu St. Mary’s Hospital, The Catholic University of Korea, College of Medicine, Uijeongbu, Gyeonggi-Do, South Korea.

RATIONALE: Community-acquired pneumonia (CAP) is a common disorder in children. The treatment options for CAP in pediatric populations are inhalation therapy and initiation of appropriate antibiotic therapy. Occasionally, CAP may progress to more severe pneumonia despite appropriate therapy. The benefit of systemic steroids such as dexamethasone as adjunctive treatment in children with CAP remains uncertain. The aim of the present study was to determine the efficacy of dexamethasone on childhood CAP whose symptoms worsened despite appropriate treatment.

METHODS: We retrospectively evaluated the effect of dexamethasone administration in 66 children with CAP whose clinical and radiographic course deteriorated despite broad-spectrum antibiotics.

RESULTS: The mean (±SD) age was 24.4 ± 17.5 months, and 35 were boys. All children had received appropriate antibiotics at presentation, but they had persistent fever and/or progressively worsening radiographic findings. In addition to broad-spectrum antimicrobial therapy, dexamethasone (0.3 mg/kg) was administered on day 2 (±1.5 days) of admission. The mean days of dexamethasone use were 2.9 ± 1.1 days. Fifty-one children became afebrile within 24 hr, and their clinical status and radiographic findings improved within several days. The mean length of hospitalization was 4.8 ± 2.1 days.

CONCLUSIONS: Dexamethasone therapy appeared to be effective in reducing morbidity and is associated with clinical and radiographic improvement. Therefore, dexamethasone treatment may be beneficial for reducing morbidity in children with community-acquired pneumonia.

660 The Association Between Strongyloides Stercoralis Infection and Allergic Skin Diseases

Dr. Lahari Rampur, MD1, Dr. Gabriele De Vos, MD2, Dr. Golda Hudes, MD, PhD3, Dr. Sunit Jariwala, MD4, 1Albert Einstein/Jacobi medical centre, Bronx, NY, 2Albert Einstein/Columbia College of Medicine, Bronx, NY, 3Albert Einstein/Montefiore Medical Center, New York, NY, 4Albert Einstein/Montefiore Medical Center, New York, NY.

RATIONALE: Studies have suggested that immune responses to helminth infections can promote allergic skin diseases. Our project aims to identify patients presenting with cutaneous symptoms found to have co-existing Strongyloides infection, and to monitor the impact of Strongyloides eradication therapy on allergic symptoms.

METHODS: We conducted a retrospective chart review of 35 patients with serologies positive for Strongyloides stercoralis, and that presented to our allergy clinic with pruritus and/or urticaria. We assessed the presenting symptoms, duration of symptoms, history of atopy, and baseline and post-treatment eosinophil levels. We also noted the baseline medications for urticaria and pruritus, and concomitant anti-histamine and/or oral steroid therapy at the time of ivermectin treatment.

RESULTS: 26 females and 9 males presented to our clinic with pruritus and/or urticaria, and the median patient age was 55 years (SD 16.6). Most patients (71%) were Hispanic, and from South America, Mexico, or the Caribbean islands; 19% of the patients were Black. 68% and 45% of patients demonstrated skin test positivity to environmental and food allergens, respectively. Following ivermectin therapy, 65% of patients reported subjective improvement or resolution of the presenting symptoms. Mean pre-therapy eosinophil count was 705 cells/ul, and mean post-therapy eosinophil count was 218 cells/ul (SD 0.318). The eosinophil count significantly improved among patients with pruritus and urticaria following ivermectin (p = 0.0078).

CONCLUSIONS: Pruritus and urticaria have been described in Strongyloides infection, and ivermectin therapy may improve these symptoms. A high index of suspicion is required for chronic Strongyloides infections in patients presenting with cutaneous symptoms.

661 Effects Of Human Rhinovirus Species On Cytokine Production and Cellular Cytotoxicity In Differentiated Sinus Epithelial Cells

Dr. Kazuyuki Nakagome, MD1,2, Dr. Yury Bochkov, PhD1, Dr. Shamaila Ashraf, PhD1, Ms. Rebecca Brockman-Schneider, MS1, Dr. James E. Gern, MD, FAAAAI1, 1University of Wisconsin School of Medicine and Public Health, Madison, WI, 2Saitama Medical University, Saitama, Japan.

RATIONALE: HRV-A and HRV-C produce more severe clinical illnesses than HRV-B, suggesting that virus characteristics might be different with species or strain of HRV. We previously reported that HRV-B types have slower replication compared to either HRV-A or HRV-C types. We now test the hypothesis that HRV-A and HRV-C cause greater cellular cytotoxicity and induce increased levels of chemokines and interferons in differentiated sinus epithelial cells.

METHODS: We cloned full-length cDNA of HRV-A16, A36, B52, B72, C2, C15 and C41 types from clinical samples, and grew clinical isolates of HRV-A7 and B6 in cultured cells. Sinus epithelial cells were differentiated at air-liquid interface. We infected cells with purified viruses (10^8 RNA copies), and collected basal medium at 24, 48, or 72 hours after infection. We measured cytokine/chemokine secretion in basal medium by multiplex ELISA, and LDH concentration as a marker of cellular cytotoxicity.

RESULTS: Infection with HRV-B induced at least 10-fold less CXCL10, CXCL11, and CCL5 at 48 hours as compared to that of HRV-A or HRV-C (p<0.05). Furthermore, HRV-B induced less IFN-α than HRV-A or HRV-C. These effects persisted even after adjusting for differences in virus load (p<0.05). Moreover, HRV-B infected cells released less LDH in basal medium at 72 hours than those infected with HRV-A or HRV-C (p<0.05).

CONCLUSIONS: Our results indicate that HRV-B types induced lower cytokine/chemokine production and cellular cytotoxicity compared to either HRV-A or HRV-C types. This characteristic may contribute to reduced cellular severity of illnesses caused by HRV-B.
662 Human Rhinovirus Bronchiolitis Predominant In Very Low Birthweight Infants In Argentina

Dr. Jodell E. Linder-Jackson, PhD1, Tatjana E. Plachco2, Lucrecia Bossi3, Gabriela Bauer3, Fernande P. Polack1, Romina P. Lüster2, Eva K. Kathryn Miller. MD, MPH1, 1Vanderbilt, TN, 2Hospital de Pediatría Garrahan, Argentina, 3Maternidad Sarda, Argentina, 1Fundación Infant, Vanderbilt University, Argentina, 2Fundación Infant, Argentina, 6Vanderbilt University Medical Center, Nashville, TN.

RATIONALE: Human rhinovirus (HRV) infections early in life may lead to asthma, especially when accompanied by recurrent wheezing. Premature infants are at increased risk for asthma, and the role of HRV in this group is largely unexplored.

METHODS: In this prospective cohort study, premature infants weighing <1500gm were enrolled in the NICU from June 2011 until October 2012. Infants were followed for the first year of life, nasal swabs collected at monthly well visits, and nasal aspirates taken during all acute respiratory infections (ARI). Real time rt-PCR for respiratory viruses was conducted on specimens.

RESULTS: Of 139 ARI samples, 66% were positive for HRV, and 53% of infants with HRV had bronchiolitis. There were 32 (26%) hospitalizations: 50% positive for HRV, 15% respiratory syncytial virus (RSV), and 15% metapneumovirus (MPV). MPV was more likely to be associated with hospitalizations than outpatient visits for ARIs (p=0.0002). Of HRV-associated ARIs, 70% were species HRVA, 7%HRVB, and 23%HRVC. Twenty-seven percent of mothers smoked during pregnancy and 55% had smokers in the home; 41% of infants had bronchopulmonary dysplasia (BPD).

CONCLUSIONS: Rhinovirus is the predominant infection associated with ARI in VLBW infants in Argentina. HRV, RSV, and MPV are all associated with infant hospitalizations. Bronchiolitis and BPD were common in this population, suggesting that many risk factors for the development of asthma later in life are affecting these premature infants and they should be targeted for preventive measures.

663 Association Of Vitamin D Status With Recurrent Wheezers and Lower Respiratory Infection In Pre-School Children

Prof. Jin-A. Jung, MD1, Prof. Ja Hyenge Kim, MD2, Prof. Ju Suk Lee, MD, PhD3, 1Dong-A University College of Medicine, Busan, 2Ulsan University Hospital, Ulsan, South Korea, 3Sungkyunkwan university, Changwon, South Korea.

RATIONALE: Recurrent wheezers are common in pre-school children and is different clinical course from lower respiratory tract infection. Although the precise mechanisms underlying vitamin D’s effects on allergic diseases have not been elucidated, vitamin D deficiency has also been inconsistently associated with atopic diseases.

METHODS: Serum 25(OH)D concentrations were measured in patients under 4 years of age admitted to hospital with a diagnosis of pneumonia or bronchitis (group A, n=58) and recurrent wheezing more than 4 times (group B, n=32) from March 2011 to February 2013 as well as in healthy patients of similar age without respiratory symptoms (control group, n=28). We also measured BMI, immunoglobulin G/A/M, WBC, platelet, AST, ALT, ALP, total eosinophil count and total IgE and reviewed their personal/family history of allergic diseases through the medical record.

RESULTS: The mean serum 25(OH)D level were similar among the3 groups (group A 23.6±10.8 versus group B 24.1±6.9 vs. group C 24.2±8.5 ng/mL). There was no significant difference in the prevalence of 25(OH)D deficiency and insufficiency among the 3 groups (for <30 ng/mL, group A 71.0% vs. group B 85.8% vs. group C 75.0%; P=0.75). BMI, immunoglobulin G/A/M, WBC, platelet, AST, ALT, ALP, total eosinophil count and total IgE were no significant differences among the 3 groups.

CONCLUSIONS: In our study, no difference was observed in vitamin D levels and other parameters among the LRI and recurrent wheezers.

664 Safety and Efficacy Of Dupilumab Versus Placebo For Moderate-To-Severe Atopic Dermatitis In Patients Using Topical Corticosteroids (TCS): Greater Efficacy Observed With Concomitant Therapy Compared To TCS Alone

Dr. Diamant Thaci, MD1, Dr. Margitta Worm, MD2, Dr. Haibo Ren, PhD3, Dr. Steven Weinstein, MD, PhD4, Dr. Neil Graham, MD4, Dr. Gianluca Pirozzi, MD, PhD5, Warren Brooks, PhD6, Dr. Marius Ardeleanu, MD1, 1Universität zu Lübeck, Lubeck, Germany, 2Charite - Universitätsmedizin Berlin. Berlin, Germany, 3Regeneron Pharmaceuticals, Inc., Basking Ridge, NJ, 4Regeneron Pharmaceuticals, Inc., Tarrytown, NY, 5Sanofi, Bridgewater, NJ.

RATIONALE: TCS are a key component of atopic dermatitis (AD) treatment. We evaluated dupilumab, a fully human monoclonal antibody against the IL-4 receptor alpha, administered concomitantly with TCS in adults with active moderate-to-severe AD (NCT01639040).

METHODS: Patients were randomized to weekly subcutaneous injections of dupilumab 300mg (n=11) or placebo (PBO; n=10) for 4 weeks plus 8 weeks of follow-up. All patients used a standardized TCS regimen. Occurrence of treatment-emergent adverse events (TEAEs) was the primary outcome. Exploratory efficacy endpoints evaluated through the treatment and follow-up periods included change in EASI, SCORAD, IGA, NRS pruritus scores, and EASI50 (≥50% improvement).

RESULTS: Thirty patients completed treatment with 41 TEAEs in 12 (57.1%) dupilumab patients and 14 TEAEs in 7 (70.0%) PBO patients; 1 serious TEAE occurred and led to treatment discontinuation (PBO patient). Most frequent TEAEs were nasopharyngitis (23.8% vs 20.0%; dupilumab vs PBO), headache, oropharyngeal pain (both 14.3% vs 10.0%). At Day 29, 100% of patients on dupilumab+TCS achieved EASI50 responses compared to 50% on PBO+TCS (p=0.0015). Significant improvements from baseline with dupilumab, relative to TCS alone, in EASI, IGA, SCORAD and pruritus NRS were achieved and persisted up to day 64. Of note, patients on dupilumab used approximately 50% less TCS during the treatment period, mean(SD) 48.7g(40.3) vs 99.4g(152.5). This was associated with faster AD lesion clearing.

CONCLUSIONS: Concomitant treatment with dupilumab+TCS was generally well tolerated. Relative to TCS alone, dupilumab+TCS provided marked, sustained, and significant improvement in clinical efficacy measures, despite use of less TCS.
A Lipid Plant Extract From Chamaecyparis Obtusa Induces Filaggrin and Human Beta-Defensin - 3

Mr. Byung Eui Kim, MD, PhD1, Mr. Gwui Cheol Kim, PhD2, Ms. Hee Jin Kim3, Donald Y. M. Leung, MD, PhD, FAAAAI1.1National Jewish Health, Denver, CO, 2Jeonnam Nano Bio Research Center.

RATIONALE: Patients with atopic dermatitis suffer from skin barrier defects and recurrent skin infections due to filaggrin (FLG) deficiency and reduced antimicrobial peptide expression. Anecdotal reports suggest that plant extracts from Chamaecyparis Obtusa have beneficial effects on skin health. However, it has not been reported whether they modulate FLG and human beta defensin (HBD)-3. Therefore, we investigated whether a lipid plant extract from Chamaecyparis Obtusa induces FLG and HBD-3.

METHODS: We prepared a lipid extract from Chamaecyparis Obtusa using the supercritical fluid extraction method. Human primary keratinocytes were differentiated and stimulated with various concentrations of the lipid plant extract in the presence and absence of IL-4 (20 ng/mL) and IL-13 (50 ng/mL). Gene expression of FLG and HBD-3 was evaluated using real time RT-PCR. We performed LDH assay to examine if the lipid plant extract is toxic to keratinocytes.

RESULTS: Gene expression of FLG (2.22 ± 0.08, P < 0.001) and HBD-3 (26.42 ± 3.41, P < 0.01) was significantly increased in keratinocytes treated with 0.001% of lipid plant extract compared with cells treated media alone (0.40 ± 0.08, 6.73 ± 2.30 respectively). FLG (1.07 ± 0.17, P < 0.05) and HBD-3 (11.68 ± 1.90, P < 0.01) was significantly upregulated in keratinocytes treated with a combination of the lipid plant extract, IL-4 and IL-13 compared with cells treated with IL-4 and IL-13 (0.24 ± 0.08, 2.71 ± 0.53 respectively). The lipid plant extract did not show toxicity to keratinocytes.

CONCLUSIONS: The lipid plant extract from Chamaecyparis Obtusa induces FLG and HBD-3, and overcomes the inhibitory effects of Th2 cytokines on FLG and HBD-3 induction. Clinical studies are needed to determine whether it can benefit skin barrier.

Identification Of Novel Gene Signatures In Atopic Dermatitis Complicated By Eczea Herpeticus

Dr. Lianghua Bin, MD, PhD1, Dr. Michael G. Edwards2, Dr. Ryan Heiser, PhD3, Mrs. Joanne Streib, BA1, Ms. Brittany Richers1, Donald Y. M. Leung, MD, PhD, FAAAAI1.1National Jewish Health, Denver, CO, 2University of Colorado at Denver.

RATIONALE: A subset of atopic dermatitis (AD) is prone to disseminated herpes simplex virus (HSV) infection, i.e. eczea herpeticus (AEDH+). Biomarkers that identify AEDH+ subjects are lacking.

METHODS: A RNA-sequencing (RNA-seq) approach was applied to evaluate global transcriptomic changes at single nucleotide resolution using peripheral blood mononuclear cells (PBMCs) from 5 AEDH+ and 6 AD without a history of EH (AEDH-). Candidate genes were confirmed by PCR or ELISA in 20 AEDH+, 20 AEDH-, and 20 non-atopic controls (NA).

RESULTS: RNA-seq analysis revealed that AEDH+ PBMCs had distinct transcriptional profiles when compared to AEDH- PBMCs following HSV-1 stimulation: 792 genes were different at a False Discovery Rate (FDR) < 0.05 (ANOVA). Ingenuity pathway analysis identified that the important innate immune regulator IRF7 signaling pathway was inhibited in AEDH+, based on the down-regulation of 16 type I and type III interferons (IFNs). Only one gene, GSTM4, was different between the two groups (FDR < 0.05, ANOVA) following sham treatment. We further validated that IFNs and IL-29 proteins were significantly decreased (p<0.05) in HSV-1 stimulated PBMCs from AEDH+ compared to AEDH- and NA by ELISA, and GSTM4 transcripts were significantly reduced in both sham (p=0.0332) and HSV-1(p=0.0009) treated AEDH+ PBMCs compared to AEDH- and NA by real-time PCR.

CONCLUSIONS: PBMCs from AEDH+ have a distinct immune response to HSV-1 exposure compared to AEDH- and NA. Inhibition of the IRF7 pathway in AEDH+ may be an important mechanism for increased susceptibility to disseminated viral infection. Additionally, GSTM4 is a novel baseline biomarker distinguishing AEDH+ versus AEDH- subjects.

Therapeutic Effects Of Recombinant Salmonella Typhimurium Expressing TLR8 miRNA On Atopic Dermatitis

Dr. Wonsuck Yoon1, Prof. Ji Tae Choung, MD2, Dr. Young Yoo, MD, PhD1.1Department of Life Science and Biotechnology, Seoul, South Korea, 2Korea Univ. Medical Center, Seoul, 3Department of Pediatrics, College of Medicine, Korea University, Seoul, South Korea.

RATIONALE: Th-2-biased immune responses are known to play a key role in the pathogenesis of atopic dermatitis. In particular, TLRs play important roles in inflammation and innate immune response to pathogens. TLR8 is a potent inducer of proinflammatory cytokines. TLRs are also correlated with disease severity in atopic dermatitis. In this study, we hypothesized the immune suppression using bacteria expressing TLR8 miRNA would be induced therapeutic effects on atopic diseases.

METHODS: The recombinant strain of Salmonella typhimurium expressing TLR8 miRNA (ST-miRTLR8) was prepared for in vivo knockdown of TLR8. The Ig-E, Interleukin-4 (IL-4), TLR8 and interferon-g (IFNγ) were examined after treatments with ST-miRTLR8 in murine atopic model. In addition, atopic patient’s blood samples were collected and examined for TLR8 expression.

RESULTS: We constructed a recombinant strain of Salmonella typhimurium expressing TLR8 miRNA (ST-miRTLR8) for the in vivo knockdown of TLR8. The TLR8 expression was decreased by treatment of ST-miRTLR8 in murine atopic model. In addition, TLR8 gene expression was higher in pediatric patients’ blood monocytes with atopic dermatitis compared to the samples taken from control groups.

CONCLUSIONS: TLR8 gene was more expressed in pediatric patients with atopic dermatitis. ST-miRTLR8 were suppressed TLR8 gene effectively and induced therapeutic effects against atopic dermatitis in mice.
669 Correlation Between Serum 25-Hydroxyvitamin D Levels and Severity Of Atopic Dermatitis In Children
Dr. Sung Soon / BUSAN MARY, BUSAN, South Korea.

RATIONALE: Allergic disease has increased over the past decades in nearly all nations. Many studies have been the association between vitamin D and allergic disease; but, is ambiguous and unclear. The aim of this study is to determine whether 25-hydroxyvitamin D level is associated with severity of allergic atopic dermatitis.

METHODS: The study was conducted on 170 non-atopic dermatitis and 170 atopic dermatitis (allergic=85, non-allergic =85) children aged 1-18 years. Using the SCORAD index, we evaluated the severity of disease and Serum 25-hydroxy vitamin D3 were determined. The relationship between serum vitamin D levels, SCORAD index, ECP, eosinophil count and total IgE were examined in atopic allergic dermatitis children.

RESULTS: We found severe, moderate and mild AD in 57(33%), 58(34%) and 55(32%) patients, respectively. In allergic atopic dermatitis children, 25-hydroxy vitamin D levels had direct and significant correlations with SCORAD index ,total IgE and age. (P<0.05) But, there were no associations between vitamin D levels and eosinophil counts, ECP, sex. (P>0.05)

CONCLUSIONS: The results from this study indicate that serum concentration of 25-hydroxyvitamin D is inversely correlated with clinical severity of allergic atopic dermatitis in children. So, we suggest that Vitamin D may play an important role in the pathogenesis of atopic dermatitis via IgE-mediated pathway.

670 Association Between Prenatal and Early Life Vitamin D Levels and Allergic Outcome At Age 2 Years
Ganesa Wegienka, PhD1, Ms. Suzanne Havstad, MA1, Kimberley J. Woodcroft, PhD1, Dr. Dennis Owby, MD FAAAAI2, Dr. Edward M. Zoratti, MD, FAAAAI1, Dr. Christine Cole Johnson, PhD, MPH, FAAAAI1; 1Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, 2Department of Pediatrics Georgia Regents University, Augusta, GA, 3Henry Ford Health System, Detroit, MI.

RATIONALE: The role of vitamin D in allergic disease remains unclear. The objective was to assess whether 25-hydroxyvitamin D [25(OH)D] levels during pregnancy, in cord blood, or at age 2 years were associated with eczema or total IgE at age 2 years.

METHODS: 25(OH)D was measured in the blood samples from women and their children enrolled in the WHEALS birth cohort study (n=218 maternal child pairs) in the Detroit area. Serum samples were collected during pregnancy, at delivery, and during a physician examination for eczema at age 2 years. Total IgE was measured at 2 years. 25(OH)D units are ng/ml and measures were adjusted for the analyses that used t-tests and Pearson correlations.

RESULTS: 25(OH)D did not significantly differ (all p>0.15) between those who did and did not have eczema among Black (prenatal: mean=19.7 (SD=9.4) versus 19.8 (10.0); cord blood: 9.1 (7.6) versus 8.9 (5.6); 2 year: 22.5 (9.1) versus 23.6 (7.2)) or White children (prenatal: 31.1 (17.8) versus 34.2 (10.7); cord blood: 14.6 (6.3) versus 15.7 (6.3); 2 year: 22.7 (5.9) versus 26.7 (8.9). Among Black children, prenatal 25(OH)D level was weakly positively correlated with total IgE (r=0.12, p=0.02). No other 25(OH)D levels were correlated with total IgE for Black or White children. Results were unchanged if 25(OH)D cutoffpoints for insufficiency (<30ng/ml) or deficiency (<20ng/ml) were used.

CONCLUSIONS: These data do not indicate an association between 25(OH)D level and eczema or total IgE in Black or White children.

671 Association Between Sun Exposure During The First 6 Months Of Life And The Cumulative Incidence Of Atopic Dermatitis In Infants
Dr. Miwa Shinohara, MD, PhD1, Dr. Kenji Matsumoto, MD, PhD2; 1Department of Pediatric Allergy and Clinical Research, Shinhizu National Hospital, Yotsukaido, Japan, 2Department of Allergy and Immunology, National Research Institute for Child Health and Development, Tokyo, Japan.

RATIONALE: Ultraviolet (UV) B radiation-induced vitamin D decreases the risk of infections, and subsequently reduces the development of autoimmune diseases by alteration of the T<sub>H1</sub>/T<sub>H2</sub> balance (Grant WB, 2008, Photochem Photobiol). Furthermore, with multiple immunomodulatory pathways, sunlight, both UVB and UVA, independently suppresses immunity in the skin and internal organs, and reduces microorganisms in environment. On the other hand, neonatal T<sub>H2</sub>-dominant immunity develops towards tolerance and/or T<sub>H1</sub>-dominant immunity by complex gene-environment interactions, such as microorganisms, diets and tobacco smoke. Therefore, we investigated whether sun exposure influences the cumulative incidence of atopic dermatitis (AD) during infancy.

METHODS: Of 1,436 parent-infant pairs, 736 (52.3%) infants with breast- and mixed-feeding and without supplementary vitamin intake were enrolled in this cross-sectional study in 2009. Postnatal infantile sun exposure, prenatal and postnatal maternal supplementary vitamin intake, parental family history of allergic diseases and physician-diagnosed AD were assessed by self-writing questionnaires. An adjusted logistic regression model was analyzed using STATA software.

RESULTS: The recovery rate was 97.2% (1,436/1,476). Infants with a family history of allergic diseases (adjusted OR, 5.72; 95% CI, 1.06-3.09 × 10) or with sun exposure during the first 6 months of life (adjusted OR, 3.70 × 10; 95% CI, 3.18 × 10-4.32 × 10<sup>3</sup>) significantly increased the cumulative incidence of AD than those without the family history or without sun exposure, respectively. Maternal supplementary vitamin intake did not significantly associate with the cumulative incidence of AD in their infants.

CONCLUSIONS: Sun exposure during early infancy may play an important immunomodulatory role in the subsequent development of AD in infants.

672 Dampness In The Water-Damaged Homes Affects The Severity Of Atopic Dermatitis In Children
Prof. Sungchul Seo1; Prof. Ji Tae Choung, MD,2 Dr. Young Yoo, MD, PhD3, Dr. Wonsuck Yoon4, Prof. Kangmo Ahn, MD, PhD2, Dr. Jihyun Kim, MD3; 1The Environmental Health Center for Asthma, Korea University, Seoul, 2Korea Univ. Medical Center, Seoul, 3Department of Pediatrics, College of Medicine, Korea University, Seoul, South Korea, 4Department of Life Science and Biotechnology, Seoul, South Korea.

RATIONALE: While low humidity is known to exacerbate the symptoms of atopic dermatitis (AD) by increasing transdermal water loss, there are a very few reports to show the effect of dampness on this disease. We determined water damage or dampness in the houses of children with AD by using the infrared (IR) camera, not simple questionnaire, and evaluated the relationship between the presence of dampness and the severity of AD.

METHODS: We visited 52 houses of patients with AD, and obtained airborne samples from the living room and child’s bedroom, respectively. Dampness was determined by thermal assessments using an IR camera and by the presence of visible mold or water stains. The concentrations of airborne mold, airborne bacteria, formaldehyde, and total volatile organic compounds were also measured. The effect of water damage on the severity of AD was analyzed by comparing dampness and other aggravating factors between water-damaged and non-damaged homes.

RESULTS: IR camera-proven dampness was observed in 31 homes (59.6%), and the concentrations of airborne mold were significantly higher in water-damaged homes than in non-damaged homes (P=0.0013). However, there was no difference in the airborne mold levels between homes with and without visible mold or water stains. Logistic regression analyses demonstrated that water-damaged home was significantly related with moderate-to severe AD (aOR, 15.10; 95% CI, 1.93 – 118.08) (P=0.0038).

CONCLUSIONS: Dampness in association with increased concentrations of airborne mold affects the severity of AD in children. An IR camera could be a promising tool for detecting dampness in water-damaged homes.
**673** Mycotoxin Aggravates Atopic Dermatitis Via TSLP Induced Th2 Inflammation

Ms. Seung-Hwa Lee¹, Ms. Ha-Jung Kim¹, Prof. Soo-Jong Hong, MD, PhD²,³; ¹Asan Institute for Life Sciences, University of Ulsan College of Medicine, ²Department of Pediatrics, Asan Medical Center, Childhood Asthma Atopy Center, South Korea, ³Research Center for Standardization of Allergic Disease, University of Ulsan College of Medicine, Seoul, Korea.

**RATIONALE:** Mycotoxins, secondary metabolites of molds, have an effect on impairment of immune system. The exposure of mycotoxin is associated with the development of atopic dermatitis (AD). However, the precise mechanisms of the allergy-promoting effect of mycotoxins remain unclear. This study was to investigate the effect of mycotoxin exposure on AD in a mouse model.

**METHODS:** To investigate the effect of mycotoxin in AD, SKH-1 hairless mice were exposed via skin to patulin (mycotoxin) during ovalbumin (OVA) sensitization for developing the mouse model of AD. Evaluation of clinical signs (erythema), transepidermal water loss (TEWL), histopathology (H&E stain), and immunohistochemistry of TSLP and IL-4 on skin was performed. In addition, serum OVA-specific IgE and OVA-specific IgG1 were measured to confirm systemic immunization.

**RESULTS:** Patulin exposure of OVA-induced mice exacerbated the phenotypes (e.g., clinical score, TEWL, and skin inflammation) of AD compared to only OVA-induced mice. In addition, the levels of OVA-specific IgE and OVA-specific IgG1 in serum were significantly increased after the application of patulin with OVA. Furthermore, the exposure of patulin with OVA increased the skin expression of TSLP and IL-4 compared to only OVA-induced mice.

**CONCLUSIONS:** The application of patulin aggravates symptoms and inflammation of AD. Exposure of mycotoxin might increases the inflammatory response in AD by systemic Th2 immunity via a TSLP dependent mechanism.

**674** Early Skin Care By “Experienced Mothers” May Prevent Sensitization In Infants With Atopic Dermatitis

Dr. Atsushi Yamashita, Dr. Mizuho Naga, MD, Ms. Kanae Furuya, Dr. Junya Hirayama, Dr. Keigo Kainuma, MD, Dr. Takao Fujisawa, MD, FAAAAI; Institute for Clinical Research, Mie National Hospital.

**RATIONALE:** Caregivers of infants with severe atopic dermatitis (AD) usually learn pivotal importance of skin care when they receive proper treatment and experience favorable outcome of AD by the treatment. Then, an ‘experienced’ mother tends to start skin care very early for her next child hoping to prevent bad outcome she went through with her first one. Since it has been suggested that epidermal barrier dysfunction in AD promotes allergen sensitization, we hypothesized that early skin care by ‘experienced’ mothers may alleviate sensitization of infants with AD, possibly through protection of skin barrier function.

**METHODS:** To investigate whether IgE sensitization levels to food and house dust mite (HDM) in AD infants of ‘experienced’ mothers are lower than those of ‘naïve’ mothers who first experienced AD in their child. Retrospective analysis of 55 infants with AD was performed. They were divided into 2 groups; 45 infants who were first-born children or had elder siblings without AD, designated as ‘naïve’ group and 10 infants who had elder siblings with severe AD, designated as ‘experienced’ group.

**RESULTS:** Severity and age at initial presentation was higher in ‘naïve’ group than in ‘experienced’ group. Serum IgE, egg white-specific IgE and HDM-specific IgE levels from 6 months to 18 months old tended to be higher in ‘naïve’ group than in ‘experienced’ group.

**CONCLUSIONS:** Early skin care presumably done by ‘experienced’ mothers may be beneficial to protect AD infants from ‘sensitization spreading’.

**675** Association Of Bathing Habits To Pruritus and Allergic Disease

Dr. Kanwaltjit K. Brar, MD¹, Dr. Rauno O. Joks, MD, FAAAAI², Dr. Hamid Moailem, MD³, SUNY Downstate Medical Center, Brooklyn, NY, ²Center for Allergy and Asthma Research, State University of New York Downstate Medical Center, Brooklyn, NY.

**RATIONALE:** Traditionally, physicians have advised limiting bathing frequency and duration for patients with pruritis. Our patient population is primarily Afro-Caribbean immigrants, whose practice of frequent bathing to stave off heat persists after migration to the cooler climate of Brooklyn. We sought to evaluate for an association between bathing habits and pruritis in our adult allergy patients. We report preliminary data from our pilot study.

**METHODS:** IRB approval was obtained, patients (n = 17) were recruited from the adult allergy clinic of University Hospital of Brooklyn, and King’s County Hospital. Our survey addressed demographics, bathing habits, medical, and environmental history. Bathing exposure time was determined by multiplying frequency of bathing with the duration of bath or shower. Pruritis was measured using a 5-D itch scale, a validated tool used to measure pruritis. Scores ranged from 5 (absent pruritis) to 25 (very severe pruritis).

**RESULTS:** Among the 17 patients, 16 (94%) were female; 11 (65%) originated from the Caribbean Islands or South America. Average bath exposure time was 33 minutes/day. Patients who had a bath exposure time of greater than 10 minutes had a mean pruritis score of 12.75, compared with patients who had a bath exposure time of less than 10 minutes who had a mean pruritis score of 10. A correlation with bath exposure time and pruritis score was not found (p = 0.83).

**CONCLUSIONS:** This is the first study to evaluate bathing habits and their association to pruritis. Bath exposure time is a novel method of quantifying bathing duration and bathing frequency.

**676** A Molecular Mechanism Underlying Atopic Dermatitis In Hyper-IgE Syndrome

Masako Saito, PhD¹, Dr. Hajime Karasuyama, MD, PhD², Dr. Yoshiyuki Minegishi, MD, PhD³; ¹Division of Molecular Medicine, Institute for Genome Research, The University of Tokushima, Tokushima, Japan, ²Tokyo Medical and Dentistry Graduate School, Tokyo, Japan, ³Division of Molecular Medicine, Institute for Genome Research, The University of Tokushima.

**RATIONALE:** Hyper-IgE syndrome (HIES) is a primary immunodeficiency characterized by extremely high serum IgE levels, atopic dermatitis, staphylococcal infections and eosinophilia. Dominant negative (DN) mutations in the STAT3 gene is a major genetic origin of the HIES. We recently established STAT3-DN knock-in mice, which did not develop atopic dermatitis spontaneously under SPF conditions. Mice were sensitized with oxazolone (Ox) on day -6, and challenged every other day from day 0. Ear thickness was measured and cells recovered from the ear skin were evaluated immunologically.

**METHODS:** Ox-sensitized and challenged STAT3-DN mice showed significantly greater ear swelling after day 10 compared to STAT3-WT mice. More CD4+ T cells, eosinophils and basophils but less neutrophils were infiltrated in STAT3-DN mice compared to STAT3-WT mice at day 15. STAT3-DN mice have significantly higher Ox-specific IgE levels compared to STAT3-WT mice. In the skin lesion, the expression of IFNg, IL-4, CXCL9, CCL17, CCL22, and CCL5 was increased in STAT3-DN mice. IFNg was predominantly expressed by CD4+ T cells, and IL-4 was expressed by basophils. CCL17 and CCL22 were expressed by DCs, and CXCL9 was expressed by CD45 negative cells. CCL5, which can recruit eosinophils, was expressed mainly by DCs. Although eosinophilia in HIES is considered to be associated with the development of atopic dermatitis, eosinophil deficient STAT3-DN mice showed equivalent ear swelling compared to eosinophil sufficient STAT3-DN mice.

**CONCLUSIONS:** These results suggest that eosinophilia is not involved in the development of atopic dermatitis in HIES.
**Racial Differences In The Relationship Of Total and Food-Specific IgE To Atopic Dermatitis In Childhood**

Dr. Gillian Bassirpour, MD, Dr. Edward M. Zoratti, MD, FAAAAI, Ganesa Wegienka, PhD, Ms. Suzanne Havstad, M.A., Alexandra Sitarik, MS, Dr. Haejin Kim, MD, Dr. Dennis Ownby, MD, FAAAAI, Dr. Christine Cole Johnson, PhD, MPH, FAAAAI, Division of Allergy and Clinical Immunology, Henry Ford Hospital, Detroit, MI, Henry Ford Health System, Detroit, MI, Department of Public Health Sciences, Henry Ford Hospital, Detroit, MI, Department of Pediatrics Georgia Regents University, Augusta, GA.

**RATIONAL: Elevated IgE is a hallmark of atopic dermatitis (AD). Although AD and elevated IgE are more prevalent in African American (AA) compared to Caucasian (C) children, it is unknown if the relationship between AD and IgE is similar between these groups.**

**METHODS: Data were analyzed from 371 AA and 138 C children in the Detroit WHEALS birth cohort. AD was defined as current or past physician diagnosis as determined at a study-located encounter at 2-3 years of age. Total and food-specific IgE (sIgE) levels for peanut, egg, and milk were determined. Univariate and multiple logistic regression models, stratified by race of child, were used to assess the association of AD with both total IgE and food sensitization. Food sensitization was included in the model as either the sum of the 3 food sIgEs or, separately, having at least one positive sIgE (>0.35 kU/L) to food.**

**RESULTS: Elevated total IgE was independently associated with AD only among Caucasian children [adjusted odds ratio (aOR) 1.81, 95% CI 1.03, 3.15, p = 0.038]. In contrast, the sum of the sIgEs for the foods [aOR 1.46, 95% CI 1.15, 1.86, p = 0.002] or the presence of ≥ 1 positive food sIgE [aOR 2.05, 95% CI 1.09, 3.87, p = 0.027] was independently associated with AD among AA children only.**

**CONCLUSIONS: The association of IgE to AD differs among AA and C children. Food sIgE is independently linked to AD among AA children. Such an association is not evident in C children after adjustment for total IgE.**

---

**Major Culprit Allergen Sensitization Patterns According To Age In Korean Atopic Dermatitis Patients**

Hye Jung Park, Jae-Hyun Lee, Kyung-Yong Jeong, Kyung-Hee Park, Yoon-Ju Kim, Jung-Won Park, Division of Allergy and Clinical Immunology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea, Institute of Allergy, Yonsei University College of Medicine, Seoul, South Korea.

**RATIONAL: Atopic dermatitis (AD) usually occur in childhood and some may be remitted but others persist to adulthood. Culprit allergens may be changed as the disease progress. In this study, we tried to distinguish important culprit allergens according to age in AD patients.**

**METHODS: Total 110 AD patients’ sera were tested to detect allergen specific immunoglobulin E (sIgE) for each 11 allergens - milk, egg white, peanut, shrimp, wheat, Dermatophagoides farinaceae (DF), Candida albicans (CA), Trichophyton rubrum (TR), Pityrosporum ovale (PO), Staphylococcal enterotoxin B (SBE), recombinant Hom s 1. Mean age of the enrolled patients was 12.2 years old (range: 1~47).**

**RESULTS: Sensitization rates of allergens were varied from 17.3% (for TR) to 52.7% (for DF). Milk and egg white sIgEs were more detected in young aged patients and their sensitization rates decreased according to age increment. Conversely, sensitization rates of shrimp, DF, SBE, CA, TR, PO and SBE increased according to age increment. There were no differences in peanut and wheat sensitization rates. Interestingly, rHom s 1 sIgE was detected more frequently in younger patients (36.5% in age 1-5 vs. 12.1% in age ≥ 18).**

**CONCLUSIONS: There is distinct difference of sensitization pattern. Milk and egg white are more important allergens in young aged patients. On the contrary, microbial and house dust mite allergens were more important in adult patients. Autoantigen can also be important cause at early stage of AD.**

---

**Protein Microarray: IgE-Profiling Of Brazilians With Atopic Dermatitis**

Lucia Camargo Lopes de Oliveira1, Roberta Faria Camilo-Araujo1, Isabel Rugue Genov1, Dr. Renata R. Cocco2, Dr. Marcia Mallozi, MD3, Prof. Nelson A. Rosario, MD, PhD, FAAAAI1, Prof. Dirceu Sole, MD, MD3, UNIFESP, Federal University of São Paulo, Brazil, Federal University of Santa Paulo, Brazil, Federal University of Sao Paulo, Sao Paulo, Brazil.

**RATIONALE: to identify for the first time the IgE-sensitization profile among Brazilian patients with different severity of atopic dermatitis (AD) using protein microarray techniques. We hypothesized the greater the severity the disease, the more common the sensitization to food allergens.**

**METHODS: 59 AD patients classified according to the severity scoring of AD index (SCORAD,SI) took part on this study. Peripheral blood samples were collected after consent approval and their IgE-sensitization profile was determined using ImmunoCAP-ISAC™ (Thermo Scientific). The study was approved by the Brazilian ethical committee (# 12551413.2.0000.5505 on www.saude.gov.br/plataformabrasil, funded by FAPESP nº 2009/53303-3). Data were expressed as mean, median and range. Kruskal-Wallis test was used to analyze differences among groups since they had no normal distribution.**

**RESULTS: patients aged from 0.75 to 23.4 years (mean = 8.25y) were distributed as following: mild (A, n = 17, median age = 12.2y, mean SI = 23.7), moderate (B, n = 13, median age = 8.5y, mean SI = 42.25), and severe (C, n = 29, median age =8.0y, mean SI = 54.6y). Mean sensitization (number of allergens per individual) to all allergens [A:8.6 (range 2-38), B:14.7 (6-41), C:13.3 (1-39)] and just to food allergens [A:1.7 (0-18); B:3.8 (0-21); 3.4 (0-19)] were not significant different between groups (Kruskal-Wallis test, p = 0.0641).**

**CONCLUSIONS: food sensitization was not related to intensity of atopic dermatitis in this Brazilian studied group.**

---

**Relationship Between Dietary Food and Nutrient Intakes and Bone Mineral Density In Childhood Eczema**

Dr. Ting Fan Leung, MD, FRCPC, FAAAAI, Ms. Flora Yin-ying Kwok, MPhil, Dr. Yvonne Yi-fong Ho, MPhil, Dr. Susan Shuxin Wang, PhD, Ms. Patty Pui-pui Tse, MSc, Prof. Gary Wing-kin Wong, MD, FRCPCH, Dr. Kam Lun Ellis Hon, MD, FAAP; Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong.

**RATIONALE: Food avoidance is common among eczema children, but there is limited data regarding effects of such practice on bone mineral density (BMD). This study evaluated nutrient intakes and BMD in Hong Kong eczema children.**

**METHODS: Chinese children with and without eczema were recruited from allergy or dermatology clinics. Their nutrient intakes were assessed by food frequency questionnaire and analyzed using Foodworks Professional software (Xyris, Brisbane, Australia). BMD was measured at mid-point of radius in the non-dominant arm and left tibia by quantitative ultrasound bone somometry (Omnisense 7000P, BeamMed, Tikva, Israel).**

**RESULTS: 114 eczema children and 60 controls were recruited. Calcium and vitamin D intakes were lower in moderate-to-severe eczema (50) and mild (64) eczema than controls (medians for calcium in mg/MJ: 0.10, 0.14 and 0.27, P = 0.001 for trend; for vitamin D in m/J: 0.88, 0.90 and 1.12, P = 0.015).**

**CONCLUSIONS: this study characterizes pattern of dietary restriction in Hong Kong eczema children, who have low calcium and vitamin D intakes. Despite this, BMD is similar between eczema and controls. Higher BMD is found in patients with higher calcium intakes. Funding: Research Committee Group Research Scheme (3110087) and Direct Grant for Research (2011.1.058), CUHK**
**681 Change Of Caregiver’s Perception Regarding Atopic Dermatitis From 2006 To 2013**

Dr. Kyung Suk Lee, MD, PhD1; Prof. Yeong-Ho Rha, MD, PhD1; Prof. Sun-Hee Choi, MD, PhD2; 1Kyung Hee University Hospital, 2Gang-dong Kyung Hee University Hospital, Seoul, South Korea.

**RATIONALE:** In the treatment and management of atopic dermatitis (AD), not only doctor’s prescription but also caregiver’s active cooperation is important. We investigated the change of caregiver’s perception about AD in their children from 2006 to 2013.

**METHODS:** We surveyed 146 caregivers of children with AD and used self-questionnaire that composed of 15 items regarding diagnosis, treatment and dietary restriction of AD. The survey results were compared to those of 2006.

**RESULTS:** 1) As the cause of AD, food was selected to be the most common and HDM has decreased from 43% to 31% in 2006-2013. The environment has increased from 25% to 35% 2) Methods of AD treatment used by caregivers were moisturizers (76%), ointments (44%), medications (13%), and immunotherapy (4%). The percentage of using moisturizers has significantly increased from 2006 to 2013. 3) The order of concerns by caregivers from AD was prolonged treatment, skin deformity, and growth, whereas in 2006, they were growth, personality disorders, asthma with rhinitis. 4) The answer of having dietary restriction decreased from 68% to 46% in 2006-2013. Restricted foods by caregiver are eggs (38%), wheat (32%), peanuts (21%), fish and shellfish (21%), milk (17%) in 2013, whereas eggs (36%), peanuts (25%), fish and shellfish (23%) in 2006.

**CONCLUSIONS:** Caregivers of children with AD paid more attention to environmental management than in 2006, but that caregiver’s level of understanding of AD is still lacking. There is a need to increase accuracy and efficiency of care through enthusiastic education of pediatrician for caregivers.

**682 Excellent Agreement Between Dermatology and Pediatric Researchers In Severity Scoring of Atopic Dermatitis (SCORAD) Index In Children**

Dr. Rodrigo Hoyos Bachiloglu, MD1, Dr. Cristian Navarrete, MD2, Dr. Cristian Vera, MD2, Dr. Sergio Silva, MD2, Dr. Lorena Cifuentes, MD1, Mrs. Carolina Iturriaga, RN4, Ms. Francisca Cristi, MS1, Dr. Arturo Borutzky, MD1; 1Division of Pediatrics, School of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile, 2Department of Dermatology, School of Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile.

**RATIONALE:** The Severity Scoring of Atopic Dermatitis (SCORAD) index is a widely applied instrument for assessing atopic dermatitis severity. Although SCORAD has been validated in several studies, few have evaluated the interobserver agreement between different disciplines.

**METHODS:** Twenty-one children with atopic dermatitis (AD) were recruited. Each was evaluated using SCORAD by: three dermatologists, two pediatricians and a pediatric nurse. All pediatric researchers were trained for standardizing SCORAD scoring between researchers from different disciplines.

**RESULTS:** Nine patients were male (43%), mean age was 2 years (range 0-25), moderate (25-50) or severe (>50). Inter-observer agreement was evaluated using the intraclass correlation coefficient (ICC). The severity of AD according to SCORAD was classified in mild (<25), moderate (25-50) or severe (>50). At 48 hours, (2) and (3) revealed pruritic, 8 mm erythematous indurations. At 96 hours, both (2) and (3) revealed 2+ erythematous indurations. Patient was advised to avoid contact stomatitis secondary to orthodontic etching and bonding products.

**CONCLUSIONS:** This case illustrates that cyclosporine may be used seasonally to prevent poison ivy dermatitis as a steroid-sparing agent. Although cyclosporine has been used in cases of severe contact dermatitis, this is the first case, to the best of our knowledge, where it was used for poison ivy.
**Contact Dermatitis Due To Topical Amorolline**

Dr. Ruperto Gonzalez Perez, Mrs. Paloma Poza-Guedes, Mrs. Immaculada Sanchez Machin, Dr. Victor Matheu, MD; Hospital del Torax-Ofisa, Sta Cruz de Tenerife, Spain.

**RATIONALE:** Contact eczema caused by allergy to antifungal drugs is uncommon. Imidazole derivatives have been described as the most sensitising agent.

**METHODS:** We report the case of a 49 year-old female non-atopic patient presenting with an extensive eczematous pruritic rash on her right great toe. She had been prescribed 3 weeks before a topical cream twice daily containing 0.25% amorolline, polyethylene glycol 40 monostearate, stearyl alcohol, parafin, carborner 934P, sodium hydroxyde, disodium edetate, 2-phenoxy ethanol and purified water. Patch test were performed with the suspected antifungal cream.

**RESULTS:** Patch test showed positive (+++) readings at 48 and 96 hours. Five control subjects obtained negative patch test with the same suspected cream. A negative result to a cosmetic battery was also included to exclude the rest of the cream components.

**CONCLUSIONS:** We describe the rare case of a contact dermatitis due to amorolline. To our knowledge only three cases have been previously reported in the literature review.

---

**Sweet's Syndrome By A Show Of Hands**

Dr. Syeda Hamadani, Dr. Anita Ravi, Dr. Seth Politoan, Dr. Eric Hsieh, Dr. Gina Rossetti; USC, Los Angeles, CA.

**RATIONALE:** Recognize an atypical presentation of Sweet’s Syndrome.

**METHODS:** Skin biopsy.

**RESULTS:** 57 year old Hispanic male with no PMH presents with new onset bilateral hand pain. Five days prior to admission, he noticed black discoloration in his fingernails. He then developed a constant pulsating pain, swelling and pruritic rash in his bilateral hands. He also complained of fevers, sweats and chills. On physical exam, patient had splinter hemorrhages on multiple fingers, marked diffuse tenderness to palpation over bilateral hands, diffuse edema of hands. Skin exam demonstrated maculopapular non-blanching erythematous rash on dorsal aspect of bilateral wrists, painful purpura on palms and fingertips bilaterally. Labs included WBC 12.9 (Neutrophil count 72.9), ESR 82, CRP 146.2. Biopsy of the hand lesion showed dense dermal neutrophilic infiltrate.

**CONCLUSIONS:** The above patient had fever, painful/erythematous rash, and neutrophilic infiltration of the skin on biopsy, leukocytosis, and responded to systemic steroids. The patients’ clinical picture, labs, and pathology were consistent with Sweet’s Syndrome. However, this case was unusual as the patient’s rash was limited to his hands. Sweet’s Syndrome clinically favors upper body and face but restriction of rash to the hands are rare. NDDH (Neutrophilic dermatosis od the dorsal hands) is a rare variant of Sweet’s Syndrome with localized lesions clinically restricted to the hands and less frequent systemic symptoms. Systemic symptoms such as fever, leukocytosis and increased ESR are observed in 1/3 of the cases. NDDH is a recent disease concept which is evolving as it has been described in only a few case studies.

---

**Mango, Pulp Fiction?**

Dr. Alexander S. Kim, MD1, Dr. Sandra C. Christiansen, MD, FAAAAI2; 1University of California San Diego, La Jolla, CA; 2Southern CA Permanente Med Grp, San Diego, CA.

**RATIONALE:** Contact reactions to mango have been previously reported. Here we present an unusual dual reaction to mango peel and pulp.

**METHODS:** Skin prick, Finn Chamber and in-vitro IgE testing.

**RESULTS:** A 23-year old gentleman was evaluated after 2 episodes of delayed reactions to mango ingestion. Both episodes involved a perioral and pruritic rash associated with dry and cracked lips developing 1 day after unpeeled mango consumption and lasting 1 week. The second episode involved significant periorbital and lip edema as well as extension of the rash to the abdomen and extremities. He denied systemic symptoms but recalled that a pruritic papulovesicular rash on his lower extremities had appeared after poison oak exposure 7 years prior. Physical exam revealed an erythematous papular rash on the left thigh and the right hand. In-vitro IgE testing was positive to dust mite but negative to mango. Skin prick testing was negative to mango skin and pulp. Epicutaneous patch testing using mango skin and pulp placed in duplicate under Finn Chambers was positive to mango skin at 72 hours and to mango pulp at 96 hours.

**CONCLUSIONS:** We present a patient with contact dermatitis to mango skin and pulp. Patch testing using Finn Chambers is an efficient method for evaluating delayed type hypersensitivity to mango fruit. It is worth considering extending the observation to 96 hours given the clinically significant reaction to pulp.
Oral Allergy Syndrome - a Spectrum Of Presentations

Dr. Parwinder Gill1, Dr. Alton Lee Melton, Jr, MD 2, Dr. Earl Poptic1, Dr. Gordon L. Sussman, FAACAA2, Jiayi Bian1, Ms. Carly Barron1; 1Cleveland Clinic, Cleveland, OH, 2University of Toronto, Faculty of Medicine, Toronto, ON, Canada.

RATIONALE: We report a case series of patients presenting with features of oral allergy syndrome (OAS) with clinical symptoms ranging from gastrointestinal upset to anaphylaxis. This highlights the possibility that OAS may present not only as local irritation of the oropharynx, but also manifest in more serious symptoms such as gastrointestinal upset, and even anaphylaxis.

METHODS: Our report consists of six individuals who presented with gastrointestinal symptoms alone, and four individuals who presented with severe allergic reactions, who underwent allergy testing for investigation.

RESULTS: In all ten cases, clinical history in addition to the results of the allergy testing was consistent with oral allergy syndrome presenting as gastrointestinal upset or anaphylaxis in response to their triggers.

CONCLUSIONS: OAS is an IgE-mediated allergic reaction resulting from cross-reactivity of pollens, mainly birch and ragweed with certain nuts, fruits and vegetables. This is generally recognised as a benign syndrome presenting as local itching of the mouth occurring after contact with these foods. However, oral allergy syndrome can manifest as gastrointestinal symptoms and even anaphylactic allergy. We report these cases to alert the possibility that oral allergy syndrome can present as a spectrum of symptoms and can result in serious systemic reactions.

Allergy To Sheep Milk With Or Without Allergy To Cow Milk

Dr. Fouseena Pazheri1, Dr. Alton Lee Melton, Jr., MD 2, Dr. Earl Poptic1, Dr. Belinda Willard1; 1Cleveland Clinic, Cleveland, OH, 2Cleveland Clinic, Cleveland, OH.

RATIONALE: Cow milk protein represents a common food allergen in children. These children often look to other mammalian milks as nutritional alternatives, including goat milk and sheep milk. Previous reports suggest significant cross-allergenicity among the caseins of different mammalian milks. Isolated allergy to sheep milk protein is unusual, with only a few reported cases. We report the analysis of two cases of sheep milk allergy, one with concomitant cow milk allergy and the other without.

METHODS: Clinical and laboratory characteristics of two children with allergy to milk proteins evaluated at a pediatric allergy clinic were reviewed. Two-dimensional SDS PAGE and immunoblotting will be performed using extracts made from sheep milk and cow milk and serum from the two patients and appropriate controls.

RESULTS: Subject 1 is a 10-year-old boy who experienced anaphylactic reactions to two sheep milk cheeses (Romano cheese and ricotta cheese). He tolerates cow milk products. IgE ELISA for cow milk was undetectable (<0.35 Ku/L) and positive for sheep milk (29.2 Ku/L). Subject 2 is a 15-year-old boy with a long history of severe allergy to cow milk, who had IgE ELISA performed for several other mammalian milks. IgE ELISA was significantly elevated for both cow milk (34.1 Ku/L) and sheep milk (48.9 Ku/L).

CONCLUSIONS: A high degree of cross-allergenicity exists between proteins from milks of different mammals, and this often limits dietary choices for children with clinical cow milk allergy. However, individual patients may display unique sensitization to a particular milk. These cases illustrate both these scenarios.

Genome-Wide Study Of Interaction Between Season Of Birth and Peanut Allergy Identifies a Region On Chromosome 3 As a Genetic Risk Factor

Corinne Keet, MD, MS1, Xiumei Hong, PhD2, Dr. Ingo Ruczinski, PhD2, Dr. Terri H. Beaty, PhD2, Dr. Jacqueline Pongracic, MD, FAACAA1, Dr. Xiaobin Wang, MD, MPH ScD3; 1Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, 2Johns Hopkins University School of Public Health, Baltimore, MD, 3Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, Chicago, IL, 4Center on Early Life Origins of Disease, Department of Population, Family and Reproductive Health, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD.

RATIONALE: Fall season of birth has been identified as a risk factor for food allergy, but underlying mechanisms remain unknown. We hypothesized that at least one common single nucleotide polymorphism (SNP) would show evidence of gene-environment interaction (GxEI) with season of birth and food allergy.

METHODS: 312 case-parent trios were included in a genome wide association study of peanut allergy using the Illumina HumanOmni1-Quad BeadChip. Analysis of GxEI between season of birth and individual SNPs was done using the package TRIO in R, which rapidly fits a conditional logistic regression model while testing for interaction. The 1 degree of freedom test comparing the dominant model with and without GxEI is reported. Season of birth was defined as fall (September, October and November) versus all other months combined. Peanut allergy was defined as history of an immediate onset of typical allergy symptoms to peanut with confirmatory positive specific IgE or skin testing.

RESULTS: Two SNPs near the genes PBRM1 & GNL3 on chr.3p21 yielded genome-wide significance in this test for GxEI (rs2590838 and rs1108842, p=9.5x10-9 and 1.2x10-8, respectively). Forty-nine SNPs in this region approached genome-wide significance (10^-5). PBRM1 is necessary for signaling by nuclear hormone receptors, including those activated by vitamin D, but has not been previously associated with any allergic diseases.

CONCLUSIONS: Genetic markers near PBRM1 on chr.3p21 appear to interact significantly with fall birth to increase risk of food allergy. More research will be needed to identify the functional significance of this statistical association.
**Orofomal Infections and Risk Of Food Allergy In Children**

**Dr. Gary Wong, MD**, Dr. Jing Li, MD, MS, Dr. Ting Fan Leung, MD, FRCPCH, FAAAAI, Prof. Nan Shan Zhong; **Chinese University of Hong Kong, Shatin, Hong Kong.**

The First Affiliated Hospital of Guangzhou Medical College, State Key Laboratory of Respiratory Disease, Guangzhou Institute of Respiratory Disease, Guangzhou, China.

**Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong.**

**Rationale:** The prevalence of food allergy is increasing in the last decade. The cause for such increase is unknown. Loss of protective factors may be a contributing factor.

**Methods:** Random samples of primary schoolchildren were recruited from urban and rural regions of Southern China. Cases and controls were then recruited for detailed assessment to evaluate for possible food allergies. Sensitization to common food allergens were tested (SPT and sIgE measurement). The presence of antibodies against common fecal-oral infections including hepatitis A, salmonella, and toxoplasmosis was performed.

**Results:** 18,342 primary school children from Hong Kong, Guangzhou city and rural Shaoguan were invited and 16,875 (92%) agreed to participate. They were screened with the EuroPrevall screening questionnaire. A random subsample 1152 subjects participated the case-control phase using standardized EuroPrevall protocol. Defining food allergy as having symptoms with a certain food within 2 hrs of ingestion and positive SPT/serum specific IgE to that food, the prevalence of probable food allergy was 2.0% in Hong Kong, and only 0.5% in mainland China. The sensitization rate was highest in Hong Kong. For milk sensitization (most common), the rates were 14.7% in Hong Kong, 6.8% in Guangzhou, and 1.9 in Shaoguan (P < 0.01). Presence of hepatitis A antibody was associated with higher prevalence of food allergy (adjusted OR 0.21;95%CI: 0.10-0.41, P < 0.01).

**Conclusions:** This is study documented a very low prevalence of food allergy and sensitization in rural China. Past hepatitis A infection was associated with lower prevalence of food allergies. The possible causal role of infections in allergies requires further studies. Supported: HKRGCGRF477110

**Peanut, Milk, and Wheat Intake During Pregnancy Is Associated With Reduced Allergy and Asthma In Children**

**Dr. Supinda Bunyavanich, MD, MPH**, Ms. Sheryl Rfas-Shiman, MPH, Thomas A. E. Platts-Mills, MD, PhD, FAAAAI, Lisa J. Workman, BA, Dr. Joanne Sordillo, ScD, Dr. Carlos Camargo, Jr, MD, DrPH, Dr. Matthew Gillman, MD, SM, Dr. Diane R. Gold, MD, MPH, Dr. Augusto A. Litonjua, MD, MPH, Division of Pediatric Allergy & Immunology, Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, Department of Population Medicine, Harvard Pilgrim Health Care Institute, Harvard Medical School, Boston, MA, Division of Asthma, Allergy & Immunology, University of Virginia Health System, Charlottesville, VA, Channing Division of Network Medicine, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA, Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, Channing Laboratory, Brigham and Women’s Hospital, Boston, MA.

**Rationale:** The relationship between maternal diet during pregnancy and childhood allergy and asthma is controversial.

**Methods:** We studied 1277 mother-child pairs from an unselected United States pre-birth cohort (Project Viva). Using food frequency questionnaires administered during the first and second trimesters, we assessed maternal intake of common childhood food allergens during pregnancy. In mid-childhood (mean age 7.9 years), we assessed food allergy, asthma, allergic rhinitis, and atopic dermatitis by questionnaire and serum specific IgE levels. We used multivariable logistic regression to examine the associations between maternal diet during pregnancy and childhood allergy and asthma.

**Results:** Food allergy was common (5.6%) in mid-childhood, as was sensitization to at least one food allergen (28.0%). Higher maternal peanut intake (each additional z-score) during the first trimester was associated with 47% reduced odds of peanut allergic reaction in mid-childhood (OR 0.53, 95%CI 0.30-0.94). Higher milk intake during the first trimester was associated with reduced odds of asthma (OR 0.83, 95%CI 0.69-0.99) and allergic rhinitis (OR 0.85, 95%CI 0.74-0.97). Higher maternal wheat intake during the second trimester was associated with reduced odds of atopic dermatitis (OR 0.64, 95%CI 0.46-0.90).

**Conclusions:** Higher maternal intake of peanut, milk, and wheat during early pregnancy was associated with reduced odds of mid-childhood allergy and asthma. The benefits of early introduction of peanut, milk and wheat on reducing childhood allergy and asthma could be entwined even before birth, as early as the first trimester of pregnancy.
695 Food Allergy Prevalence In Parents Of Food-Allergic Children Based On Self-Report, Serologic Testing and Physician Diagnosis
Melanie M. Makhija, MD1,2; Dr. Rachel Glick Robison2,3; Deanna Caruso, MS4; Miao Cai, MS2; Dr. Xiaobin Wang, MD, MPH ScD3; Dr. Jacqueline Pongracic, MD, FAAAAI1,2; 1Ann and Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, 2Division of Allergy & Immunology, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, 4Johns Hopkins University School of Public Health, Baltimore, MD, 5Division of Allergy & Immunology, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL.

**RATIONALE:** Food Allergy (FA) prevalence and gender difference in adults has not been extensively studied. We sought to determine the FA in parents of food-allergic children, hypothesizing that parents may under-report FA due to increased awareness.

**METHODS:** 1252 mothers and 1225 fathers of food-allergic children answered standardized questionnaires, including self-report and physician(MD) diagnosis of FA, history of atopy and characteristics of food allergy in themselves and their children. Skin prick tests(SPT) and specific IgE(sIgE) serum tests were performed to 9 common food allergens. Data was analyzed in SAS.

**RESULTS:** 14.5% of mothers and 12.7% of fathers reported current FA, 13.3% of mothers and 8.9% of fathers reported MD-diagnosed FA. Only 17.7% of mothers and 21.1% of fathers reporting current food allergy had positive SPT, detectable IgE and MD diagnosis of FA. Of parents reporting FA who had positive SPT and detectable IgE to any food, 78.3% of fathers vs. 96.6% of mothers had an MD diagnosis of food allergy (P<0.01). 37.6% of mothers and 16.6% of fathers reporting an allergy to peanut had positive SPT, detectable peanut-specific IgE and MD diagnosis. For milk allergy, only 5% of mothers and 16.7% of fathers had positive SPT, detectable milk-specific IgE and an MD diagnosis.

**CONCLUSIONS:** Among parents of food-allergic children who reported FA, only a small proportion had positive SPT, detectable IgE and an MD diagnosis of FA. MD diagnosis was significantly higher in mothers. More parents who reported peanut allergy had clinical markers of allergy than those reporting milk allergy.

696 The Effect Of Neighborhood Level Poverty and Urbanization On The Prevalence Of Food Allergy In The National Health Interview Survey (NHIS)
Dr. Emily C. McGowan, MD1,2; Dr. Meredith C. McCormack, MD2, Dr. Roger Peng, PhD2; Dr. Elizabeth Matsui, MD2; Corinne Keet, MD, MS1; 1Johns Hopkins University School of Medicine, Baltimore, MD, 2The Johns Hopkins University School of Medicine, Baltimore, MD, 3Johns Hopkins University School of Public Health, Baltimore, MD, 4Johns Hopkins University School of Medicine, Baltimore, MD.

**RATIONALE:** Although some studies have suggested that the prevalence of food allergy (FA) in inner-city children is high, the relative contributions of neighborhood poverty, urbanization, and race/ethnicity to FA prevalence in inner-city children have not yet been examined.

**METHODS:** Data were obtained from the 2009-2011 NHIS, where self-reported food allergy among children over the past year was assessed by questionnaire. Place of residence was linked to census level household poverty prevalence, with a “poor” neighborhood defined as > 20% of households below the poverty level. Urbanization was defined as urban, suburban, medium metro or rural. Risk factors for self-reported food allergy were assessed by logistic regression, using weights and survey strata for all analyses.

**RESULTS:** 35,128 children were surveyed between 2009 and 2011. The overall prevalence of self-reported FA was 5.1%, and those living in poor urban neighborhoods had the lowest prevalence (3.1%; 95% CI 2.4-4.0%). Neighborhood-level poverty, urban location (compared to suburban), and Hispanic race/ethnicity (compared to non-Hispanic white) were protective (OR 0.81; 95%CI:0.69 – 0.96; p=0.01, OR 0.82; 95%CI:0.69 – 0.98; p=0.02, and OR 0.72; 95%CI:0.60 – 0.84; p<0.001, respectively), while black race/ethnicity was a risk factor for self-reported FA (OR 1.24; 95%CI:1.04 – 1.47; p=0.02), in multivariate models also including sex and age.

**CONCLUSIONS:** In this analysis, although children of black race/ethnicity had the highest prevalence of self-reported FA, neighborhood-level poverty and urbanization were actually protective for this condition. Whether this is due to a true protective effect of the environment or to disparities in reporting FA warrants further study.

697 Prevalence Of IgE-Mediated Food Sensitisation and Food Allergy In Unselected 12-36 Month Old South African Children
Dr. Maresa Botha, MBChB, FCPaed1, Prof. Michael E. Levin, MBChB, FCPaed, Dip Allergology, MMEd(Paeds), PhD, EAACI allergy exam (UEMS), Certificate Allergology, FAAAAI1,2; 1University of Cape Town, Cape Town, South Africa, 2Red Cross War Memorial Children’s Hospital, Cape Town, South Africa.

**RATIONALE:** The prevalence of IgE-mediated food allergy seems to differ across ethnic groups in South Africa. However no robust prevalence data exists of food allergy in South Africa or Africa, a shortfall this study addresses.

**METHODS:** This cross-sectional prevalence study of IgE-mediated food sensitisation and allergy in unselected 12 - 36 month old children (1200 in urban Cape Town and 400 in rural Eastern Cape) compares prevalence and various risk factors between sub-cohorts of Caucasian, Mixed race and black African urban children and between urban and rural black African children. All participants complete a questionnaire and undergo skin prick tests (SPT). Oral food challenges are performed in participants with SPT>1mm who are not tolerant to assess for diagnosis of IgE-mediated food allergy. Population specific cut-off levels for SPT with 95% positive predictive values will be generated.

**RESULTS:** Pilot phase response rates in the first 10% (118) of the urban sample were 56% (66) but with high participation (90.9% (60)) and completion rates (83% (55)). Changed recruitment strategies increased the response rate to 75%. Of the participants 6.7%, 28%, and 65% were Caucasian, Mixed race and Black African respectively. Overall prevalence rates for SPT>1mm was 18% (10), for SPT>3mm 10.9% (6), for SPT>7mm 7.3% (4) and OFC confirmed food allergy 1.8% (1).

**CONCLUSIONS:** This study was found to be acceptable and feasible. This first prevalence study of its kind in Africa will bring further opportunities for studying risk factors in a population possibly only at the beginning of the food allergy epidemic.
Prevalence Of Peanut Allergy: A Systematic Review

Dr. Heather Mackenzie1, Dr. Carina Venter, PhD, RD2, Dr. Sally Kilburn1, Ms. Harriet R. Moonesinghe1, Dr. Antonella Cianferoni, MD, PhD3; 1Children’s Hospital of Philadelphia, Philadelphia, PA, 2333 Walnut Street, Philadelphia, PA, 3Children’s Hospital of Philadelphia, Philadelphia, PA

Rationale: There is relatively little information about geographical variations in the prevalence of peanut allergy, as many studies have used different diagnostic criteria and methods of diagnosis.

Methods: The review methodology was employed. Studies identified by searching Web of Science and PubMed, and by consultation with experts and screened for eligibility according to pre-specified criteria.

Results: Prevalence data for peanut allergy was presented by 62 included studies; 28 presented data from one or more European countries and 26 from one or more non-European countries. Self-reported peanut allergy ranged from 0.0% (95% CI: 0.0-1.5%) to 15.0% (95% CI: 13.0-17.3%) in European countries, and from 0.0% (95% CI: 0.1-2.0%) to 8.4% (95% CI: 6.2%-11.2%) in non-European countries. Sensitisation ranged from 0.0% (95% CI: 0.0-12.0%) to 12.2% (95% CI: 9.7-15.2%) in European countries, and in non-European countries from 0.3% (95% CI: 0.0-2.1%) to 13.5% (95% CI: 11.6-15.7%). Reported prevalence in European countries ranged between 0.0% (95% CI: 0.0-4.2%) and 1.4% (95% CI: 0.9-2.3%) using open food challenges and a good clinical history, and between 0.0% (95% CI: 0.0-2.0%) and 2.8% (95% CI: 1.8-3.8%) using DBPCFC and a good clinical history. The single non-European study to base on open food challenges.

Conclusions: Based on open food challenges.

Prevalence Of Fish and Shellfish Allergy: A Systematic Review

Ms. Harriet R. Moonesinghe1, Dr. Sally Kilburn1, Dr. Heather Mackenzie1, Dr. Paul J. Turner, FRACP PhD2, Dr. Carina Venter, PhD, RD3, Ms. Kellyn Lee1, Prof. Taranath Dean1, University of Portsmouth, School of Health Sci, Portsmouth, United Kingdom, 2Imperial College London, United Kingdom, 3The David Hide Asthma and Allergy Research Center, Isle of Wight, United Kingdom

Rationale: Accurate information on prevalence of food allergy allows a more evidence-based approach to planning of allergy services. Additionally reporting on the totality of evidence relating to specific food allergy can establish geographical variation which may exist.

Methods: Searches were conducted using two databases; Web of Science and PubMed. Initially 958 studies were identified; 902 were excluded at title/abstract screen, 17 at full text screen and a further 7 during data extraction. 59 studies were included in the review.

Results: Thirty-four studies reported the prevalence of fish/shellfish allergies in Europe. Prevalence rates based on self-reported allergy were presented in 22 studies, sensitisation rates were assessed in 8 studies using skin prick tests and 5 studies reported on serum IgE, sensitisation plus clinical history was obtained in 4 studies and 7 studies based prevalence data on food challenges. Depending on the assessment criteria prevalence ranged between 0% - 7%. Twenty-seven studies looked at the prevalence of fish/shellfish allergy across the rest of the world. Self-reported allergy was presented in 16 studies, 10 studies combined clinical history and clinician diagnosis, 7 studies measured sensitisation rates with a further 3 studies reporting a convincing clinical history plus sensitisation. Only 2 studies used food challenges to confirm suspected allergy. Depending on the assessment criteria prevalence ranged between 0% - 24.5%.

Conclusions: Very few studies have established the prevalence of fish/shellfish allergy using the gold standard challenge criteria. Where this is used the worldwide prevalence rates of fish allergy ranges between 0%-1% and 0.2%-0.9% for shellfish allergy.

Prevalence Of Food Allergy To Uncommon Foods Based On Oral Food Challenges

Dr. Gita Ram1, Christina Gustafson1, Dr. Jonathan M. Spergel, MD, PhD, FAAAAI2, Dr. Antonella Cianferoni, MD, PhD3; 1Children’s Hospital of Philadelphia, Philadelphia, PA, 2The Children’s Hospital of Philadelphia, Philadelphia, PA, 33615 Civic Center Boulevard, The Children’s Hospital of Philadelphia, Philadelphia, PA

Rationale: There is substantial food allergy (FA) research on milk, egg, peanut, wheat and soy, but there remains limited data on other foods. We evaluated the clinical characteristics of patients undergoing oral food challenge (OFC) to these less common foods.

Methods: Retrospective chart review of all children undergoing OFC to any food excluding milk, egg, peanut, wheat and soy from 2004-2012.

Results: Patients aged 1-18 years (median 6) underwent 366 OFCs. Challenged foods included tree nuts (36.6%), meats (15.8%), seeds (11.7%), shellfish (9%), fish (6.8%), fruits and vegetables (6%), grains excluding wheat (5.7%), legumes excluding peanut (4.9%), and miscellaneous foods (3.2%). 90.7% of patients had other FA, 71.6% asthma, and 48.1% eczema. Overall, 81.1% of children passed OFC with similar pass rates within each food category. Only 6.3% of challenges required epinephrine administration. Highest pass rates were among OFCs to miscellaneous foods (91.7%) and lowest to grains excluding wheat (71.4%). Failure rate was associated with history of other FA (OR 8.2, P<0.04), but there was no correlation to age, history of prior reaction, time since last ingestion, or history of asthma or eczema. Wheat size was slightly larger in those who failed (5mm vs. 4mm), and this was markedly significant (OR 1.16, P<0.001).

Conclusions: FA to uncommon allergens is becoming increasingly prevalent. Patients with other FA are more likely to have true allergy to these foods. Overall, pass rates appear to be significantly higher than OFCs to milk, egg, peanut, wheat and soy, suggesting that allergy to these uncommon foods may be overdiagnosed.
**702** Prevalence Of Food Allergy In Patients With Irritable Bowel Syndrome

Erin L. Leigh, MD, MS1, Dr. Javed Sheikh, MD, FAAAAI1, Anna Kvolszki, MD, MD, Beth Israel Deaconess Medical Center, Boston, MA, 2Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA.

**RATIONALE:** Patients with irritable bowel syndrome (IBS) are often referred to allergists for food allergy (FA) testing even when they lack immediate-type hypersensitivity symptoms (ITHS). The clinical utility of FA testing in this population is uncertain. We hypothesized that patients with IBS who lack ITHS have a FA rate comparable to the general population.

**METHODS:** We performed a cross-sectional, epidemiological study by medical record review of 247 adult patients with IBS who had FA testing at Beth Israel Deaconess Medical Center. We recorded food-related symptom triggers, presence of ITHS, and FA testing results. Chi-square test was used for analysis.

**RESULTS:** Patients with IBS had higher rates of positive FA testing compared to the NHANES asymptomatic general population [n=93 (38%); 95% CI, 32-44% vs. 6.4%; p<0.001], and higher rates of FA compared to the general population [n=45 (18%); 95% CI, 13-23% vs. 4%; p<0.001]. Of the 45 patients with FA, 41 (91%) had ITHS while only 4 (9%) had gastrointestinal symptoms attributable to FA. Milk (28%) and wheat (23%) were the most common self-reported gastrointestinal symptom triggers, but sensitization to these foods was rare (1.2% and 0.4%, respectively).

**CONCLUSIONS:** Patients with IBS who lacked ITHS had a rate of FA that was similar to the general population, while patients with ITHS had a significantly higher rate of FA. ITHS in patients with IBS may be a useful screening tool for assessing the utility of FA testing in this population.

---

**703** Clinical Characteristics Of Seafood Allergy In Canadian Children

Dr. Victoria Cook1, Dr. Edmund S. Chan, MD, FAAAAI2, Dr. Ann Elaine Clarke, MD, MSc3, Mr. Greg Shand, Dr. Moshe Ben-Shoshan, MD, MSc4, 1Department of Pediatrics, University of British Columbia, BC Children’s Hospital, Vancouver, BC, Canada, 2Department of Pediatrics, Faculty of Medicine, University of British Columbia, 3Division of Allergy and Clinical Immunology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada; 4Division of Clinical Epidemiology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada.

**RATIONALE:** There is minimal data describing presentation of seafood allergy. We have characterized first reactions in seafood-allergic children.

**METHODS:** Children with seafood allergy were recruited from allergy clinics at the Montreal Children’s Hospital from March 2011 to May 2013. Questionnaires assessed demographics, cause, location, diagnosis, severity, and management of first reaction.

**RESULTS:** Twenty-one fish and 18 shellfish-allergic patients responded (36.2% and 51.4% response rate). Age, sex, trigger and reaction severity were comparable between respondents and non-respondents. Median age at initial reaction was 5 years (range 2-17). Most reactions occurred at home (61.9% and 83.3%). Average age at diagnosis following initial reaction was 8 months (fish) and 10 months (shellfish). Most (85%) reactions were classified as moderate to severe, yet only 21% (9.6% to 39.4%) of these patients sought medical attention. At the time of questionnaire administration, all children had seen a physician, but 33.3% (15.5% to 56.9%) of patients with fish allergy and 52.9% (28.5% to 76.1%) of those with shellfish allergy were not prescribed an auto-injector.

**CONCLUSIONS:** Seafood allergy presents at an early age and the most common causative foods are tilapia and shrimp. Following initial reaction, there appears to be a delay in physician diagnosis and low rates of auto-injector prescription.

---

**704** Changes In Total IgE Levels To Predic Food Challenge Test Outcomes

Dr. Kenta Horimukai1, Dr. Masami Narita, MD, PhD2, Dr. Ichiro Nomura, MD, PhD3, Dr. Kenji Matsumoto, MD, PhD3, Dr. Yukihiro Ohya, MD, PhD3, Dr. Kenta Horimukai, 1Jikei University Katsushika Medical Center, Tokyo, Japan, 2National Center for Child Health and Development, Tokyo, Japan, 3National Center for Child Health and Development, Setagaya, Japan.

**RATIONALE:** Probability curves using food-specific IgE antibodies have transformed them into a more accessible tool; nevertheless, decision factors may be different for various facilities conducting Oral food challenge(OFC). This study aimed to determine whether the combination of total serum IgE and specific IgE values affected the prediction of OFC results.

**METHODS:** Between April 2010 and February 2013, we recruited 315 patients (males, 208; females, 107; median age, 43 months; range 5 months–14 years) with suspected egg allergy who completed the open OFC test by consuming heated egg whites (total, 3.5 g), and 245 patients (males, 168; females, 77; median age, 53 months; range, 7 months–13 years) with suspected milk allergy who completed the open OFC test by consuming raw milk (total, 3.1 mL). Serum total and specific IgE antibodies levels (ovomucoid and milk) were determined by ImmunoCAP within 180 days before OFC. Binary logistic regression analyses evaluated the associations between the allergen-specific serum IgE and positive OFC results.

**RESULTS:** Each probability curve (Ovomucoid-specific IgE, Milk-specific IgE) was compared with three total IgE concentration groups [low (<250 UA/mL), intermediate (250–750 UA/mL), and high groups (>750 UA/mL)] using either ovomucoid-specific IgE or milk-specific IgE. Consequently, lower the total IgE levels higher the positive ratio for OFC.

**CONCLUSIONS:** Total serum IgE levels affected the prediction of OFC results.
706 Possession of Epinephrine Auto-Injectors (EAI) in a Vulnerable Canadian Population With Food Allergies

Dr. Sabrine Cherkaoui, MD1, Ms. Lianne Soller, MSc2, Dr. Moshe Ben-Shoshan, MD, MSc3, Daniel Harrington, MA, PhD4, Dr. Sebastien La Vieille, MD5, Dr. Joseph Fragapane, MD6, Dr. Lawrence Joseph, PhD7, Mr. Yvan St-Pierre, MSc8, Prof. Susan Elliott, PhD9, Dr. Ann Elaine Clarke, MD, MSc7,10; 1Division of Internal Medicine, Department of Medicine, University of Montreal, Montreal, QC, Canada, 2Division of Clinical Epidemiology, Department of Medicine, McGill University Health Center, Montreal, QC, Canada, 3Division of Paediatric Allergy and Clinical Immunology, Department of Paediatrics, McGill University Health Center, Montreal, QC, Canada, 4McMaster University - School of Geography, Hamilton, ON, Canada, 5Food Directorate, Health Canada, Ottawa, ON, Canada, 6McGill University, Dorval, QC, Canada, 7Division of Clinical Epidemiology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, 8Division of Allergy and Clinical Immunology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, 9Applied Health Sciences, University of Waterloo, ON, Canada, 10Division of Allergy and Clinical Immunology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada.

RATIONALE: To determine the percentage prescribed and carrying an epinephrine auto-injector (EAI) in a vulnerable Canadian population with food allergies.

METHODS: We performed a random cross-Canada telephone survey between September 2010 and September 2011 targeting Canadians of low income, New Canadians, and Aboriginal people using 2006 Canadian Census data. Those reporting a physician diagnosed allergy to at least one of peanut, tree nut, fish, shellfish, sesame, milk, egg, wheat, or soy were identified and queried on whether they had been prescribed and were always carrying an EAI. Multivariate regression was performed to examine potential predictors of being prescribed and carrying their prescribed EAI.

RESULTS: Of the 12,762 households reached, 5,734 households, representing 15,022 individuals, completed the survey (45.0% response rate). Of the 348 patients with physician diagnosed food allergy, 44.0% (95%CI, 38.7%-49.4%) were prescribed an EAI. Among individuals with EAI prescriptions, 56.9% (48.6%-64.8%) reported always carrying the EAI. Children (OR 3.6, 95%CI 2.1-6.3), subjects with peanut, tree nut or sesame allergy (OR 3.1, 1.9-5.1), those reporting diagnostic testing (OR 2.8, 1.3-6.1) or those in a non-low income household (OR 2.6, 1.3-5.3) were more likely to be prescribed an EAI. Adults with a post-secondary degree (OR 3.2, 1.2-8.5) were more likely to carry their prescribed EAI.

CONCLUSIONS: Less than half of vulnerable Canadians with physician diagnosed food allergy are prescribed an EAI, and among them 43% don’t carry the EAI at all times. Further education on the potentially fatal hazards of food allergy and the importance of always carrying an EAI is needed.

707 Food Allergy In Daycare Centers: Prevalence, Management, and Knowledge Of Directors

Dr. Lisanne Newton, MD, Dr. Brian Schroer, MD; Cleveland Clinic, Cleveland, OH.

RATIONALE: Food allergy (FA) affects 6-8% of children, with young children affected the most. FA reactions may commonly occur at daycares; however, little is known about FA knowledge and preparation in daycare settings.

METHODS: IRB approval was obtained to distribute a 43 item web-based questionnaire to daycare directors around Cleveland, OH. Fisher exact tests calculated associations between daycare characteristics and responses.

RESULTS: 29/81 (36%) questionnaires were completed. 41.3% from national chains, 48.2% single sites, 10.3% local chains. Of 3,155 children, 6.8% had reported FA. Peanut was most common (3.1%), then milk (2.7%), tree nut (1.6%), egg (1.2%). All centers accepted children with FAs. 69% restricted peanuts. All centers had training on epinephrine administration; most had formal training on FAs (82.8%). 93.1% had FA Action Plans. Only 51.7% had epinephrine for each child. One center reported a generic epinephrine available for a first reaction; 24% would administer another child’s epinephrine to a child having a severe reaction. The majority answered general knowledge questions correctly. National chains vs. single sites (p=0.047) and peanut-free centers (p=0.05) were more likely to have epinephrine available.

CONCLUSIONS: This web-based questionnaire on FAs in daycares found that all centers had at least one child with FA. The directors’ knowledge about FAs was high. Only half of centers had epinephrine available for each child with FA. The availability of a generic epinephrine was rare and most would not administer another child’s epinephrine in an emergency. National chains and peanut-free centers were more likely to have epinephrine available, which may be helpful for patient counseling.

708 Assessment Of Food Insecurity and Health Literacy In a Tertiary Care Pediatric Allergy Population

Dr. Meredith A. Dilley, MD1,2, Ms. G. Lynn Christie, MS, RD, RD1, Ms. Mary Price2, Ms. Connelly Weeks3, Malikkarjuna Rettiganti, PhD1,2, Maria Melguizo Castro1, Dr. Amy M. Scurlock, MD1,4, Dr. Tamara T. Perry, MD1,2, Dr. Robbie D. Pesek1,2, Dr. Matthew C. Bell, MD1,2, Joshua L. Kennedy, MD1, Ms. Erin O’Brien1,2, Ms. Sklar McGrath4, Mr. Jared Hogan5, Megan Patterson1, Julia Aronson1, Dr. Patrick Casey, MD1,2, Stacie M. Jones, MD3,5; 1University of Arkansas for Medical Sciences, Little Rock, AR, 2Arkansas Children’s Hospital, Little Rock, AR, 3University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Little Rock, AR, 4University of Arkansas for Medical Sciences/Little Rock Children’s Hospital, Little Rock, AR, 5Arkansas Children’s Hospital Research Institute, Little Rock, AR.

RATIONALE: Food insecurity (FI), defined as limited food availability or uncertain ability to acquire food, is linked to poor health. Arkansas has the highest rate of FI (19.7%) in the nation. Food allergy (FA) introduces dietary limitations by necessity of food avoidance. To test our hypothesis that dietary limitations associated with FA contributes to increased FI, we examined FI and health literacy (HL) in food allergic (FA) and non-food allergic (non-FA) children.

METHODS: FA and non-FA children (1-17 years) were recruited from Arkansas Children’s Hospital allergy clinics. The 18-item USDA Food Security Questionnaire and the Newest Vital Sign HL questionnaire were administered. Quality of life (QOL) was measured in FA subjects. Chi-squared test, two-sample t-tests, and two-way ANOVA were utilized for midpoint analysis.

RESULTS: Subjects (n=295) included 197 FA and 98 non-FA; mean (SD) age was 7.9 (4.2) years; 62% Caucasian. FI was not different between FA and non-FA groups (17.8% vs. 19.4%, p=0.734). HL was lower in FI compared to food secure subjects (4.8 (1.4) vs. 3.7 (1.9), p<0.001); no difference was noted between FA and non-FA groups (p=0.50). In FA subjects, better QOL was reported in food secure vs. FI subjects (4.6 (2.2) vs. 5.3 (2.3), p=0.04).

CONCLUSIONS: Despite high overall rates of food insecurity, preliminary results suggest that rates are not different between FA and non-FA children. Consideration of risk factors for FI, including reduced HL and lower QOL, may be important for design and implementation of active intervention strategies to improve health outcomes for food insecure children.
709 Environmental and Sociodemographic Factors Associated With Food Allergy: A Nested Case-Control Study
Dr. Moshe Ben-Shoshan, MD, MSc1, 2, Ms. Lianne Soller, MSc2, Daniel Harrington, MA, PhD2, Ms. Megan Knoll, MSc1, Dr. Sebastian La Vieille, MD3, Dr. Joseph Fragapane, MD2, Dr. Lawrence Joseph, PhD4, Mr. Yvan St. Pierre, MSc2, Dr. Kathi Wilson5,6,7,8, Dr. Joseph Fragapane, MD2, Dr. Lawrence Joseph, PhD4, Mr. Yvan St. Pierre, MSc2, Dr. Kathi Wilson5,6,7,8. 1Division of Paediatric Allergy and Clinical Immunology, Department of Paediatrics, McGill University Health Center, Montreal, QC, Canada, 2Montreal Children’s Hospital, Montreal, Canada, 3Division of Clinical Epidemiology, Department of Medicine, McGill University Health Center, Montreal, QC, Canada, 4McMaster University - School of Geography, Hamilton, ON, Canada, 5Division of Clinical Epidemiology, Department of Medicine, McGill University Health Center, Montreal, QC, Canada, 6McGill University Health Centre, Montreal, QC, Canada, 7Health Canada, Ottawa, ON, Canada, 8Food Directorate, Health Canada, Ottawa, ON, Canada, 9McGill University, Dorval, QC, Canada, 10Division of Clinical Epidemiology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, 11Department of Geography, University of Toronto, Toronto, ON, Canada, ON, Canada, 12McGill University Health Centre, Montreal, Canada.

RATIONALE: To determine the influence of the environment on the development of food allergy.

METHODS: We performed a cross-Canada, random telephone survey. Cases consisted of individuals with probable food allergy (i.e. self-report of convincing symptoms and/or physician diagnosis) to peanut, tree-nut, shellfish, fish, milk, egg, wheat, soy or sesame. Controls consisted of non-allergic individuals matched for age within the same household (when available) or non-allergic households. Cases and controls were queried on dietary habits during pregnancy, lactation and infancy, day-care attendance, vaccination, infections, pet ownership, living on a farm, and personal and family atopy. Multivariate logistic regressions were used to assess potential determinants.

RESULTS: Between September 2010 and September 2011, 612 cases and 5254 controls completed the questionnaire: For all 9 allergens, probable allergy was associated with maternal or sibling food allergies [odds ratio = OR, 2.9 (95%CI, 2.0, 4.4), 2.8 (2.1, 3.8) respectively] as well as personal history of eczema, asthma, hay fever or other food allergies [2.4 (1.9, 3.0), 2.3 (1.8, 3.0), 2.1 (1.6, 2.6) and 1.9 (1.3, 2.5)]. High income (top 20%) was associated with higher odds [1.6 (1.2, 2.0)] while recent adult immigrants (< 5 years) had lower odds [0.4 (0.2, 1.0)]. Individual food allergies had similar associations with personal and family atopy. High income was associated with peanut and shellfish allergy and higher education (college and above) with tree-nut allergy. Tree-nut allergy was less common in immigrants and shellfish allergy was more common in children who immigrated in the last 10 years.

CONCLUSIONS: Our results reveal that atopy, socioeconomic status, education, and immigration are associated with probable food allergy.

710 Differences In Empowerment and Quality Of Life Among Mothers and Fathers Of Children With Food Allergy
Mr. Christopher Warren, BA1, Dr. Rochi Gupta, MD, MPH2, Mr. Nannit Li3, Min-Woong Sohn, PhD4, Dr. Craig Garfield, MD4, Dr. Jacqueline Pongracic, MD, FAAAAAF5, Dr. Xiaobin Wang, MD, MPH ScD6, 1University of Southern California, Los Angeles, CA, 2Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL. 3University of Michigan, Ann Arbor, MI. 4Northwestern University, Chicago, IL. 5Johns Hopkins, Chicago, IL.

RATIONALE: Living with food allergy has been found to strain familial relationships, limit social activities and diminish quality of life. Past studies on the psychosocial consequences of pediatric food allergy on caregivers have focused overwhelmingly on mothers. This study describes the impact of pediatric food allergy on mothers and fathers, assessing the relationship between parental empowerment and food allergy quality of life (FAQOL).

METHODS: 940 families of children with food allergy were included as part of a family-based cohort. Food allergy was determined by objective symptoms developing proximate to ingestion, skin prick, and specific IgE testing. Parental empowerment and FAQOL were assessed via an adapted Family Empowerment Scale and FAQOL—Parental Burden (PB) scale. Maternal and paternal scores were compared by t-test. Multivariate regression models examined the association of parental empowerment with FAQOL.

RESULTS: Mothers reported greater empowerment (P<.001) and reduced FAQOL (P<.0001) compared to fathers, regardless of food allergy severity, type, or comorbidities. However, no significant association was found between empowerment and FAQOL for mothers (P=.57) or fathers (P=.98). Though parents of children with peanut, milk, egg and tree nut allergy were similarly empowered, milk and egg allergy were associated with reduced FAQOL (P<.01). FAQOL-PB items that most strongly impacted parental FAQOL involved fears of allergen exposure in social situations away from home.

CONCLUSIONS: Parental empowerment and FAQOL vary significantly among mothers and fathers of children with food allergy. Empowerment to manage a food allergy is insufficient to ensure adequate FAQOL given widespread parental concern regarding allergen exposure in the broader social environment.

711 Prevalence Of Misconceptions Regarding Egg Allergy and Measles Mumps and Rubella Vaccine Contraindications
Dr. Vylma Velazquez, MD, Dr. Carmen Rivera, Dr. Monique Adorno; Hospital Episcopal San Lucas, Ponce, PR.

RATIONALE: Despite current guidelines concerning the administration of Measles, Mumps and Rubella (MMR) vaccine and revised contraindications, there are still misconceptions, especially when dealing with egg allergy and the vaccine. Our study proposes to evaluate eligibility criteria used at the time of immunization, in Ponce, Puerto Rico.

METHODS: A brief questionnaire was answered by voluntary participants (N=55), parents of children between the ages of 1-4 years, regarding certain variables, which may influence a child’s immunization status.

RESULTS: Of the surveyed parents, 20% were asked if their children had been exposed to eggs prior to vaccine trial, 29% was asked if there is any history of egg allergy, and 4% were asked about gelatin allergy. 7% of parents were asked about lack of egg exposure, 13% were asked about any family history of adverse reaction to vaccine and 16% of parents were asked if their children had any allergic reaction to the first dose of MMR vaccine. Of the parents who answered yes to any of the screening questions 4% of the children were referred to allergist, 4% vaccination were delayed to a later date, and in 4% of children the vaccine was not administer.

CONCLUSIONS: Our results demonstrated that some children with egg allergies or lack of exposure to eggs were wrongly delayed or denied the administration of the MMR vaccine. The pre-immunization screening question regarding egg allergy or exposure remains prevalent and is taken into consideration in deciding to whom to administer the vaccine.
712 Prenatal and Postnatal Factors Associated With IgE-Mediated Wheat Allergy In Infants: A Study In Asian Population
Dr. Suparat Sirivimonpan, MD; Chulalongkorn University, Bangkok, Thailand.
Rationale: Wheat allergy is a growing problem in Asian countries. Factors associated the diseases from western studies may not apply to the population because of genetic, geographical and dietary differences. Early life circumstances may affect development of sensitization and food allergy. We aimed to determine prenatal and postnatal factors associated with wheat allergy.
Methods: Using case-control design, 47 infants with IgE-mediated wheat allergy and 188 gender and age matched controls were enrolled. Personal histories and associated factors were analyzed.
Results: Ninety-two percent of wheat-allergic infants had symptoms on first exposure, suggested the role of sensitization intrauterine or via breast milk. Anaphylaxis occurred in 19% of subjects. Parental atopic histories and high socioeconomic status significantly increased the risk of wheat allergy. IgE-mediated wheat allergy was independently associated with maternal wheat consumption during pregnancy (bread: 3 pieces per week, adjusted odds ratio, 3.7; 95% confidence interval, 1.8 to 7.5; P = 0.001), and breast feeding beyond 6 months (adjusted odds ratio, 2.3; 95% confidence interval, 1.1 to 4.8; P = 0.03). Delayed wheat introduction after 6 months of age had trend toward the association with IgE positivity to wheat (adjusted odds ratio 1.8; 95% confidence interval, 0.9 to 3.9; P = 0.09).
Conclusions: Several factors during prenatal and early life period associated with the risk of IgE-mediated wheat allergy. Our findings demonstrated that genetic predisposition and socioeconomic status strongly increased risk of wheat allergy. Maternal consumption of wheat during pregnancy and prolonged breast feeding were significantly associated with the disease. Developing the strategies to prevent wheat allergy requires consideration of all these factors.

713 Maternal Healthy Diet and Development Of Allergic Disease
Dr. Carina Venter, PhD, RD1, Ms. Harriet R. Moonesinghe2, Prof. Hasan Ashraf3,4, Prof. Taraneh Dean5,6, Mrs. Jane Grundy7, Mrs. Gill Glasbe8, Dr. Veeresh Patil9,10, The David Hide Asthma and Allergy Research Center, Isle of Wight, United Kingdom, University of Portsmouth, School of Health Sci, Portsmouth, United Kingdom, The David Hide Asthma and Allergy Centre, Newport, United Kingdom, University of Southampton, Southampton, United Kingdom, The David Hide Asthma and Allergy Centre, Newport.
Rationale: Maternal healthy diet may play a role in the development of allergic diseases and need further investigation.
Methods: Pregnant women (n = 969) were recruited at 12 weeks gestation; a FFQ was completed at 36 weeks. Reported symptoms of allergic disease were obtained during infants first three years, and at 10 years. Children were skin prick tested to a panel of food and aero-allergens and food challenges conducted. Healthy Eating Index (HEI) was calculated as: multivitamin/mineral intake (2) + folic acid (1) + omega-3 fatty acids (1) + regular white fish (1)/ fatty fish intake (2) + citrus fruit (1) + ≥ 5/day fruit and vegetables (2) = 10
Results: Maternal diets scored low on HEI: 949/969 (97.9%) scored 0-5 and 20/969 (2.1%) scored 6-10. Using this binary HEI factors, no association with atopy (+ SPT) (3 years; p = 0.589 and 10 years; p = 0.519), reported allergic diseases (3 years; p = 0.489 and 10 years; p = 0.636) and food allergy (FA) (3 years; p = 0.450 and 10 years; p = 0.365) was seen. HEI as continuous variable was associated with FA by 3 years (p = 0.010; OR 1.244 [95% CI: 1.055 – 1.468]) even after adjusting for maternal allergic history and smoking, pet exposure and sibship. FA at 10 years showed no association (p = 0.128, OR 0.723 [0.475 – 1.099]). Fatty fish intake was associated with increased risk of atopy by 3 years (p = 0.023).
Conclusions: The role of healthy diet on development of allergic disease need more investigation using a robust method measuring food intake and sufficient numbers of healthy eating mothers.

714 Effect Of Annual Income On Parental/Family Burden Of Food Allergy
Dr. David A. Petty, DO1, Jay A. Lieberman, MD2, Nhu Quynh Tran, PhD3,1 University of Tennessee Allergy fellowship program, Memphis, TN, 2University of Tennessee, Memphis, TN, 3University of Tennessee Department of Preventive Medicine.
Rationale: Having a child with food allergies can cause a significant burden for families. We hypothesized the effect that a child’s food allergy would have on the family’s quality of life would be different among different socio-economic classes.
Methods: Parents of pediatric patients with physician-diagnosed food allergies were recruited from both a university and a private allergy clinic. Participants completed the Food Allergy Quality of Life-Parental Burden (FAQL-PB) questionnaire. Background and demographic data were also collected, family incomes were reported in quintiles (< $25,000, $25,000-50,000, $50,000-75,000, $75,000-100,000, and > $100,000). Wilcoxon rank sum tests were used for univariate analyses. Multiple linear regression was used to model the relationship between exploratory variables and the FAQL-PB scores.
Results: Data from 77 respondents were analyzed. The mean age of the food-allergic child was 6.69 years (range 1-17). 86% of respondents were mothers. The majority of respondents were either black (46%) or white (42%). In the univariate analysis, there was a significant difference in the FAQL-PB scores among different family income levels (P = 0.01), with the lowest scores seen in the $75,000-100,000 income quintile. This significance held in the multivariable analysis (P = 0.02). Factors associated with a decreased quality of life in the univariate analysis included if the respondent was the child’s mother (P = 0.03) and if the child was allergic to milk (P = 0.01) or wheat (P = 0.04).
Conclusions: In this survey study, there was a statistically significant variance in FAQL-PB scores among different family income levels, with the least perceived family burden seen in families reporting income levels between $75,000-100,000.

715 Food Allergy and Anaphylaxis Educational Needs Assessment, Training Curriculum and Assessment Of Knowledge Of Urban Child Care Center Workers
Dr. Bruce J. Launer, MD1, Dr. Ronina A. Covar, MD2, David Mark Fleischer, MD, FAAAAI1, Dr. J. Andrew Bird, MD, FAAAAI2, National Jewish Health, Denver, CO, 1UT Southwestern Medical Center, Dallas, TX.
Rationale: More than half of preschool aged children are enrolled in child care, and nearly 10% between ages 3 and 5 have a food allergy. The need exists for food allergy and anaphylaxis educational needs assessment and training curriculum for child care center workers.
Methods: An online educational needs assessment and live training curriculum with pre and post-test were created, reviewed by experts and piloted with a focus group of child care workers to obtain content and face validity. A SurveyMonkey link to the needs assessment was sent to email addresses from the state licensing agency to centers in Dallas and Tarrant Counties. The curriculum and eighteen question test addressed the areas of understanding labeling and the definition of food allergy, recognizing a reaction and treatment.
Results: Seventy-three workers responded to the online needs assessment, with 43% having food allergy training. They identified their sources of information as parents (73%), self-taught (54%), educational curricula (21%) and conferences (19%). The majority felt they have a high or moderately high proficiency in food allergy management. Forty-five workers participated in the training curriculum, presented at regional child care conferences. Total scores improved from 54% correct on pre-test to 83% on post-test, (p < 0.0001). Categorical sub-analysis reveals similar results, with statistically significant improvement in all areas.
Conclusions: Child care center workers have diverse educational backgrounds and infrequently experience standardized training about food allergies. There is a significant lack of knowledge regarding food allergies and anaphylaxis. The curriculum was successful at educating workers to more safely care for children with food allergies.
Food Allergy Survey Among Food Service Workers

Bruce M. Preston, MD, John Hollingsworth, PA, Ron Oliver, Linnet Brew, LVN, Allergy Partners of San Diego, San Diego, CA.

Rationale: The number of individuals with food allergy has grown significantly in recent years, and it is a problem for children and adults. Restaurant workers have been noted to have an improper understanding of how allergic reactions occur. The purpose of this questionnaire/survey is to examine awareness of restaurant personnel regarding the seriousness of anaphylaxis caused by accidental ingestion of allergenic food.

Methods: The survey consisted of ten multiple-choice or true/false questions in English only on food allergens, food allergy reactions, and anaphylaxis. Individuals responding to the questionnaire were asked to respond according to their position in the food establishment. We graded the surveys and examined the results according to workers’ job function. Descriptive results are provided for the proportion (%) of correct answers to the 10 questions among workers.

Results: Survey responses were obtained from a total of 120 workers at 5 food industry establishments. The average score across workers was 79%, with average scores among bussers, hostesses, kitchen staff, servers, management, and bartenders as well as chefs of 58%, 73%, 75%, 80%, 89%, and 90%, respectively. Among kitchen staff at 3 restaurants, scores ranged from 55% to 93%. Kitchen staff at 2 hospitals had scores of 61% and 91%, respectively. Among kitchen staff at 3 restaurants, scores ranged from 55% to 93%. Kitchen staff at 2 hospitals had scores of 61% and 91%. The average score across workers was 79%, with average scores among bussers, hostesses, kitchen staff, servers, management, and bartenders as well as chefs of 58%, 73%, 75%, 80%, 89%, and 90%, respectively. Among kitchen staff at 3 restaurants, scores ranged from 55% to 93%. Kitchen staff at 2 hospitals had scores of 61% and 91%.

Conclusions: Knowledge of allergy among food industry workers is variable, showing the need for a program conducted by physicians and properly educated chefs for food service workers. This will be based on the program developed by the original FAAN (Food Allergy and Anaphylaxis Network) to provide detailed information on food allergens and anaphylaxis.

Bullying and Food Allergy – Longitudinal Follow-Up

Scott H. Sichener, MD, FAAAAI, Melissa Rubes, Chloe Mulbarkey, Mordechai Abramese, Nogu Ravid, Kelley Chung, Rachel Annunziato, Eyal Shemeshe, Mount Sinai School of Medicine, New York, NY; Fordham University, NY. Tchaan School of Medicine at Mount Sinai, NY.

Rationale: Bullying is frequently reported by children with food allergy (FA), but no longitudinal studies have been reported regarding persistence.

Methods: Identical questionnaires were mailed ~1 year (T2) following baseline (T1) assessments of 251 children with FA attending the Jaffe Food Allergy Institute clinical practice. Questionnaires included bullying and allergy characteristics, quality-of-life (QoL), demographics, and anxiety, as previously reported for this cohort (Pediatrics. 2013;131(1):e10-17).

Results: 124 (49%) patient-parent packets were returned. Reported bullying due to food allergy decreased significantly: 31.5% in T1, 28.2% in T2. There were 8 new cases of bullying in T2 (6.5% of the T2 sample). QoL scores did not differ between patients who were bullied in both T1 and T2 (persistent bullying) compared with those who were bullied only in T2 (t=−1.37, p=0.18). Regarding T2 completers who reported being bullied in T1, logistic regression showed that both a younger age (p < 0.01), and a parental report that the parent “did something about the bullying”, predicted resolution of bullying at T2 (p = 0.05). Children’s report of telling the parent about being bullied, or parents’ report that they knew about the bullying, did not significantly predict resolution (p = 0.20).

Conclusions: New and persistent bullying had a similar impact on QoL, reinforcing previous conclusions that any bullying (long or short term) is associated with lower QoL. The results also suggest that resolution of bullying required an active parental intervention; parents’ merely knowing that bullying occurred was not enough.


Ms. Taiye M. Oladipo, MPH, Dr. Stefano Luccioli, MD, FAAAAI; Center for Food Safety and Applied Nutrition, Food and Drug Administration, College Park, MD.

Rationale: Limited data are available on the frequency and characteristics of consumer-reported allergic adverse events to food products. The FDA’s Center for Food Safety and Applied Nutrition Adverse Events Reporting System (CAERS) is a passive surveillance system that collects adverse event reports (AERs) indicating regulated foods and cosmetics.

Methods: AERs to food products that were received between 2007 and 2011 and, that cited allergy, hypersensitivity, or anaphylaxis were reviewed to ascertain probable food allergic (non-anaphylactic) and anaphylactic events, as well as to understand the frequency and characteristics of indicated food allergens and product categories.

Results: Of 11,027 AERs involving consumption of conventional foods, 637 (5.8%) indicated allergy, hypersensitivity, or anaphylaxis. Of these reports, 258 (2.3%) were ascertained as probable non-anaphylactic events; 58 (0.5%) met anaphylaxis guideline criteria. No trend was observed in the number or frequency of probable food allergic events by year. The majority of probable events involved a consumer concern of an undeclared allergen in the food. For non-anaphylactic events, the food allergens most commonly identified included peanuts (13.2%), milk (11.2%), and egg (7.0%). For anaphylactic events, the food allergens most commonly identified included milk (31.0%), peanuts (20.7%), and tree nuts (19.0%); the main food categories included bakery (16.3%), cereal/breakfast food (10.0%), and ice cream (6.7%). For anaphylactic events, the food allergens most commonly identified included milk (31.0%), peanuts (20.7%), and tree nuts (19.0%); the main food categories included bakery (20.8%), and chocolate (15.3%).

Conclusions: Consumer-reported probable allergic events represent 2-3% of all food AERs in CAERS. Review of these reports revealed differences in food allergens and food categories indicated in reports of non-anaphylactic vs. anaphylactic events.

Impact Of School Peanut-Free Guidelines On Epinephrine Administration

Dr. Lisa M. Bartnikas, MD, Dr. Michelle F. Huffaker, MD, Dr. William J. Sheehan, MD, Dr. Watcharoot Kanchongkitiphon, MD, Paul D. Jr., Mr. Carter Petty, MA, Ms. Anne Sheetz, RN, BSN, MPH, Dr. Robert Leibowitz, PhD, Dr. Michael C. Young, MD, FAAAAI, Dr. Wanda Phipatanakul, MD, MS, FAAAAI, Dr. Lisa M. Bartnikas, MD, Dr. Michelle F. Huffaker, MD, Dr. William J. Sheehan, MD, Dr. Watcharoot Kanchongkitiphon, MD, Paul D. Jr., Mr. Carter Petty, MA, Ms. Anne Sheetz, RN, BSN, MPH, Dr. Robert Leibowitz, PhD, Dr. Michael C. Young, MD, FAAAAI, Dr. Wanda Phipatanakul, MD, MS, FAAAAI, Dr. Lisa M. Bartnikas, MD, Dr. Michelle F. Huffaker, MD, Dr. William J. Sheehan, MD, Dr. Watcharoot Kanchongkitiphon, MD, Paul D. Jr., Mr. Carter Petty, MA, Ms. Anne Sheetz, RN, BSN, MPH, Dr. Robert Leibowitz, PhD, Dr. Michael C. Young, MD, FAAAAI, Dr. Wanda Phipatanakul, MD, MS, FAAAAI, Dr. Lisa M. Bartnikas, MD, Dr. Michelle F. Huffaker, MD, Dr. William J. Sheehan, MD, Dr. Watcharoot Kanchongkitiphon, MD, Paul D. Jr., Mr. Carter Petty, MA, Ms. Anne Sheetz, RN, BSN, MPH, Dr. Robert Leibowitz, PhD, Dr. Michael C. Young, MD, FAAAAI, Dr. Wanda Phipatanakul, MD, MS, FAAAAI.
AB208 Abstracts

FEBRUARY 2014

720 Comparison Of Germfree and Conventional Mice For Evaluating The Potential Allergenicity Of Dietary Proteins Using Model Allergenic and Non-Allergenic Proteins
Nathan L. Marsteller1,2, Mr. Kwame Andoh-Kumi1, Daniel A. Peterson3, Richard E. Goodman1, Joe L. Baumert1, 1Food Allergy Research and Resource Program, University of Nebraska-Lincoln, Lincoln, NE, 2School of Biological Sciences, University of Nebraska-Lincoln, 3Johns Hopkins School of Medicine, Baltimore, MD.

RATIONALE: Currently no animal model of food allergy has proven to be predictive of human responses in ranking purified dietary proteins in prevalence or potency of allergy. Since the intestinal microbiota is thought to influence oral tolerance, we hypothesize that a germfree mouse model will more accurately predict human responses than conventional mice.

Preliminary studies were undertaken to test the sensitizing and eliciting responses to a potent dietary allergen, β-lactoglobulin (BLG), compared to a non-allergenic dietary protein, soy lipoygenase (LOX).

METHODS: Conventional and germfree C57/HeN mice were sensitized with BLG or LOX by three weekly intraperitoneal injections (IP) with alum adjuvant. One week following the final sensitization an IP challenge of 500 μg BLG or LOX was administered. Thirty minutes post-challenge clinical scores were graded (0 = no symptoms to 5 = death) and body temperatures recorded. Specific IgE and mast cell protease serum concentrations were determined by ELISA.

RESULTS: Upon challenge conventional mice sensitized with BLG exhibited significantly more severe clinical scores (average 4) compared to conventional mice sensitized with LOX (average 1). The mean temperature drop post-challenge for BLG and LOX sensitized mice was 8°C and 2°C, respectively. Germfree mice sensitized with BLG elicited stronger responses than conventional mice sensitized with BLG.

CONCLUSIONS: BLG and LOX results in conventional mice indicate that this model could differentiate between potent and non-allergens based on temperature drop and clinical scores 30 minutes post challenge. Preliminary results suggest there is less clinical variance when the mice are germfree. Tests with additional proteins are required to estimate predictive power.

721 The Role Of Lipopolysaccharide In Skeewing The Sensitization Potential Of Purified β-Lactoglobulin In A Mouse Model
Mr. Kwame Andoh-Kumi1, Richard E. Goodman1, Daniel A. Peterson2, Joe L. Baumert1, Nathan L. Marsteller1,2, 1Food Allergy Research and Resource Program, University of Nebraska-Lincoln, Lincoln, NE, 2Johns Hopkins School of Medicine, Baltimore, MD.

RATIONALE: Published studies have reported that lipopolysaccharides (LPS) present in protein sources used to sensitize mice skew the immune response towards a Th1, non-allergic response. Initial tests with bovine LPS in BLG-A was high (2561 EU/mg protein) compared to LPS in BLG-B (<5 EU/mg protein). Toward the development of better allergens, we hypothesized that a germfree mouse model will more accurately predict human responses in ranking purified dietary proteins in prevalence or potency of allergy.

METHODS: Alum was added to each protein source to achieve a constant concentration of 3 μg/mg protein. A total of 260 oral food challenges were performed to egg (n=63), milk (n=63) and peanut (n=63). Mean age of patients was 5.1 years (range: 1-16). The majority were male (70.8%) and Caucasian (79.3%).

RESULTS: Post-challenge body temperature loss was less pronounced in GF mice treated with BLG-A (5.9°C) compared to BLG-B (7.5°C). No differences in body temperature loss (8°C) or lethality (2/9) were observed between the conventional mice sensitized with either BLG or LOX.

CONCLUSIONS: Higher levels of LPS in the sensitization dose seemed to have skewed the immune response toward less pronounced allergy in germfree, but not in mice with conventional microbiota.

722 Oral Co-Administration Of Peanut and Cholera Toxin Subunit B During Pregnancy and Lactation Blocks Anaphylaxis and Induces Epigenetic Modifications In Peanut Allergic Murine Mothers
Dr. Ying Song, MD1, Dr. ChangDa Liu1, Dr. Kamal D. Srivastava, PhD1, Dr. Jia Chen, ScD1,2, Dr. Rachel L. Miller, MD, FAAAI1, Dr. Xia-Min Li, MD1,2,1Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, 3Prevention, Icahn School of Medicine at Mount Sinai, NY, 2Division of Pulmonary, Allergy and Critical Care Medicine, Columbia University, New York, NY.

RATIONALE: The prevalence, severity of reactions, and life-long nature of peanut allergy (PNA) lead particular urgency to develop strategies to treat PNA. We previously showed that maternal consumption of low dose PN plus the nontoxic mucosa-binding B subunit of cholera toxin (CTB) induced tolerance to active peanut sensitization in offspring of peanut allergic mothers. We hypothesized that this approach may also have a beneficial immunotherapeutic effect on peanut allergic mothers.

METHODS: Peanut allergic female mice were received PBS (Sham) or 10 mg PN mixed with 20μg CTB (PN+CTB) during pregnancy and lactation weekly for 6 weeks. CTB and PN consumption alone were employed as controls. Anaphylactic reactions, plasma histamine levels, sera PN-IgE and fecal PN-IgA levels, cytokine levels in spleenocyte cultures, and peripheral blood leukocytes (PBL) DNA methylation at CpG sites of Foxp3 and IL-4 promoters were determined.

RESULTS: As compared to sham-fed mice, PN+CTB-fed mice exhibited weaker anaphylactic reactions, reduced PN-specific IgE and plasma histamine levels, and increased PN-IgA levels (all p<0.05). PN stimulated cultured spleenocytes exhibited increased IL-10, and reduced IL-4 production. PBL Foxp3 promoter DNA methylation was decreased, whereas IL-4 promoter methylation was increased (p<0.05–0.01).

CONCLUSIONS: PN+CTB consumption during pregnancy and lactation protects against peanut anaphylaxis. Induction of regulatory cytokines and epigenetic mechanisms are associated with the immunotherapeutic effects.

723 Worsened Reaction Severity In Oral Food Challenges Confirms Need For In-Office Procedure
Dr. Annie Esquivel, Dr. Girish V. Vitalpur, MD, FAAAAI, Dr. Kirsten Kloepfer, MD, Dr. Frederick E. Leickly, MD, MPH, FAAAAI, Riley Hospital for Children at Indiana University Health, Indianapolis, IN.

RATIONALE: Oral food challenges (OFCs) determine food tolerance/reactivity. We examined OFC failures to assess predictive factors for a failed challenge.

METHODS: A retrospective chart review analyzed patients undergoing OFCs to egg, milk, and peanut at Riley Hospital for Children’s Allergy Clinic from January 2008 to December 2012. Families were offered OFC when food specific IgE was below an established critical cut-off. Data were analyzed by SPSS.

RESULTS: 260 oral food challenges were performed to egg (n=120), peanut (n=77) and milk (n=63). Mean age of patients was 5.1 years (range: 1-16). The majority were male (70.8%) and Caucasian (79.3%). Overall, 46/260=17.7% failed. The most common reaction was urticaria/angioedema (14/46=30.4%). The second most common was anaphylaxis (12/46=26.1%). Of the 12 patients with anaphylaxis, 10 occurred with egg. Forty percent (4/10) of egg anaphylaxis occurred in baked egg challenges. Only 25% (3/12) with anaphylaxis during OFC had initial presentation of anaphylaxis. Egg accounted for 50% of the failed challenges (23/46). There were no significant differences between OFC successes and failures with regard to food type, specific IgE level, family history of atopy, or history of atopic dermatitis, asthma or other food allergies.

CONCLUSIONS: 18% of patients failed the OFC. Egg was the most common failure, and serious reactions were more common to egg. Of the 12 patients with anaphylaxis, 75% had less severe reactions initially. Thus, serious reactions can occur in children who never experienced such a reaction before. Due to this risk, the OFC should be performed in a controlled clinical environment.

All abstracts are strictly embargoed until the date of presentation at the 2014 Annual Meeting.
Oral Allergy Challenge Outcome Among Children With a Negative Skin Prick Test Result

Dr. Wipa Jessadapakorn, MD1, Dr. Prapastri Kalalert, MD2, Dr. Araya Yuenyongwisat, MD3, Dr. Pasaprue Sangsupawanich, MD4. 1Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat-Yai, Songkhla, Thailand, 2Prince of Songkla University, Songkhla, Thailand, 3Prince of Songkla University, Songkhla, Thailand, 4Prince Songkhlana garind hospital, Hatyai, Thailand.

Rationale: Oral food challenges (OFCs) are procedures to make an accurate diagnosis of food allergy and are usually performed in the hospital because of risks of systemic and life-threatening reactions. However, the disproportionate numbers of patients and allergists make the OFCs in the hospital impractical. Thus, we aimed to examine the outcome of OFCs among children with histories of non-severe food reactions.

Methods: A retrospective chart review of children with negative skin prick test (SPT) results who underwent OFCs at the Pediatric Allergy Clinic of Songklanagarind Hospital between July 2011 and August 2013 was performed. Children with histories of severe food reactions were excluded. SPTs were performed using commercial food extracts.

Results: We performed 88 OFCs in 69 children (30 males, 39 females). The mean age of children who participated in OFCs was 20 months (range, 2 months – 8 years). Most children (53.6%) were presented with atopic dermatitis. Cow’s milk was the most commonly tested food (60%). Sixteen of the 88 OFCs (18%) failed the challenges. Most reactions occurred after 24 hours and were self-limited. Only 1 out of 16 developed sneezing and rhinorrhea at 2 hours after the OFC and was treated with oral antihistamine. No systemic or severe reactions were observed.

Conclusions: Although OFCs can cause severe allergic reactions and should be done in a hospital, our data found that most patients with negative SPTs who experienced only eczema or mild allergic reactions had a low risk for OFCs. In selected patients, OFCs can be done at home safely.

Abbreviated Oral Food Challenge As a Safe and Effective Alternative For Diagnosing Food Allergy In A Pediatric Clinic

April L. Goolsby, BS1, Heather Minto, MD, MS2, Amy Perkins, MS2, Kelly M. Maples, MD1,2, Eastern Virginia Medical School, Norfolk, VA, 2Children’s Hospital of The King’s Daughters, Norfolk, VA.

Rationale: Along with the increasing prevalence of food allergy (FA), comes increased misdiagnosis and unnecessary food avoidance. Skin prick tests (SPT) and specific IgE testing have a high false positive rate and alone are insufficient for FA diagnosis. Traditional oral food challenges (OFC) are the gold standard for FA diagnosis but are also lengthy, costly, and impractical for many allergy clinics. A two-step abbreviated oral food challenge (AOFc) may be as reliable and safe in FA diagnosis in selected populations while improving cost, efficiency, and availability of food challenges.

Methods: A retrospective chart review of 2-18 year-olds who completed an OFC or AOFc at our children’s hospital between January 2010 and December 2012 was performed to assess the safety, efficacy, and reliability of AOFc compared to OFC. Demographics, history, and allergic sensitizations by SPT and IgE were collected. OFC and AOFc were compared by challenge pass rates, frequency of epinephrine usage, and time to completion of the food challenge.

Results: 203 AOFc and 232 OFC were completed. In each group, 10% of patients failed and 90% passed the challenge. 14% of patients given AOFc and 17% of patients given OFC required epinephrine after failure. Mean AOFc time to completion was 112.2 minutes, and mean OFC time was 246.2 minutes (P<0.001).

Conclusions: In carefully selected patients, AOFc is a safe, effective alternative to OFC in FA diagnosis. AOFcs reduce the length of food challenges and unnecessary food avoidance while increasing availability of testing and office productivity.

Safety Of Ungraded Oral Food Challenges In Ruling Out Peanut Allergy In Children

Dr. Darlene Kassab Mansoor, MD, MS1, Amit Singal, BS2, Shweta Bansil, BS2, Dr. Hemant P. Sharma, MD, MHS, FAAAI1, Children’s National Medical Center, 2George Washington University School of Medicine.

Rationale: Indiscriminate testing may misdiagnose peanut allergy (PA) due to false positive results. Oral food challenges (OFC) are the gold standard for ruling out PA, but are time-consuming and costly. A one-step, ungraded OFC versus traditional graded OFC may more efficiently rule out PA in select low-risk patients, but its safety is unknown.

Methods: A retrospective chart review was conducted of peanut OFC performed between 2011 and 2013 at a pediatric allergy referral center. Patients were offered ungraded OFC if they had: no prior peanut exposure or reaction history inconsistent with PA, peanut IgE <2kU/L, and peanut skin prick test (SPT) wheal diameter <8mm. Ungraded OFC delivered the goal peanut dose in one dose, while graded OFC used six gradually escalating doses. OFC outcome was compared between the two groups.

Results: 86 OFC were conducted, 11 of which were ungraded. Mean peanut-SPT was smaller in ungraded versus graded OFC (1.1mm and 5.6mm, p<0.01), but peanut-IgE did not significantly differ (0.8kU/L and 2.1kU/L respectively, p=0.24). Mean age did not differ between ungraded and graded OFC (4.2 and 6.0 years respectively, p=0.12), nor did prevalence of comorbid atopic disease. 11/11 ungraded OFC were passed, compared to 49/75 (65%) graded OFC (p=0.02). 2/11 patients undergoing ungraded OFC developed mild self-limited symptoms (sneezing and perioral rash); 0/11 required treatment with antihistamine or epinephrine. 14/75 (18.7%) of graded OFC required epinephrine treatment.

Conclusions: In carefully selected patients with a low pre-test probability of PA, ungraded OFC may be a safe and efficient way to rule out PA.

Safety Of Oral Food Challenges To Extensively Heated Egg In Children

Dr. Cindy Nguyen, MD1, Shweta Bansil, BS2, Amit Singal, BS2, Dr. Hemant P. Sharma, MD, MHS, FAAAI1, Children’s National Medical Center, Division of Allergy and Immunology, Washington, DC, 2George Washington University School of Medicine, 3Children’s National Medical Center, Division of Allergy and Immunology, DC.

Rationale: A majority of egg-allergic children tolerate extensively heated or baked egg products in their diet, and this is often initially determined through an oral food challenge (OFC) to baked egg. However, the characteristics of children who react to baked egg during OFC and the severity of their reactions are poorly defined.

Methods: A retrospective chart review was conducted of baked egg OFC performed at an allergy referral center between 2011 and 2013. Egg-allergic subjects strictly avoided all egg prior to OFC. Challenges were performed following a standardized protocol with incremental dosages to a total amount of cake containing ¼ egg. Patient characteristics were compared between passed and failed OFC.

Results: Baked egg OFC was conducted in 34 children. Eighteen (53%) passed, 7 (21%) refused to eat the total goal dose, and 9 (26%) failed due to reactions requiring treatment. The most common reaction symptoms were skin and gastrointestinal complaints. Of those who reacted, 4 (44%) required treatment with epinephrine, but none required multiple doses. Comparing passed versus failed OFC, no significant differences were observed in mean age (5.8y and 3.7y respectively, p=0.11), prevalence of comorbid atopic disease, or symptoms on prior accidental egg exposure. Egg skin prick test wheat size did not differ between passed and failed OFC (9mm and 9.7mm respectively), nor did egg white-specific IgE (8.9 and 31.1kU/L respectively, p=0.27).

Conclusions: While the majority of children tolerated baked egg OFC, 44% of those who reacted required epinephrine treatment. Baked egg OFC should take place in medically supervised settings.
All abstracts are strictly embargoed until the date of presentation at the 2014 Annual Meeting.

729 Risk Of Oral Food Challenges In Children - a Prospective Multicenter Study -
Dr. Toshiko Itazawa, MD, PhD1, Dr. Motokazu Nakabayashi, MD, PhD1, Dr. Yasunori Ito, MD, PhD, Dr. Yoshie Okabe, MD, PhD1, Dr. Yoko S. Adachi, MD, PhD1, Dr. Yuichi Adachi, MD, PhD1, Dr. Komei Ito, MD, PhD2, Motohiro Ebisawa, MD, PhD, FAANAI1, 1Department of Pediatrics, University of Toyama, Toyama, Japan, 2Aichi Children’s Health and Medical Center, Obu, Aichi, Japan, 3Clinical Research Center for Allergy and Rheumatology, Saga University National Hospital, Kanagawa, Japan.  
Rationale: Oral food challenges (OFCs) are essential to the diagnosis of food allergy or tolerance to a food. However, there are few multicenter studies about risk of OFC.  
Methods: A prospective multicenter study was performed to evaluate provoked symptoms in OFC. Each center was asked to register all OFCs or a maximum of 100 consecutive OFCs during 6 months.  
Results: Data of 5,270 OFCs were enrolled. Data of OFC for rush immunotherapy, patients older than 19 years old and insufficient questionnaire information were excluded. A total of 5,063 OFCs (median: 3.7 years old, male: 65.0%) from 113 hospitals and 6 clinics were analyzed. Most frequently tested foods were egg (n=2,462), milk (n=1,094), and wheat (n=609), with the following positive rate for each food; egg 43.3% (1,067), milk 54.5% (596), and wheat 54.2% (330). Among children with positive response to egg, cutaneous reactions were most common (69.5%), followed by gastrointestinal (51.6%) and respiratory (32.6%) symptoms. Similarly, cutaneous reactions were most common (79.2%), followed by respiratory (52.1%) and gastrointestinal (17.3%) symptoms.  
Conclusions: OFCs can result in not only mild allergic reactions but also systemic or severe reaction. OFC should be carried out only under the close supervision by trained physicians. This study was performed by Oral Food Challenge Survey Group.

730 A Double-Blind Randomized Controlled Trial Of A Thickened Amino-Acid-Based Formula In Children Allergic To Cow’s Milk And To Protein Hydrolyzates  
Prof. Nicolas Kalach, MD, PhD1, Dr. Elena Bradtana2, Prof. Alain Lachaux3, Dr. Francois Payot1, Prof. Frederic de BLAY4, Dr. Lydie Guenard-Bilbaux5,6, Dr. Riad Hatahet2, Dr. Sandra Muller8, Prof. Christophe Dupont, MD, PhD7, 1Hopital Saint Vincent de Paul, Groupement des Hopitaux de l Institute Catholique de Lille (GH-ICL), Lille, France, 2Department of Pediatrics, Regional Hospital, Namur, Belgium, 3Gastroenterology, Hepatology and Nutrition Unit, University and Pediatric Hospital of Lyon, France, 4CHRU Strasbourg, France, 5Regional University Hospital, Strasbourg, Strasbourg, France, 6Allergologist, Illkirch-Graffenstaden, France, 7Pediatrician Allergologist, Forbach, France, 8Queen Fabiola Children’s, University Hospital, Brussels, Brussels, Belgium, 9Hopital Necker Enfants Malades, Paris, France.  
Rationale: Children with cow’s milk allergy (CMA) may also be allergic to extensively hydrolyzed protein formulas (ehF). Amino acid-based formulas (AAFs) are recommended in such cases, though no AAF has been clinically tested in infants allergic to ehF.  
Methods: 86 infants were randomized in a double-blind controlled trial comparing a “thickened” AAF (Elementa, United Pharmaceuticals) and a commercially available “reference” AAF. Only patients whose symptoms did not improve with an ehF were included. CMA was confirmed through a double blind placebo controlled food challenge. Digestive, cutaneous and respiratory symptoms as well as growth parameters were assessed at 1, 3 and 6 months.  
Results: Data at 1 month show that both formulas were tolerated (100% of children for “thickened” AAF and 95% for “reference” AAF). CMA and ehF allergy were confirmed in 75 children; all of them tolerated the tested formulas. The main allergic symptom disappeared completely within 1 month in 26/42 (61.9%) and 17/33 (51.5%) respectively with the “thickened” and the “reference” AAF (ns). Infants had significantly more normal stools (90.5% vs 66.7%, p=0.011) with the “thickened” AAF versus the “reference” AAF. Regurgitations disappeared completely in 65.4% vs 42.3% (ns) respectively. Weight-for-age z-score increased by 0.1±0.3 (mean±SD) for the “thickened” AAF and 0.2±0.4 for the “reference” AAF (ns). BMI z-scores increased respectively by 0.2±0.6 and 0±0.7 (ns).  
Conclusions: This is the first demonstration of AAF efficacy in CMA associated with ehF allergy. The “thickened” AAF was tolerated by all infants and growth parameters were appropriate.
731 Impact Of Formula Containing Docosahexaenoic Acid, Prebiotics, and Beta-Glucan On Allergic Manifestations In Young Children

Dr. Deolinda Scalabrini, MD, PhD1, Suzanne Stolz1, Weihong Zhuang1, Mariana Pontes2, Angela de Matos3, Indhira Almeida2, Carolina Godoy2, Sara Gatto2, Vivian Leal2, Gabriela Cabral2, Tereza Ribeiro2, Hugo Ribeiro1, I Mead Johnson Nutrition, Evansville, IN. 2 Federal University of Bahia, Brazil.

RATIONALE: Nutrients such as docosahexaenoic acid (DHA), prebiotics, and beta-glucan have been associated with reduced incidence of respiratory illnesses and allergic manifestations. Our objective was to assess if a cow’s milk-based formula enriched with these and other nutrients, including zinc, vitamin A, and iron, reduced the incidence of respiratory infections and diarrheal disease and secondarily the occurrence of allergic manifestations (AM) in healthy children.

METHODS: In this double-blind, randomized, controlled trial, healthy children (1-4yrs) from 2 daycare centers in Brazil were fed 3 servings per day of a follow-up formula (FF; n = 125) containing DHA, the prebiotics polydextrose (PDX) and galactooligosaccharides (GOS), and beta-glucan, or a control cow’s milk (C; n = 131) for up to 28 weeks. The occurrence of respiratory infection, diarrheal disease, and allergic manifestation was assessed by study pediatricians and analyzed with the Cochran-Mantel-Haenszel test.

RESULTS: The FF group had fewer episodes of AM, which included allergic rhinitis, conjunctivitis, wheezing, allergic cough, eczema, and urticaria, compared to the C group (p = 0.021). The hazard ratio for AM was lower in the FF group compared to control (HR, 0.64; 95% CI 0.47-0.89; p = 0.007). There was no difference in the incidence of respiratory infections and diarrheal disease between groups.

CONCLUSIONS: A cow’s milk-based formula containing DHA, PDX/GOS, and beta-glucan, and enriched with micronutrients including zinc, vitamin A, and iron, when consumed 3 times per day for 28 weeks by 1-to-4 year-old children, was associated with fewer episodes of allergic manifestations in the skin and the respiratory tract, as compared to cow’s milk.

732 Parents’ Perception Of The Likelihood Of Future Life-Threatening Events In Their Children With Food Allergies

Dr. Peter Arkwright, MD, PhD, FAAAAI1, Ms. Jennifer Ogg1, Dr. Naomi Davis2, Dr. Ming Wan1; 1 University of Manchester, Manchester, United Kingdom, 2 Royal Manchester Children’s Hospital, United Kingdom.

RATIONALE: In children suffering from food allergies, factors determining parents’ perception of future risk of life-threatening events are largely unknown. A better understanding of this will help to tailor advice and support to parents who are most in need.

METHODS: Questionnaires were completed by parents bringing their children to regional pediatric allergy outpatient clinics with food allergies, and for comparison, parents of children attending an adjoining pediatric orthopaedic clinic after sustaining a fracture. Data were collected on parents’ demographics and the nature of the allergy or injury. Using validated scoring systems, parents’ perceived risk and severity of future events, as well as anxiety and depression scores were also assessed.

RESULTS: Data were collated from 69 parents of children with food (38%) nut allergy and 73 parents of children with fractures. There was no difference in educational level, depression or anxiety scores between the two groups. Compared with parents of children suffering from fractures, parents of children with food allergies perceived a significantly higher risk of future severe (59% versus 10%, P < 0.05) and fatal events (28% versus 3%; P < 0.02). Parents of children with food allergies who had higher anxiety scores perceived a greater risk their child dying from their allergy (40% versus 7%; P < 0.05).

CONCLUSIONS: Parents of children suffering from food allergies, particularly those with higher anxiety scores, are significantly more likely to be concerned that their child may die of future events than those whose children have suffered a fracture.

733 Can Training Improve Allergists’ Ability To Accurately Identify Anxiety In Children With Food Allergy?

Melissa Rubes1, Anna Podolsky2, Nicole Caso1, Rachel Annunziato1, Dr. Amand A. Cox, MD2, Dr. Jennifer S. Kim, MD, FAAAAI, Dr. Anna H. Nowak-Wegrzynek, MD, FAAAAI, Dr. Julie Wang, MD, FAAAAI, Scott H. Sicherer, MD, FAAAAI, Eyal Shemesh; 1 Fordham University, NY, 2 Icahn School of Medicine at Mount Sinai, NY, 3 Mount Sinai School of Medicine, New York, NY.

RATIONALE: Anxiety is common in children with food allergy and is associated with decreased quality of life; we therefore evaluated a brief workshop to improve allergists’ detection of anxiety.

METHODS: 39 food-allergic children aged 8-17 years and their allergists separately completed the Screen for Child Anxiety Related Disorders (SCARED), a validated questionnaire. The 5 participating allergists attempted to estimate their patient’s responses. We analyzed the differences between patients’ and allergists’ reports. A child psychologist and a psychologist delivered a 60-minute workshop, in which four items with the highest rate of discrepant answers were discussed, and specific verbal screening questions were suggested. Following the workshop, the same allergists completed the SCARED for a different cohort of 39 children.

RESULTS: Following the workshop, clinicians’ “do not know” responses to questionnaire items decreased from 70% to 5%. However, the correlation between clinician and child responses remained insignificant (r = .31, p = .32, before workshop; r = .30, p = .068, after). 20% (8 patients) of the first cohort exceeded the SCARED threshold score for clinically meaningful anxiety, 10% (4 patients) met that threshold in the second cohort. Clinicians identified 1/8 of the cases in the first; and 1/4 of the cases in the second. Two clinicians reported that evaluating anxiety interfered with their practice and 3 of 5 indicated they would not continue to use the screen.

CONCLUSIONS: This brief educational workshop was neither useful nor acceptable in improving allergists’ ability to screen for anxiety, and different modalities, such as self-administered screens, are likely needed.

734 Nutritional Status Impairment In Patients With Food Allergies

Dr. Gesmar Segundo, Mrs. Larissa Costa, Mrs. Erica Rezende; Universidade Federal de Uberlandia, Uberlandia, Brazil.

RATIONALE: Food allergy (FA) is a common disease that is rapidly increasing in prevalence for reasons that remain unknown. The aim of this study was to analyse the clinical characteristics and nutritional status of patients with food allergies followed in a tertiary centre of allergy and immunology.

METHODS: A retrospective study was performed that assessed the data records of patients with food allergy diagnosis, covering a period from February 2009 to February 2012. 354 patients were evaluated in the period; 226 (69.1%) patients had a confirmed FA diagnosis, while the remaining 128 (30.9%) had a diagnosis of FA excluded.

RESULTS: The age of patients with an FA diagnosis was lower (median=36.5 months, IC=1-216 months). There were no statistical differences in sex, gestational age, birth type, breastfeeding period and age of introduction of complementary formulas based on cow milk protein. The z-scores for weight-for-age, height-for-age, and body mass indices-for-age showed lower significant values in the FA group compared with the non-FA group by Mann Whitney test, with significance values of p=0.0005, p=0.0030, and p=0.0066, respectively.

CONCLUSIONS: FA patients had a lower growth rate in comparison with patients without FA. The early recognition of food allergies with the establishment of protein-implicated diet exclusion, in association with an adequate nutrient replenishment, is important to reduce the nutritional impact of food allergies.
AB212 Abstracts

735 Everyday Life Impact On Food Allergy Spanish Children. Caregivers Perception
Dr. Elena Alonso-Lebrero, PhD1, Dr. Julio Monleone, MS2, Alberto Alvarez-Perea, MD3, 1Hospital Materno Infantil Gregorio Marañon Pediatric Allergy Section, Madrid, Spain, 2Santa Barbara, Madrid, Spain, 3Hospital Materno Infantil Gregorio Marañon, Pediatric Allergy Department, Madrid, Spain.

RATIONALE: Food allergies (FA) affect family’s activities. Our aim was to determine FA impact on Spanish parents/caregivers.

METHODS: 325 parent’s FA children from public pediatric hospital filled-out an anonymous self-administered, 42 items (3 steps scale) questionnaire and a free commentary. Data was quantitative and qualitative analyzed.

RESULTS: Clinical data. Age: 4 years 2m median (1-15y), Asthma: 42.2%, Atopic Dermatitis: 15.4%. Number/Types foods: median 2 (1-6). Milk 36.9%, Egg 56%, Fish 26.5%, Legumes 13.2%, Nuts/peanut 26.8%, Fresh fruits 13.8%, Shellfish 11.4%, Others 5.5%. Quantitative Results Family Burdens: 28.6% suffer high extra-expenses, 30.2% domestic work overburden, and 35.1% daily life vital changes. Family Worries: nutritional deficit 59.2%, afraid about a severe reaction 60.4% Information: 82.9% thought FA is a bad known disease. School problems: 74.4% experienced canteen problems. 81.3% reported troubles in school field trips. Adverse/Accidental Reactions (AAR): 65.6% suffered AAR last 2 years and 21.3% consulted Emergency Room last 12m. AAR self-management: Parents 69.9%, other family members 54.2%, staff 45.2%. Number foods increase expenses, canteen problems, AAR, nutritional deficit. Fish and legumes FA associated more fear nutritional deficit. Organizations: 13.7% are members of nonprofit Food Allergy Spanish Association (Asociación Española de Padres de Niños con Alergia a Alimentos AEPNA). Qualitative Results A qualitative approach to the free comment section show: economic support required, school meal integration problems, nutritional deficit fear and ask for best food labeling and population FA knowledge.

CONCLUSIONS: FA cause relevant impact on Spaniard family’s daily life. Our data will help us develop specific strategies adapted to local environment.

736 The First 4 Central American Cases Of Delayed Meat Allergy With Galactose-Alpha-1,3-Galactose Positivity Clustered Among Field Biologists In Panama
Dr. Paige G. Wickner, MD1, Scott P. Commins, MD, PhD2, 1Bigham and Women’s Hospital, Division of Rheumatology, Immunology and Allergy, Chesnut Hill, MA, 2University of Virginia Health System, Charlottesville, VA.

RATIONALE: Serological positivity to galactose-alpha-1,3-galactose has been associated with delayed meat anaphylaxis and tick bite exposure. This entity has been reported in Australia, North America and Europe. Here we report the first 4 Central American cases of delayed meat anaphylaxis clustered among field biologists in Panama.

METHODS: Subjects describing a history of urticaria, food allergy, or systemic reactions may occur following deliberate elimination diets. Health care provider. All were positive on a medically supervised graded open oral testing and graded oral challenge.

RESULTS: Within this group of subjects reactions ranged from hives and joint swelling to respiratory distress requiring emergency room visit after an unknown number of tick bites. Alpha-gal sIgE antibodies were measured using our modification of the ImmunoCAP assay with streptavidin on the solid phase.

CONCLUSIONS: Tick bites are common among international and local biologists working near the Panama Canal. In the forested and aquatic areas surrounding the canal, an estimated 15-20 tick species are found, at a density of 8500 ticks per 300 m2 of forest. Human bites are dominated by the Amblyomma cajennense species. We report 4 cases of delayed meat allergy among field biologists. This group represents a unique cohort in which the natural history of sensitization to alpha-gal can be studied.

737 Incidence Of New Onset Food Allergy In Renal, Cardiac, and Hepatic Transplant Recipients and Correlation With Immunosuppression Protocol
François Graham, MD, MSc1, Frédéric Racicot2, Luminita Iuliana Jamali, MD1, Marie-Jeanne Lebel, MD1, Hugo Chapdelaine, MD1, Fernando Alvarez, MD2, Véronique Phan Cong, MD2, Marie-Josée Raboisson, MD2, Louis P. Paradis, MD, FRCP; FAAAAI2, Anne M. Des Roches, MD, FRCP, FAAAAI2; CHUM, Hôpital Notre-Dame, Montreal, QC, Canada, 2Centre Hospitalier Universitaire Sainte-Justine, Montreal, QC, Canada.

RATIONALE: New onset food allergy (NOFA) is a serious and poorly understood complication after pediatric liver transplantation. The objective of this study was to compare the incidence of NOFA after liver, renal and cardiac transplantations and to determine whether the type of solid organ transplantation and immunosuppression protocol played a role in the development of NOFA.

METHODS: The study population consisted of 146 liver, 41 cardiac, and 49 renal transplant recipients at Sainte-Justine Hospital, transplanted between the age of 1 month and 19 years. All data was collected retrospectively from patients’ medical charts.

RESULTS: NOFA developed in 12 patients with liver transplants, 3/4 of patients receiving cyclosporine (3%), and 9/52 receiving tacrolimus (17%). The higher incidence of NOFA in the tacrolimus-treated patients was statistically significant (RR 5.42; 95% CI 1.54 – 19.16, p = 0.008). NOFA was observed in 1/32 patients of the cyclosporine group of cardiac transplants (3%), whereas none were observed in the tacrolimus group. No NOFA were found in renal transplant recipients in both tacrolimus and cyclosporine groups. The median age of liver transplant (3.2 years) was significantly lower (p < 0.001) than renal and cardiac transplants (12 years).

CONCLUSIONS: Exposure to tacrolimus after pediatric liver transplantation was associated with an increased risk of NOFA. NOFA was not observed after renal transplant and in only one case after cardiac transplant, although similar immunosuppressive regimens were used. Younger age at time of liver transplant may play a role in these observations. Prospective studies are needed to further elucidate the pathophysiology of NOFA after pediatric transplantation.
739 Food Allergy Testing Practices Of Primary Care Pediatricians In Illinois
Hector Rodriguez, MD1,2, Ms. Claudia Lau1, Dr. Ruchi Gupta, MD, MPH1,2, Melanie M. Makhija, MD1,3, 1Ann and Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL, 2Northwestern University Feinberg School of Medicine, Chicago, IL, 3Division of Allergy & Immunology, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL.

RATIONALE: There is increasing need for pediatricians to appropriately diagnosis and manage food allergies given rising prevalence. As recently as 2010, physicians acknowledged limitations in their understanding of food allergy and the interpretation of its diagnostic studies. It is in this context that we assessed the food allergy management practices of pediatricians in Illinois.

METHODS: Online surveys were distributed to pediatricians in Chicago and surrounding area (urban and suburban Illinois). The survey assessed current food allergy testing and management practices. Basic statistical tests and chi-squared analyses were performed using STATA/SE 12.1.

RESULTS: 217 physicians responded to the survey. 57% estimated a food allergy prevalence in their practice of >6%. Specific IgE testing was ordered by 78%, with food reaction being the most common reason for testing (95%) followed by eczema (66.2%), parental request (62.6%) and environmental allergy (49.6%). Restriction of diet was recommended by 45.8% of respondents to prevent development of food allergy. 17.5% of respondents to prevent atopic dermatitis and 5.2% of respondents to prevent asthma. Food restriction was recommended by 33% to manage atopic dermatitis. Of those who manage children with food allergy, 94% of respondents consistently prescribed autoinjectable epinephrine, 82.1% offered education on allergen avoidance and 67.9% provided emergency action plans.

CONCLUSIONS: Pediatricians order testing for allergies and recommend food avoidance for both the prevention and management of various atopic diseases. Most pediatricians in the Chicagoland area offer education and prescribe autoinjectable epinephrine for their food allergy patients.

740 Understanding The Role Of Online Resources For Childhood Food Allergies
David Goese1, Ves Dimov, MD2, 1University of Chicago Pritzker School of Medicine, Chicago, IL, 2University of Chicago Medicine, Chicago, IL; Section of Allergy, Asthma and Immunology, Department of Pediatrics, Department of Medicine, University of Chicago, Chicago, IL.

RATIONALE: 59% of US adults searched for health information online within the past year. The largest online childhood food allergy forum, Kids With Food Allergies Foundation (KWFA), has 30,000+ users. Use of such web resources remains uncharacterized. This study aims to define KWFA user demographics, identify important KWFA features, and understand how KWFA affects the lives of food-allergic families.

METHODS: A 23-question mixed-methods quantitative and qualitative survey was administered starting June 7, 2013 on the KWFA forum website, KWFA Facebook page, and KWFA e-newsletter. N = 104 study participants met inclusion criteria of being a KWFA user over 18 years old. All data was collected anonymously.

RESULTS: Survey respondents were 93% women, 89% Caucasian, and 62% were between age 36-50. 69% had dealt with food allergies for 3 or more years. The most commonly used resources were KWFA’s e-newsletter, forum, and recipe index. Users reported the forum as the most valuable resource. 24% of respondents visit the forum once a day or more. Reasons for use include getting information about latest allergy treatments, support from peers, and ability to get second opinions. 13% chose a physician based on forum information or recommendations. Most users agree that KWFA reduces stress (76%) and influenced purchasing decisions (71%). 94% would recommend KWFA to other families raising food-allergic children.

CONCLUSIONS: Children With Food Allergies Foundation online resources influence users’ behavior, provide valuable information and support, and may have a role in the spectrum of childhood food allergy care as a source of information and stress alleviation.

741 Clinical Features, Diagnosis, Management and Natural History Of Food Protein-Induced Enterocolitis Syndrome In a National Cohort
Dr. Todd David Green, MD, FAAAAI, Dr. Matthew J. Greenhawt, MD, MBA, MSc2, Dr. Tammy S. Jacobs, MD, MA1, Fallon Schultz2, 1Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA, 2Department of Internal Medicine, The University of Michigan Medical School, Division of Allergy and Clinical Immunology, Ann Arbor, MI; 1International Association for Food Protein Enterocolitis (IAFFPE).

RATIONALE: Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergic reaction. Current descriptive studies are regionally limited to referral center populations.

METHODS: An internet survey examining characteristics of FPIES was distributed nationally via email and social media networks of two support organizations (International Association for Food Protein Enterocolitis and Kids With Food Allergies Foundation).

RESULTS: Among 263 respondents to date, the most common triggers were rice (61%), milk (57.9%), oat (48.8%), soy (47.2%), sweet potato (26%), wheat (23.6%), and egg (23.2%). 70.1% reported breastfeeding for >6 months, and 42.1% reported a reaction triggered through breast-milk exposure. Co-morbid atopic conditions included eczema (60.4%), allergic rhinoconjunctivitis (36.3%), IgE-mediated food allergy (33.2%), and asthma (19.5%). 13.7% reported carrying an epinephrine auto-injector for FPIES. Median reported age of milk FPIES onset was 2 months, soy 5 months, and for the most common solid foods between 5-7 months. 56.3% of milk and 28.2% of soy reactions reportedly occurred before age two months. Profuse vomiting occurred with 56.3% of milk, 82.1% of soy, and 95.8% of rice reactions; lethargy occurred in 46% of milk, 79.5% of soy, and 87.4% of rice reactions. Over half who outgrew FPIES reported undergoing at-home challenge for initial re-introduction.

CONCLUSIONS: Common FPIES triggers were similar to previous reports, though reported ages of onset for liquid and solid FPIES were younger and the frequency of FPIES to oat and rice was higher. More respondents than expected reported reactions triggered through breast milk, carry epinephrine for FPIES reactions, and underwent at-home challenge for food re-introduction.
742 Health Literacy Is Associated With Medication Adherence In Adolescents and Young Adults With HIV-1 Infection

Dr. Amrita Khokhar, MD1, Dr. Robert Spertier, MD2, Dr. David Rosenthal, DO1; 1Department of Medicine, Hofstra North Shore-LIJ School of Medicine, 2Division of Allergy/Immunology, Departments of Medicine and Pediatrics, Hofstra North Shore-LIJ School of Medicine, Kathryn Kilkenny, Division of Allergy/Immunology, Departments of Medicine and Pediatrics, Hofstra North Shore-LIJ School of Medicine, 3Division of Allergy/Immunology, Departments of Medicine and Pediatrics, Hofstra North Shore-LIJ School of Medicine, Great Neck, NY.

RATIONALE: Patient adherence to antiretroviral therapy (ART) is of critical concern, because noncompliance decreases HIV viral suppression, leads to disease progression, and to antiviral resistance. Medication adherence and viral control in adolescents and young adults with HIV were examined to identify a relationship with health literacy.

METHODS: Medical records from 2012 of 68 patients, ages 13-22, with HIV-1 infection were reviewed. Data abstracted included self-reported medication adherence (excellent, good, fair, or poor), HIV-1 RNA viral load (VL), and a measure of health literacy (REALM-Teen score). Data were analyzed via Fisher exact test (GraphPad Instat).

RESULTS: Among patients who self-reported "excellent" or "good" adherence at all clinic visits during 2012, 80% had an undetectable VL (<200 copies/mL) at all points the same year, whereas patients who self-reported "fair" or "poor" adherence at any point were less likely (46%, p=0.03) to have undetectable VL at all points. Among the patients with a REALM-Teen score of 0, signifying reading ability of medical words at or above grade level, 85% reported "excellent" or "good" adherence at all points, compared to 56% of patients with below grade level reading (p=0.03). Patients with a REALM-Teen score of 0 tended to have undetectable VLs throughout the year (p=NS).

CONCLUSIONS: Greater health literacy was associated with better ART adherence, which was associated with optimal viral control. This suggests that efforts directed at improving health literacy may also improve treatment adherence in adolescent and young adult patients with HIV infection. A longitudinal study of these patients is now in progress.

743 Variability In Measurement Of Allergen Skin Testing Results Among Allergy-Immunology Specialists

Dr. Tiffany Jean1, Dr. Kenny Y. Kwong1, Dr. Nasser Redjal, MD, FAAAAI2; 1Harbor-UCLA Medical Center, 2Harbor-UCLA Medical Center, Torrance, CA.

RATIONALE: Epicutaneous skin testing for sensitization to Aeroallergens in patients with allergic diseases requires measurement of skin wheal and erythema in response to antigens. This may be variable between different providers, and especially among patients with dark skin pigmentation. Purpose of this study is to determine whether Allergy-Immunology specialists vary in their measurement of epicutaneous skin tests in patients with differential skin pigmentation.

METHODS: Three patients with differing skin tones were skin tested using various concentrations of histamine to produce increasing sizes of skin wheal and erythema reaction. High resolution photographs of these were taken and sent to 20 board certified/eligible Allergy-Immunologists to measure the wheal and erythema size. Intra-class correlations were calculated to assess reliability of the provider measurements for each patient.

RESULTS: Overall, the wheal measurement (ICC = 0.464) had fair to good agreement and the flare measurement (ICC = 0.834) had excellent agreement among specialists. For the lightest skin tone, the reliability was fair for wheal (ICC= 0.579) and excellent for flare (ICC= 0.902). For medium tone, the reliability was good for wheal (ICC= 0.657) and also excellent for flare (ICC= 0.792). However for dark tones, the correlation across specialist ratings was poor for both wheal (ICC = 0.067) and flare (ICC= 0.060).

CONCLUSIONS: Measurement of skin test results in patients with dark skin pigmentation may have significant variability even among specialists. In vitro tests may be appropriate in these patients.

744 Serologic Specific IgE (sIgE) Testing In a Closed Healthcare System

Dr. Daniel A. Steigelman, MD, Dr. Tonya S. Rans, MD; Wilford Hall Ambulatory Surgical Center, Joint Base San Antonio - Lackland AFB, TX.

RATIONALE: Serologic allergen testing is widely available to providers across healthcare settings. This study describes sIgE utilization by all providers in United States Air Force (USAF) healthcare facilities.

METHODS: Since 2007, a centralized USAF laboratory has processed all sIgE testing in the USAF. Electronic records from 2007-2012 catalogued sIgE requests by year, facility, and quantity.

RESULTS: From 2007-2012, 120,333 requests for 1,335,695 sIgE tests were processed at a disposable materials cost of $6,237,947. Aeroallergen sIgE panels (34.9% of total) were most frequently requested, followed by individual food tests (34.3%), food panels (13.6%), individual aeroallergens (13.1%), and miscellaneous (2.2%). Combined, sIgE testing for hymenoptera and medications were least requested (1.6%). The lab serviced 34 facilities in 2007, 63 in 2008, and 67 in 2012. While total ordering facilities increased 6% since 2008, utilization snowballed. By 2012, sIgE requests increased 87.4%, number of tests analyzed increased 207.3%, average tests per request increased 64%, and annual disposable materials cost increased 210.5%. sIgE panels were requested at a 21.0% median annual increase (interquartile range 18.5-25.0%) compared with 9.2% (1.6-20.7%) for individual tests. While total annual sIgE requests increased a median of 15.3% (13.3-19.2%), total sIgE tests increased a median of 29.7% (23.6-39.0%), annually increasing costs by 30.0% (23.8-39.5%).

CONCLUSIONS: From 2007 to 2012, USAF providers requested sIgE testing with increasing frequency and have preferentially requested panels of tests to individual tests. Future studies may correlate sIgE testing with clinical outcomes and compare sIgE utilization by allergists versus non-allergists.
745 Outcomes After Implementation of an Inpatient Antibiotic Prescribing Pathway for Patients With Penicillin or Cephalosporin Allergy

Dr. Kimberly Blumenthal, MD1, Dr. Erica Shenoy, MD, PhD2, Ms. Christy Varughese, PharmD3, Dr. David Hooper, MD, PhD4, Dr. Aleena Banerji, MD5, 1Allergy and Immunology, Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 2Division of Infectious Disease and Infection Control Unit, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Department of Pharmacy, Infection Control Unit, Massachusetts General Hospital, Boston, MA, 4Division of Infectious Disease and Infection Control Unit, Department of Medicine, Massachusetts General Hospital, Boston, MA, 5Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA.

RATIONALE: Standardized guidelines for inpatient providers on drug allergy history taking and antibiotic prescribing for penicillin (PCN) or cephalosporin-allergic patients are lacking.

METHODS: An antibiotic prescribing pathway was developed to assist providers in drug allergy history taking, antibiotic prescribing, and performance of test doses with and without Allergy/Immunology (AI) consultation for inpatients with PCN or cephalosporin allergy. The pathway was implemented at a 947-bed tertiary care facility beginning April 2013. All test doses through the pathway were performed by the primary inpatient team unless the pathway directed AI consult. A retrospective pre/post analysis compared test doses, hypersensitivity reactions (HSRs), and use of PCN skin testing quarterly in the year prior to implementation of the pathway to the first quarter following implementation.

RESULTS: Prior to pathway implementation, an average of 11 test doses per quarter were performed, all with AI consult. In the post-period, 39 test doses were performed of which 7 (18%) were with AI consult. There were only 3 HSRs among all test doses with no difference in rate between the pre and post periods (p>0.5). In the post-period, 100% of test doses performed with AI required PCN skin testing, which was a significantly higher rate than prior to pathway implementation (48%, p=0.012).

CONCLUSIONS: The implementation of an antibiotic prescribing pathway resulted in an almost 4-fold increase in the number of test doses to PCN and cephalosporin antibiotics. The pathway increased the efficiency of AI consultation for PCN allergy while maintaining patient safety.

746 The Effect of Panel Ordering on Utilization of In Vitro Specific IgE Testing by Primary Care Physicians in a Large HMO

Dr. Bruce J. Goldberg, MD, PhD, FAAAAI1, Dr. John S. Kaptein, PhD2; 1Kaiser Permanente, Los Angeles, CA, 2Southern California Permanente Medical Group, Los Angeles, CA.

RATIONALE: In 1999, allergists at an HMO created a panel of 8 foods in order to facilitate evaluating children with atopic dermatitis. Since 2005 when the organization adopted an EHR, there has been tremendous growth in the use of in vitro allergy testing by primary care physicians. Due to the organization’s focus on the “Choosing Wisely” initiative, usage patterns by primary care physicians were reviewed.

METHODS: EHR and LIS records for the food allergy panel were reviewed for the number of requests and the associated diagnoses ordered by allergists, internists, family practitioners and pediatricians.

RESULTS: By 2012, 98% of the eight foods were ordered as a complete panel while only 2% were ordered individually. Panel ordering increased from 1,864 tests prior to EHR implementation to 19,472 tests the year immediately following EHR implementation to 146,699 tests by 2012. Family practice and pediatrics had the highest utilization with internal medicine having the lowest (79,595, 47,200 and 19,904 tests respectively). Common diagnoses associated with the panel orders included urticaria, allergic rhinitis and screening in addition to atopic dermatitis. Due to the volume ordered by primary care and the perception that ordering was not always appropriate, the food panel was deactivated. Follow up analysis revealed a 77.5% decrease per month in ordering of the 8 food allergens comprising the panel.

CONCLUSIONS: Facilitating the ordering of multiple allergens in an EHR with a single click resulted in increased and often inappropriate utilization by primary care physicians. Removing this ability reduced ordering with a resultant significant cost savings.

747 Premature Discontinuation of Allergy Immunotherapy: Inadequate Reimbursement by Health Insurers as a Major Factor

Dr. Surender K. Vaswani, MD, FAAAAI1, Ravi Vaswani2, Dr. Njideka Udoh3, Rajiv Karam4, Dr. Leena Parikh5, 1Allergy & Asthma Clinical Center, Columbia, MD, 2New York University School of Medicine, 3Howard County General Hospital/Johns Hopkins, 4University of Cincinnati School of Medicine, 5St. Agnes Hospital.

RATIONALE: Despite proven efficacy of allergy immunotherapy, many patients discontinue allergy injections prior to the recommended duration of 3-5 years, thereby not deriving expected benefit. This study was undertaken to examine the causes of premature discontinuation of allergy subcutaneous immunotherapy.

METHODS: The data was collected on patients who stopped allergy subcutaneous immunotherapy prior to the completion of the prescribed duration. The patients were contacted in the office, via phone or letter to identify the reason for stopping allergy injections.

RESULTS: A total of 555 patients with Allergic Rhinitis, Asthma or both terminated immunotherapy prematurely. Sixty eight percent were on maintenance dose and 32% were in the escalation phase. Two hundred and thirteen (38.2%) were males and 342(61.6%) were females. The reasons cited by patients for early dropout from immunotherapy were – requirement of co-payment for allergy injections, payment for allergen extract, or both by their health insurer (40%), inconvenience of travel (15%), change of residence (8%), concurrent health problems (5%), patient-perceived ineffectiveness (4%), patient perceived lack of need to continue (2%), and adverse side effects (local reaction– 1%; systemic reaction– 0.5%). The remaining 24.5% of the patients did not provide any reason for withdrawing from subcutaneous immunotherapy.

CONCLUSIONS: Inadequate reimbursement of allergen extract and allergy injections by health insurers is a major contributing factor for premature discontinuation of allergy subcutaneous immunotherapy by patients.
Adherence To Labeling Guidelines Of Inhalant Allergen Immunotherapy Practice Parameter 2011 At The University Of Michigan Health Service

Dr. Marilyn Karam, MD1, Kiela Samuels2, Cynthia Hernandez, RN2, Dr. Christine L. Holland, MD3, Dr. Matthew J. Greenhawt, MD, MBA, MSc1, 1The University of Michigan, Division of Allergy and Clinical Immunology, Ann Arbor, MI, 2University of Michigan Health System, Ann Arbor, MI, 3Department of Internal Medicine, The University of Michigan Medical School, Division of Allergy and Clinical Immunology, Ann Arbor, MI.

RATIONALE: To assess non-University allergist adherence to inhalant allergen immunotherapy (IT) labeling guidelines recommended by the Immunotherapy Practice Parameters (PP).

METHODS: Patient identifiers, volume/volume (v/v) concentration, color or alphanumeric coding, allergen content, and expiration date were checked on the IT labels of 111 patients with non-University formulated IT administered at the University of Michigan Health Service (UMHS). Data were analyzed by logistic regression.

RESULTS: Among the 111 outside IT labels, 100% listed an expiration date, 70% listed ≥2 patient identifiers, 71% listed v/v concentration, 55% listed allergen content, 51% were color coded, and 3% had alphanumeric coding. Labels listing ≥2 patient identifiers (OR 3.21, p=0.009, 95%CI 1.3-7.7), specific extract content (OR 2.7, p=0.021, 95%CI 1.16-6.35), and color-coded vials (OR 10.4, p<0.001, 95%CI 1.9-12.3), and labels with both v/v concentration and color-coding significantly increased with each personal identifier listed (OR 4.81, p=0.001, 95%CI 1.9-12.3), and labels with both v/v concentration and color-coding had significantly higher odds of having ≥2 patient identifiers listed (OR 6, p<0.001, 95%CI 2.2-16.3). Comparatively, 58/58 patient labels from University-formulated IT administered at UMHS were color-coded, had ≥2 patient identifiers, v/v concentration, extract content and expiration date.

CONCLUSIONS: Adherence to standardized labeling guidelines is recommended by the PP to prevent errors in extract administration. Color-coding, listing ≥2 patient identifiers or listing v/v concentration increased the odds of labeling compliance by non-University allergists per PP recommendations. Further study is warranted to explore variations in labeling compliance and their effects.

The Prevalence Of Allergic Rhinitis Among High- School Male Military Recruits In Jordan

Dr. Mansour Fuad Karadsheh, MD, Dr. Suleiman Soudi; Royal Medical Services, Madaba, Jordan.

RATIONALE: The prevalence of physician- diagnosed allergic rhinitis varies between countries; and even between different regions in the same country. This may be related to environmental and genetic factors that modify the allergic response in different groups. This study aims to look at the prevalence of allergic rhinitis in high- school (Tawjihi) males who presented for admission to Mutah University military division during the school year 2011-2012.

METHODS: As part of screening tests for students for admission to Mutah University, a single examiner performed otolaryngologic examination using standard halogen light, and Killian nasal dilators (anterior rhinoscopy); diagnosis was made from both positive history or findings noted by the examiner according to the known practice guidelines.

RESULTS: A total of 832 subjects took part in the study; the age range was 17- 19 years. Of them 48(5.8%) had a physician- diagnosed allergic rhinitis. There was no statistically significant difference between governors; comparison between our study and other studies from Arab, Middle Eastern and international studies was performed.

CONCLUSIONS: The prevalence of allergic rhinitis in our study of adolescent males was 5.8% in Jordan. There was a great difference in the prevalence of allergic rhinitis in different countries and groups in the same country. Further studies are needed in different age groups, and gender are needed to increase the awareness, and detection of this disease among Jordanians.

Allergen Sensitivity Patterns Among Atopic Individuals At A Tertiary Allergy Center

Dr. Lukena U. Karkhanis, MD, Dr. Sarena Sawlani, MD, Dr. Andrew Kau, MD, PhD; Washington University School of Medicine, St. Louis, MO.

RATIONALE: Studies have identified an association amongst atopic diseases and allergic sensitization to Aeroallergens. Our study examines relationships among specific aeroallergen sensitivity and demographics, geographical location, and allergic diseases in the St. Louis region.

METHODS: Using retrospective chart analysis, aeroallergen sensitivities by percutaneous skin testing (standardized panel of 7 trees, grasses, weeds each, 21 molds, 2 dander, 2 dust mites, cockroach) (tests graded 0-4), demographics, geographical location, seasonality patterns, and allergic disease history from 105 patients were reviewed. Principal coordinate analysis was used to determine patterns of allergen sensitivity. Data were analyzed using correlation analysis, t-test and/ or ANOVA.

RESULTS: Overall, rural patients have lower total allergen sensitization versus urban. Suburban patients have more tree sensitization versus rural (e.g. Oak 1.66 vs. 0.33, p-value: <0.02). Urban patients have more grass (e.g. Timothy 1.93 vs. 0.33), cockroach (1.55 vs. 0.33), and D. pteronyssinus (2.3 vs. 1.11) sensitization versus rural (p-values <0.048, 0.03, 0.036 respectively). Rural residents have lower Ragweed sensitization versus suburban/ urban (0.66 vs. 1.95, 1.88, p-value: 0.02, 0.037 respectively). Men have more grass (e.g. Timothy 2.26 vs. 1.41), White ash (2 vs. 1.11) and Birch (2.1 vs. 1.17) sensitization over women (p-values <0.02). Non-pet owners have higher Red fescue sensitization versus pet owners (2.02 vs. 1.29, p-value: 0.02).

CONCLUSIONS: Knowledge of sensitization patterns in relation to geography and allergic diseases could be beneficial to tailor skin prick testing, and could yield important prognostic information regarding the severity of allergic diseases. Additionally, our data supports the notion that rural residence confers protection against allergic sensitization.
751 Assessing Quality Of Life In Patients With AERD After Aspirin Desensitization
Dr. Melissa Lammate, MD1, Dr. Autumn Chandler Guyer, MD2, Dr. Rebecca Saff, MD, PhD3, Dr. Eric Holbrook, MD4, Dr. Stacey Gray, MD4, Dr. Aidan Long, MD, FAAAAI4, Dr. Aleena Banerji, MD5, 1Massachusetts General Hospital, 2Cincinnati Children’s, 3Massachusetts General Hospital, Boston, MA, 4Massachusetts General Hospital, Harvard Medical School, Boston, MA, 5Allergy and Clinical Immunology, Massachusetts General Hospital, Boston, MA, 3Allergy and Clinical Immunology, Massachusetts General Hospital, Boston Medical School, Boston, MA. 3Allergy and Clinical Immunology, Massachusetts General Hospital, Boston Medical School, Boston, MA, 3Allergy and Clinical Immunology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 3Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston Medical School, Boston, MA.
RATIONAL: Previous studies have shown that aspirin desensitization with subsequent daily aspirin treatment is associated with clinical improvement in patients with aspirin-exacerbated respiratory disease (AERD). However, few studies have assessed whether aspirin desensitization improves quality of life in patients with AERD.
METHODS: We evaluated patients with AERD who underwent aspirin desensitization in our outpatient Allergy/Immunology clinic between April 2012 and August 2013. Quality of life (QOL) was assessed at baseline and six months after aspirin desensitization using the self-administered Asthma Quality of Life Questionnaire with Standardized Activities (AQLQ(S)) and the Sino-Nasal Outcome Test-22 (SNOT-22). Questionnaire v4. The AQLQ(S) data were analyzed according to the following domains: symptoms, activity limitation, emotional function and environmental stimuli. Composite scores for the SNOT-22 were compared. Wilcoxon signed-rank test was used to analyze the data.
RESULTS: Six AERD patients underwent successful outpatient aspirin desensitization and completed all QOL assessments. The majority of patients were male (83%) and Caucasian (100%) with a mean age of 58 years. All patients had prior sinus surgery (median 28 months, IQR [8-41]). At 6 months, patients reported improvement in symptoms (p = 0.006 for AQLQ(S); p = 0.006 for SNOT-22), activity limitation (p = 0.006) and environmental stimuli (p = 0.038). There was no statistically significant improvement in emotional function (p = 0.087).
CONCLUSIONS: Quality of life is improved at six months in patients with AERD who were successfully desensitized to aspirin as measured by reported improvement of symptoms, activity limitation and environmental stimul. However, no statistically significant improvement is noted in emotional function.

752 Published Findings On Dust Allergens May Be Inaccurate Due To Improper Handling Of Values Below The Lower Limit Of Detection

Henry Lynn, Mr. Agustin Calatroni, MA, MS, Katy Jaffee, MS, Rebecca A. Zabel, Samuel J. Arbes, Jr, Rho, Inc., Chapel Hill, NC. 2Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA, 3Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA, 3Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA, 3Division of Pulmonary and Critical Care Medicine, Massachusetts General Hospital, Boston, MA.
RATIONAL: When dust allergen levels are below the lower limit of detection (LLOD), the common practice in many studies is to replace them by the LLOD/2 value. Such ad hoc substitutions can lead to biased mean and standard deviation (SD) estimates and biased associations with atopy.
METHODS: Data from the Urban Environment and Childhood Asthma (URECA) study are used to provide examples and simulation models to quantify the bias when allergen levels below LLOD are substituted with LLOD/2. Estimates of the mean and SD of the allergen levels are calculated, and odds ratios between allergen and skin test and specific immunoglobulin enzyme (sIgE) are estimated using logistic regression. Maximum likelihood and multiple imputation methods are applied to handle values below LLOD, and their performances in estimation are compared to the substitution method.
RESULTS: In URECA, 1%, 25%, 31%, 33%, 49%, 87% of the bedroom Muc m1, Can f1, Fel d1, Der f1, Bla g1, Der p1 data, respectively, were below the LLOD. Substituting these values with LLOD/2 produced inflated mean and SD estimates and biased odds ratios (e.g., with 50% below LLOD, mean and SD estimates were 103% and 37% larger, and odds ratio with skin test was 24% larger). In contrast, the bias of these estimates from maximum likelihood and multiple imputation methods was about 10%.
CONCLUSIONS: The default method of substituting allergen levels below LLOD with LLOD/2 can lead to substantial bias. Maximum likelihood and multiple imputation methods have better statistical properties and should be recommended instead.

753 Patient-Reported Factors That Influence Diphenhydramine Use In Children and Adults In An Allergy Specialty Practice
Dr. Prakash Navaratnam1, Dr. Robert Anolik, MD, FAAAAI, Dr. Howard Friedman, MS, PhD1, Dr. Eduardo Urdaneta, MD2, 1DataMed Solutions LLC, New York, NY, 2Allergy and Asthma Specialists, PC, Blue Bell, PA, 3McNeil Consumer Healthcare, Fort Washington, PA.
RATIONAL: To examine the association between over-the-counter (OTC) diphenhydramine (DPH) use and patient-reported attributes, satisfaction, and preferences in medically-managed adults and children with allergic rhinoconjunctivitis.
METHODS: Adult and pediatric DPH users, diagnosed with allergic rhinitis and managed during 2012 in an allergy practice, were identified. Their DPH utilization histories were evaluated with a 1-year retrospective electronic medical record (EMR) review. Eligible adults and parents of eligible children completed an on-line survey measuring attitudes, behaviors, preferences, and treatment satisfaction.
RESULTS: Two-hundred-seventy-two patients with linked EMR and survey responses (N = 137 children, N = 135 adults) were identified. The most desirable DPH attributes on a ranking scale (1 = least important to 7 = most important) were “effectiveness in relieving symptoms” (Mean rank score [MRS]: 5.4, children; 5.6, adults) and “safety” (MRS: 4.9, children; 4.4, adults). For both cohorts, the most important influencers to use DPH were “doctor recommendation” (MRS: 7.2, children; 6.5, adults) and “prior successful use” (MRS: 5.9, children; 6.8, adults). Both groups reported that “cost” (79.8%, children; 67.7%, adults) and “convenience” of obtaining DPH (78.7%, children; 77.6%, adults) were preferred over prescription medications. Over 75% of patients were “strongly satisfied”/”satisfied” with DPH and were “very likely”/”likely” to recommend DPH to friends/family.
CONCLUSIONS: OTC DPH has an important role in the treatment of allergic rhinoconjunctivitis, even in a medically-managed population treated by allergy specialists.
754  The Efficacy and Safety Of The Short Ragweed Sublingual Immunotherapy Tablet MK-3641 Is Similar In Asthmatic and Nonasthmatic Subjects Treated For Allergic Rhinitis With/Without Conjunctivitis (AR/C)

Dr. Jennifer Maloney, MD1, Dr. David I. Bernstein, MD, FAAAAI2, Dr. Jacques Hébert, MD2, Dr. Martha White, MD2, Dr. Robert Fisher, MD3, Dr. Thomas B. Casale, MD, FAAAAI4, Dr. Amarjot Kaur, PhD5, Dr. Hendrik Nolte, MD, PhD6, 1Merck, Whitehouse Station, NJ, 2Bernstein Allergy Group, Cincinnati, OH, 3Centre de Recherche Appliquée en Allergie de Québec, Quebec City, QC, Canada, 4Institute for Asthma & Allergy, Wheaton, MD, 5Allergy Research & Care, Milwaukee, WI, 6Univeristy Of South Florida Morsani College Of Medicine, Tampa, FL.

RATIONALE: Asthma is a frequent comorbidity of allergic rhinitis with/without conjunctivitis (AR/C). However, patients with asthma may be at higher risk of adverse reactions and/or benefit differently from AR/C immunotherapy.

METHODS: Data from two trials evaluating short ragweed sublingual immunotherapy tablet (SLIT-T), MK-3641 (Merck/ALK; Ambrosia artemisiifolia) were pooled. Subjects with ragweed-pollen-induced AR/C were randomized to once-daily MK-3641 (6 or 12 Amb a 1-U doses) or placebo for approximately 52 weeks. Subjects with reported stable asthma not requiring medium- or high-dose inhaled corticosteroids, and ≥70% predicted FEV1, were eligible. Efficacy and safety outcomes included AR/C total combined score (TCS; combined symptom+medication scores) and adverse events (AEs) in asthma and non-asthma subjects.

RESULTS: Among AR/C asthma subjects receiving MK-3641 6 or 12 Amb a 1-U, TCS was reduced by 17% (−1.27; 95%CI: −3.48, 0.93; n = 56) and 22% (−1.68; 95%CI: −3.69, 0.33; n = 64), respectively, versus placebo (mean TCS = 7.65, n = 64) over the 15-day peak season. Among non-asthma subjects receiving MK-3641 6 or 12 Amb a 1-U, TCS was reduced by 21% (−1.83; 95%CI: −2.84, −0.82; n = 261) and 27% (−2.34; 95%CI: −3.33, −1.35; n = 247), respectively, versus placebo (mean TCS = 8.73; n = 269). At least one treatment-related AE was experienced by 33%, 63%, and 65% of placebo and MK-3641 6 and 12 Amb a 1-U asthma subjects, respectively, versus 24%, 54%, and 60% of non-asthma subjects. No treatment-related serious or life-threatening AEs or hypersensitivity or systemic reactions were observed.

CONCLUSIONS: The ragweed SLIT-T treatment MK-3641 did not have clinically meaningful differences in efficacy or safety in ragweed AR/C subjects with and without asthma.

755 Compliance With Guidelines In The Use Of Allergen Immunotherapy

Dr. Pudupakkam K. Vedanthan, MD1, Ms. Christina Cutter, MSc, BA2, Ms. Phuong Dinh, BS2, Mr. Peter DeWitt, MS2, 1University of Colorado, Lakewood, CO, 2University of Colorado - Anschutz Medical Campus, Aurora, CO.

RATIONALE: This study seeks to appraise whether asthma/allergy practices are complying with prescribed guidelines for allergen utilization and handling. It also compares the prevalence of allergic conditions afflicting staff at asthma/allergy and family practice centers.

METHODS: A cross-sectional study was performed through evaluation of 325 surveys completed by randomly selected United States asthma/allergy practices (N=223) and family practice centers (N=102). The questionnaire sought to elucidate information about practice environment, behavioral procedures regarding preparation of allergens, and prevalence of select allergic conditions amongst staff members before and after employment. Compliance scores were ascribed to responses, employing both a binary and a graded scale, to reflect congruence with peer-reviewed published guidelines. Prevalence of allergic conditions before and after employment was compared between the two practice types.

RESULTS: A total of 144 clinics were evaluated for guideline compliance. The binary and graded analyses revealed compliance scores of 0.55 (95%CI=0.51-0.59) and 2.29 (95%CI=2.16-2.42) respectively. There was no difference between the asthma/allergy (N=184-185) and family practice centers (N=79) when testing for variation in the number of staff members afflicted with allergic conditions before and after employment.

CONCLUSIONS: This study highlights an important deficit in the translation of published allergen handling parameters into clinical practice. Research should be pursued to identify barriers for guideline utilization to facilitate improved future compliance. Further studies should assess individual staff-level data to elucidate whether impaired allergen handling guideline compliance correlates to increased staff affliction with allergic conditions.

756 Efficacy Of Short Ragweed Sublingual Immunotherapy Tablet (SLIT-T) In Mono-Sensitized and Poly-Sensitized Subjects

Dr. David I. Bernstein, MD, FAAAAI1, Kevin R. Murphy, MD2, Dr. Hendrik Nolte, MD, PhD3, Dr. Amarjot Kaur, PhD4, Dr. Jennifer Maloney, MD5, 1Bernstein Allergy Group, Cincinnati, OH, 2Boys Town National Research Hospital, Boys Town, NE, 3Merck, Whitehouse Station, NJ.

RATIONALE: Immunotherapy may be less effective in allergic rhinitis with/without conjunctivitis (AR/C) patients with multiple sensitizations. However, this was not observed in recent trials with standardized timothy-grass sublingual immunotherapy tablet (SLIT-T), MK-7243 (Merck/ALK; 2800 BAU Phleum pratense). The relevance of multiple sensitizations to treatment effect of short ragweed SLIT-T, MK-3641 (Merck/ALK; 12 Amb a 1-U Ambrosia artemisiifolia) is not known.

METHODS: A prospective subpopulation efficacy analysis between mono- and poly-sensitized ragweed-pollen-induced AR/C was performed in subjects treated with MK-3641. Pooled data from 2 randomized controlled trials investigating MK-3641 (6 and 12 Amb a 1-U doses) were used. Efficacy outcomes included the total combined score (TCS=symptom+medication scores) during the 15-day peak season.

RESULTS: For the whole population, peak TCS improvements from placebo for the pooled MK-3641 6 and 12 Amb a 1-U groups were 20% (−1.70; 95%CI, −2.55 to −0.86) and 23% (−2.02; 95%CI, −2.87 to −1.17), respectively (P<0.0001 for both). Differences vs placebo in the mono-sensitized ragweed MK-3641 pool (n = 175) were 15% (−1.34; 95%CI, −3.40 to 0.73) and 19% (−1.72; 95%CI, −3.63 to 0.20) for 6 and 12 Amb a 1-U, respectively. In the poly-sensitized MK-3641 pool (n = 784) differences vs placebo were 21% (−1.78; 95% CI, −2.80 to −0.75) and 27% (−2.27; 95% CI, −3.27 to −1.28) for 6 and 12 Amb a 1-U, respectively.

CONCLUSIONS: In the whole study population, treatment with MK-3641 6 and 12 Amb a 1-U for ragweed-induced AR/C was superior to placebo. In the subpopulations, numerical trends suggest a greater treatment effect in poly-sensitized subjects.
757 Trends In Prescribing Of Specific Immunotherapy For Grass Pollen Allergy In Germany: 2005-2012
Prof. Ulrich Wahn, Prof Dr Med1, Amanda McDonnell2, Catrina Richards2, Dr. Felicia C. Allen-Ramey, PhD3, Mr. Jakob N. Andreassen1, Charles Hawes2, Dirk Derneth4; 1Charlie, Berlin, Germany, 2D.Health, United Kingdom, 3Merck & Co, Inc, West Point, PA, 4ALK, Denmark.

RATIONAL: Sublingual allergen immunotherapy for grass pollen allergies in tablet form became available in Germany in 2006. This study examined the impact of the introduction of sublingual immunotherapy (SLIT) tablets on prescribing of subcutaneous immunotherapy (SCIT) and SLIT drops over time in Germany, a market which closely reflects current US treatment options and access to allergy care.

METHODS: An electronic medical records review of grass pollen allergen immunotherapy (AIT) prescriptions (ATC code: V01AA02) written for >18,000 allergic rhinitis patients from 2005-2012 was conducted using IMS Disease Analyzer. Administration modality was determined by the first prescription identified during each prescribing year (September-August). McNemar’s test was used to evaluate prescribing trends over the study period for the total patient population and age subgroups.

RESULTS: Nearly all patients (96%) with grass AIT prescriptions in study year 1 (2005/2006) were prescribed SCIT with greatest AIT use generally among adults (61% of prescriptions), with pediatric patients (<18 years) accounting for 39% of AIT prescriptions. A statistically significant increase in the proportion of patients prescribed SLIT-tablets was observed, from 8% (2006/07) to 29% (2011/12) (p<0.001). The proportion of patients prescribed SCIT therapies declined from 87% to 67% (p<0.001), while use of SLIT-drops was rare (~4% of patients annually) from 2006/07 to 2011/12. Similar trends were observed for both children and adults.

CONCLUSIONS: The proportion of patients prescribed SLIT-tablets increased significantly following their introduction to the market. Despite this increase, SCIT remained the primary modality prescribed to patients with grass pollen allergies over the study period.

758 Efficacy Of 300IR 5-Grass Pollen Sublingual Tablets In The Treatment Of Rhinitis Symptoms In Patients With Grass Pollen-Induced Allergic Rhinoconjunctivitis
Prof. Claus Bachert, MD, PhD1, Prof. Alain Didier, MD, PhD2, Ms. Laurence Ambroisine, Msc3, Dr. Kathy Abiteboul, PharmD4, Dr. Robert K. Zeldin, MD, PhD5; 1Université Libre de Bruxelles Belgium, 1Darney Allergy and Asthma Specialists, San Antonio, TX, 1Peninsula Research Associates, Rolling Hills Estates, CA, 1Hospital Medica Sur, Mexico D.F., Mexico.

RATIONALE: The efficacy of 300IR 5-grass pollen sublingual tablets has been demonstrated using a score which combines rhinitis and conjunctivitis symptoms. Here, we present the results of an analysis of its efficacy in the treatment of rhinitis symptoms alone.

METHODS: Patients with grass pollen-induced allergic rhinoconjunctivitis (ARC) were enrolled in one of four randomized, double-blind trials (two single-season adult trials, one single-season pediatric trial, and one long-term adult trial [primary endpoint at year 3]). They received placebo or 300IR 5-grass pollen sublingual tablet daily starting 4 months before the expected onset of the grass pollen season and continuing for its duration. Each day, participants recorded the severity of four nasal symptoms (i.e., sneezing, rhinorrhea, nasal pruritus, nasal congestion) on a 0-3 scale (absent to severe) yielding a daily Total Nasal Symptom Score (TNSS; 0-12 scale). For each study, the daily TNSS was analyzed by a repeated measures linear mixed model.

RESULTS: Data from 1,468 adults and 266 adolescents/children were analyzed. In each study, the adjusted mean of the daily TNSS in the 300IR (4M) group was significantly lower than that of the placebo group (p<0.02 in each of the adult studies and p=0.025 in the pediatric study). Relative adjusted mean differences ranged from -18.6% to -36.0% in the adult studies and were -22.1% in the pediatric one.

CONCLUSIONS: Pre- and co-seasonal treatment with 300IR 5-grass pollen tablet provides relief from nasal symptoms (sneezing, rhinorrhea, nasal pruritus and nasal congestion) in patients with grass pollen-induced allergic rhinoconjunctivitis.

759 Allergen Immunotherapy Safety While Using "High Risk" Medication: A Survey Of AAAAI Members
Dr. Matthew A. Rank, MD, FAAAAI1, Dr. David W. Hauswirth, MD, FAAAAI2, Dr. Christopher W. Calabria, MD3, Dr. Lawrence D. Sher, MD, FAAAAI4, Dr. Désirée E. S. Larenas Linnemann, MD, FAAAAI5; 1Mayo Clinic, Scottsdale, AZ, 2Nationalwide Children’s Hospita, Columbus, OH, 3Dilley Allergy and Asthma Specialists, San Antonio, TX, 4Peninsula Research Associates, Rolling Hills Estates, CA, 5Hospital Medica Sur, Mexico D.F., Mexico.

RATIONALE: Problems with individuals who are taking certain “high risk” medications on allergen immunotherapy (AIT) are not well described.

METHODS: AAAAI members were surveyed using a web-linked questionnaire. Major problems were defined for the responders as systemic reactions or discontinuation of AIT for medical reasons. Minor problems were defined as dose-reduction or postponed dose and AIT continuation.

RESULTS: The response rate was 9.3% (507/5433). Demographics of the responders were: 89% US-based, 41% urban and 54% suburban, 77% non-academic, 62% with 16+ years experience, and only 1% who report using lower AIT doses than recommended by practice parameters. The following percentage of responders report experience with high risk medications: angiotensin receptor blockers (84%), ACE-inhibitors (78%), anti-hormonal therapies (63%), anti-arrhythmia (62%), ocular β-blockers (44%), chemotherapeutic immunosuppressants (41%), biological immunosuppressants (37%), and oral β-blockers (34%). The total number of patients that responders had experience with, by medication type, was 1,758 ACE-inhibitors, 1,450 angiotensin receptor blockers, 1,175 oral β-blockers, 607 anti-arrhythmia, 437 ocular β-blockers, 427 anti-hormonal, 336 chemotherapeutic immunosuppressants, and 184 biological immunosuppressants. The percentage of major (minor) problems, by medication type and per responder, were 3.7% (7.0%) oral β-blockers, 1.3% (1.9%) chemotherapeutic immunosuppressants, 0.8% (2.4%) biological immunosuppressants, 0.8% (3.8%) ACE-inhibitors, 0.8% (1.1%) angiotensin receptor blockers, 0.7% (0.7%) anti-hormonal, 0.5% (2.0%) ocular β-blockers and 0.5% (1.9%) anti-arrhythmia.

CONCLUSIONS: A survey of AAAAI membership found that the use of “high risk” medication concomitantly with AIT is common and is associated with an overall low frequency of major and minor problems.
**760 Venom Immunotherapy Use With Contraindicated Medication: A Survey Of AAAAI Member’s Experience**

Dr. David W. Hauswirth, MD, FAAAAI, Dr. Matthew A. Rank, MD, FAAAAI, Dr. Desiree E. S. Larenas Linnemann, MD, FAAAAI, Dr. Lawrence D. Sher, MD, FAAAAI, Dr. Christopher W. Calabria, MD, Buckeye Allergy, Columbus, OH; Nationwide Children’s Hospital, Columbus, OH, Mayo Clinic, Scottsdale, AZ, Hospital Medica Sur, Mexico D.F., Mexico, Peninsula Research Associates, Rolling Hills Estates, CA, Diller Allergy and Asthma Specialists, San Antonio, TX.

**RATIONALE:** Several medications are considered contraindicated for use with Venom Immunotherapy (VIT). The aim of this study is to determine medication use patterns during VIT.

**METHODS:** An English language survey was sent to members of the AAAAI using Survey Monkey, and online survey tool.

**RESULTS:** A total of 507 responses (of 5433 surveys, response rate of 9.3%) were collected. These responses represent more than 4170 patients on VIT. The majority (88.5%) use 100mcg venom as the maintenance dose with no age limit. A total of 64.7% (306/473) do, or would use, VIT in patients on oral β-blockers. This number increases to 78.2% for ocular β-blockers. ACE inhibitors were used, or would be used by 85.7% of the survey respondents. Immunosuppressive chemotherapy was not felt to be a contraindication by 82.6% of survey participants; biological therapy was not a contraindication to 83.8% of respondents. For β-blockers, experience with 435 patients is reported in more depth; 5% of survey participants (10/204) reported minor problems (dose-reduction or doses postponed) and 2% (4/204) report to have had major (activation of underlying disease and/or VIT not well tolerated [systemic adverse events] and/or VIT discontinued for medical reasons) problems. Major problems were report by 1.4% of participants using VIT in patients on ACE inhibitors.

**CONCLUSIONS:** This survey examined AAAAI member’s experience with VIT and medication use. A majority of respondents report simultaneous use of VIT and contraindicated medications. These data suggest that more study is necessary to define specific (and relative) medications contraindicated with VIT.

**761 Simultaneous Measurement Of Multiple Proteins In Blatella Germanica Extract Using Antibody-Based Multiplex Assay**

Dr. Taruna Khurana, PhD, Ms. Maggie Collision, Dr. Jay E. Slater, MD, CBER FDA, FDA/CBER/OVRR/DBPAP, Rockville, MD.

**RATIONALE:** German cockroach (GCr) allergen extract contains multiple allergens of varying stability. Understanding GCr composition and potency may enhance the safety and efficacy of this product for diagnosis and therapy. We have reported that overall allergenicity of GCr extracts does not correlate with known specific allergens. We have developed a multiplex antibody/bead-based assay for measuring potency and composition of allergen extracts. In this report we describe our findings for GCr extracts using this assay.

**METHODS:** Highly purified scFv antibodies were coupled to activated carboxylated beads as previously described. Rabbit polyclonal sera generated against GCr extract (E6Cg), rBla g 1, 2, 3, and 4, were used for detection. As part of the assessment of the bead-based assay, E6Cg and multiple commercial allergen extracts were assayed. E6Cg extract was specifically depleted of Bla g 3, Bla g 7 or Bla g 2 using specific rabbit polyclonal sera for further analysis.

**RESULTS:** Mean fluorescence intensity signals were measured at multiple extract concentrations, and parameter values determined four-parameter fit using Prism software (GraphPad). Signal from negative control extracts (cat, ragweed, Alternaria) was negligible. EC50 values for specific targets were determined for GCr extracts, and various strategies were adopted to estimate the overall potencies of the commercial extracts relative to E6Cg. Assay of specifically-depleted E6Cg confirmed the specificity of the depletions and the assay.

**CONCLUSIONS:** An scFv antibody-based multiplex assay has been developed that can be used to simultaneously measure different proteins in a complex mixture, and to determine potency and composition of allergen extracts.

**762 Characterization and Protein Composition Of Food Allergen Extracts**

Dr. Greg A. Plunkett, PhD, Dr. Tricia Moore, PhD, ALK-Abelló, Inc, Round Rock, TX.

**RATIONALE:** Food diagnostic extracts used in the USA are non-standardized with no measurement of potency. Most food diagnostics have not been extensively characterized or allergen proteins identified. This study analyzed the protein composition of several foods extracted under varying conditions.

**METHODS:** Animal and plant foods were defatted with acetone and extracted overnight in 50% glycerin or aqueous extraction fluid using multiple extraction techniques. Extractions were performed at 4°C or room temperature and blended or stirred. Following extraction, all samples were adjusted to contain 50% glycerin, centrifuged and sterile filtered. The extracts were then evaluated for protein profiles and concentrations using Coomassie or silver stained SDS-PAGE and Bradford methods.

**RESULTS:** The food extracts showed a wide range of protein content. For example, tree nut allergens, almond and Brazil nuts were over 10 mg/mL whereas pecan and walnut were 1-3 mg/mL. For most foods the protein profiles within the same species were similar for the differing extraction conditions and correlated with the final protein concentrations. Walnut extraction, however, produced final protein concentrations that varied significantly according to the extraction method. Glycerin extraction resulted in an average final concentration of 2-3mg/mL, versus 0.3mg/ml for aqueous extraction. Room temperature extraction resulted in higher protein yields (2.5mg/ml), when compared to extraction at 4°C (1.7mg/ml), and persistent stirring was the superior method of agitation.

**CONCLUSIONS:** SDS-PAGE profiles and total protein content were obtained for many food extracts in several food groups in order to optimize extraction conditions and to eventually monitor for allergen content, potency and stability.

**763 Stability and Compatibility Of Cat, Dog, Dust Mite, and Cockroach Extracts In Indoor Allergen Mixtures and Dilutions For Immunotherapy**

Dr. Silvia Huebner, MD, Dr. Saryen Manilal Gada, MD, Dawn Hall, BS, Dr. Thomas Grier, MD, Evans Army Community Hospital, Fort Carson, CO, Walter Reed National Military Medical Center, Bethesda, MD, Greer Labs.

**RATIONALE:** Immunotherapy with mixtures of multiple low-protease and high-protease indoor allergens is a common practice in many allergy clinics, but the compatibilities of these preparations have not been determined. The objective of this study was to assess the recoveries of cat, dog, dust mite, and cockroach allergen activities in 4-component mixtures and dilutions stored for up to 12 months.

**METHODS:** Test mixtures and single-extract controls were analyzed for major allergen content (cat Fel d 1 radial immunodiffusion, dog dander Can f 1 ELISA) or multi-allergen IgE-binding potency (dog epithelia, D. farinae, or cockroach ELISA inhibition) after incubation for 1, 3, 6, 9 and 12 months at 2-8 degrees C.

**RESULTS:** All component allergens exhibited near-complete compatibilities in 50% glyceral (concentrates) and HSA d10 diluent (1:10 dilutions of concentrate), compared with corresponding control sample reactivities. Cockroach allergens were stabilized by mixing with other indoor allergen extracts.

**CONCLUSIONS:** Extracts of common indoor allergens possess very favorable stabilities and mixing compatibilities. These findings support the utility of combining these allergens in the same formulation when administering allergen immunotherapy.
764 Interest Of Mass Spectrometry-Based Quantification Of Relevant Allergens To Improve The Standardization Of Allergen Extracts

Thierry Batard, PhD1, Emmanuel Nony2, Christel Dayang, PhD2, Julien Bouley, PhD2, Maxime Le Mignon, PhD2, Christelle Berrouet2, Aurélie Lautrette, PhD2, Marie Naveau, PhD2, Henri Chabre, PhD2, Dr. Philippe Moingeon, PhD3; 1Stallergenes, Antony, France, 2Stallergenes, France, 3Stallergenes SA, Antony, France.

RATIONALE: Because of their clinical importance, relevant allergens should be quantified in allergenic extracts used to diagnose and treat type 1 allergies. The results obtained with antibody-based techniques of quantification such as ELISA cannot be considered absolute. Especially, antibodies used are often specific for selected isoforms only, hence leading to underestimate the allergen concentration. To overcome those limitations, we developed and validated mass spectrometry (MS)-based assays for the comprehensive quantification of grass pollen group 1 allergens and house dust mite (HDM) group 2 allergens.

METHODS: Allergens were purified by liquid chromatography (LC) and characterized by LC coupled to tandem MS (LC-MS/MS). Allergen quantification was performed by LC-MS/MS after digestion with trypsin.

RESULTS: Grass pollen group 1 and HDM group 2 allergens were purified, and their variants characterized, allowing the identification of consensus peptides. Two corresponding MS quantification assays were developed on this basis and validated. The two assays were selective, linear (R² > 0.98), accurate (recovery close to 100%) and sensitive (level of detection below 0.5 ng/mL). For both assays, intra- and inter-run precisions were better than 10-fold higher. CONCLUSIONS: Focusing on two important allergens, we confirm that MS-based assays allow the quantification of relevant allergens in a sensitive, accurate, repeatable and comprehensive manner. As such, MS-based assays offer an attractive alternative to antibody-based assays, especially when the latter rely upon antibodies that are too specific.

765 Baseline Predictors Of Symptom Severity Following Exposure To House Dust Mite In An Antigen Challenge Chamber (ACC)

Daniel Ramirez, MD1, Robert L. Jacobs, MD1, Cynthia Rather, CCRC1, Andrew Carrillo, BS2,3, Weijing He, MD2,3, Nathan Harper, BS2,3, Charles Andrews, MD1, Sunil K. Ahuja, MD2,3, 1Biogenics Research Chamber, San Antonio, TX, 2Department of Medicine, University of Texas Health Science Center, San Antonio, TX, 3Veterans Administration Center for Personalized Medicine, South Texas Veterans Health Care System, San Antonio, TX.

RATIONALE: The relationship between factors that influence symptomatology following exposure to a perennial allergen such as house dust mite in the environment versus ACC is unknown.

METHODS: 23 mite-sensitive participants underwent 4 consecutive 3-hour exposures in an ACC to mite, purified mite body preparation of Dermatophagoides pteronyssinus. This elicitation response will allow for testing of novel pharmacological specific therapies.

RESULTS: Of the 23 participants, 19 (out of 23) had positive skin test results for D. pteronyssinus. The results obtained with antibody-based techniques of quantification such as ELISA cannot be considered absolute. Especially, antibodies used are often specific for selected isoforms only, hence leading to underestimate the allergen concentration. To overcome those limitations, we developed and validated mass spectrometry (MS)-based assays for the comprehensive quantification of grass pollen group 1 allergens and house dust mite (HDM) group 2 allergens.

METHODS: Allergens were purified by liquid chromatography (LC) and characterized by LC coupled to tandem MS (LC-MS/MS). Allergen quantification was performed by LC-MS/MS after digestion with trypsin.

RESULTS: Grass pollen group 1 and HDM group 2 allergens were purified, and their variants characterized, allowing the identification of consensus peptides. Two corresponding MS quantification assays were developed on this basis and validated. The two assays were selective, linear (R² > 0.98), accurate (recovery close to 100%) and sensitive (level of detection below 0.5 ng/mL). For both assays, intra- and inter-run precisions were better than 10-fold higher. CONCLUSIONS: Focusing on two important allergens, we confirm that MS-based assays allow the quantification of relevant allergens in a sensitive, accurate, repeatable and comprehensive manner. As such, MS-based assays offer an attractive alternative to antibody-based assays, especially when the latter rely upon antibodies that are too specific.

CONCLUSIONS: Co-factors in the environment unrelated to dust mite lead to high run-in TSS values, accounting for their modest capacity in predicting TSS specific to dust mite exposure in the ACC. Accordingly, baseline predictors of TSS during the run-in and ACC were only partly overlapping. Thus, the ACC has high value for evaluating dust mite-specific therapies.

766 Validation Of Biogenics Research Chamber For Elicitation Of Symptoms To Dust Mite Antigen (Der p1)

Robert L. Jacobs, MD1, Cynthia Rather, CCRC1, Fabio Jimenez, BS2,3, Hernan Martinez, MD2,3, Weijing He, MD2,3, Daniel Ramirez, MD1, Charles Andrews, MD1, Sunil K. Ahuja, MD2,3, 1Biogenics Research Chamber, San Antonio, TX, 2Department of Medicine, University of Texas Health Science Center, San Antonio, TX, 3Veterans Administration Center for Personalized Medicine, South Texas Veterans Health Care System, San Antonio, TX.

RATIONALE: This study was performed to determine the operational characteristics of the Biogenics Research Chamber for elicitation of symptoms in dust mite allergic individuals.

METHODS: Twenty-five dust mite sensitive and 15 normal controls (32% male, mean age 40) were enrolled to undergo 4-consecutive 3-hour chamber exposures to a milled, purified mite body preparation of Dermatophagoides pteronyssinus. A 5-day run-in assessed symptoms in the natural setting. Symptoms were monitored at baseline and 30 minute intervals. Airborne samples were collected from 5 stations for 10 minutes at hourly intervals through a modified nylon filter for measurement of Der p1 by ELISA, and an Allergenco cassette sampler for microscopic evaluation of mite particles.

RESULTS: Thirty-eight participants completed 4 consecutive chamber exposures. Mean Der p1 levels on days 1, 2, 3 and 4 in the chamber were 81, 78, 110, and 101 ng/m³, respectively. 70% of sensitive subjects had Maximum Total Nasal Symptom Scores of ≥2 (out of 16). 65% of sensitive participants had Maximum Total Symptom Scores (TSS) of ≥15 (out of 28). Three of 15 normal controls had TSS of 1, 2, and 4, and the remaining did not exhibit any symptoms.

CONCLUSIONS: Administration of dust mite preparations containing an average of 92 ng/m³ of Der p1 levels induced symptoms in 70% of sensitive participants. The delivery and dispersal system of the Biogenics Chamber with dust mite was as efficient as previously reported for various pollens. This elicitation response will allow for testing of novel pharmacological agents.
Magnitude Of Changes In Patient Symptom and Medication Scores In Grass Allergy Immunotherapy Trials: Dependency On Levels Of Pollen Exposure

Dr. Hendrik Nolte, MD, PhD1, Prof. Stephen R. Durham, MA, MD, FRCP2, Dr. Harold S. Nelson, MD, FAAAAI1, Dr. David I. Bernstein, MD, FAAAAI1, Dr. Peter S. Creticos, MD, FAAAAI1, Dr. Ziliang Li, PhD1, Dr. Jens Andersen, PhD1, Merc, Whitehouse Station, NJ, 2Imperial College London, London, United Kingdom, 3National Jewish Health, Denver, CO, 4Bernstein Allergy Group, Cincinnati, OH, 5Johns Hopkins Division of Allergy & Clinical Immunology, 6ALK-Abelló, Horsholm, Denmark.

RATIONALE: While symptomatic therapy trials for seasonal allergic rhinitis with or without conjunctivitis (AR/C) begin while subjects have symptoms, pollen immunotherapy trials generally begin treatment pre-seasonally and assess efficacy during seasonal exposure. We investigated the impact of pollen exposure variability on magnitude of recorded immunotherapy treatment effect.

METHODS: Data from 7 North American and European randomized placebo-controlled trials of standardized Timothy grass sublingual immunotherapy tablet (SLIT-T), MK-7243 (Merck/ALK; 2800 BAU of *Phleum pratense*) were included (omitting 1 trial, as lack of pollen-count/symptom relationship suggested etiology other than grass pollen exposure). Predefined preseasonal treatment ranged from 8-16 weeks. Boundaries of 3 consecutive days with pollen count ≥10 grains/m³ defined grass pollen season (GPS). We assessed correlation of between-treatment difference in total combined score (TCS; combined symptom/medication scores) per trial or trial year to first-20-days-of-GPS cumulative grass pollen count and entire-GPS average pollen count.

RESULTS: Data included 1798/1765 MK-7243/placebo subjects. TCS for both groups increased with grass pollen counts. Treatment effect in TCS in each trial (or trial year) was correlated to cumulative grass pollen count during first 20 days of GPS (R²=0.803). Correlation was also seen between TCS and average pollen count over entire GPS (R²=0.464).

CONCLUSIONS: Post hoc analysis of 7 MK-7243 trials demonstrates that treatment effect magnitude was highly correlated to pollen exposure. Difference in pollen-exposure levels should be considered when comparing results among pollen immunotherapy trials and should also be considered with other methodological differences when comparing to symptomatic medication trials. The early-season-exposure/efficacy correlation does not confirm prevailing theories regarding priming.

Evaluation Of Acoustic Rhinometry In Histamine Nasal Provocation Test In Children and Adolescents

Dr. Fausto Y. Matsumoto1, Dr. Gustavo Wandalsen, MD2, Dr. Aline Mendes2, Prof. Direceu Sole, MD, PhD1, Federal University of São Paulo, São Paulo, Brazil, 2UNIFESP, São Paulo, Brazil, 3Federal University of São Paulo, Brazil, 4Federal University of Sao Paulo, Sao Paulo, Brazil.

RATIONALE: although acoustic rhinometry (AR) is considered a well established technique to evaluate nasal patency its role in nasal provocation tests is still to be defined, especially in children and adolescents.

METHODS: Twenty patients with allergic rhinitis and 18 controls were submitted to histamine nasal provocation test. AR and anterior active rhinomanometry were performed after bilateral instillation of 0.14ml of nasal saline and histamine (0.12, 0.25, 0.5, 1, 2, 4 and 8mg/ml) until 100% increase in total nasal airflow resistance (NAR). Different AR parameters were recorded (nasal volume in first 5cm [V5] and 4cm, minimal cross sectional area between 0 and 2.2cm [MC1] and between 2.2 and 5.4cm [MC2]).

RESULTS: Among all analyzed parameters, V5 showed to have the best inverse correlation with NAR both in the rhinitis and in the total group (r=-0.62, p<0.004 and r=-0.56, p<0.001, respectively). At the end of the provocation test a mean increase of 127% (CI95%: 113% to 141%) in NAR was observed in the rhinitis group that corresponded to a mean decrease of 24.5% (CI95%: 22.5% to 26.5%) in V5. Twenty percent fall in V5 showed to have the best balance between sensitivity (88.2%) and specificity (97.1%) among all analyzed endpoints (14% to 34% fall in V5).

CONCLUSIONS: AR is able to discriminate children and adolescents with allergic rhinitis from controls when submitted to histamine nasal provocation test. V5 showed the highest correlation with NAR among all studied AR parameters and 20% fall in V5 was identified as the best endpoint in such challenges.

EQ-5D Health Utility Values In The Treatment Of Seasonal Grass Pollen Induced Rhinoconjunctivitis

Mr. Jakob N. Andreason1, Dr. Chris Poolec2, Dr. Christian Bannister3, Dr. Jens Andersen, PhD4, Mr. Niels Serup-Hansen1, 1ALK, Denmark, 2Cardiff University, Cardiff, Wales, 3Cardiff University, 4ALK-Abelló, Horsholm, Denmark.

RATIONALE: Standard clinical efficacy endpoints in allergen immunotherapy trials include the daily Rhinoconjunctivitis Symptom Score (RSS) and daily Rhinoconjunctivitis Medication Score (RMS). However, measurement of subjects’ QoL in terms of health utility is also necessary to characterise changes in health status. In this study, we aimed to determine a relationship between standard efficacy endpoints and the health utility.

METHODS: Data from a 5-year DBPC phase III trial (GT-08, ALK, Denmark) in subjects with grass pollen induced rhinoconjunctivitis were analysed. During each pollen season, subjects recorded daily their RSS and RMS and weekly the EQ-5D index. A two-stage model was constructed: 1) binomial modelling of subjects with “perfect health” (EQ-5D utility=1) and 2) Gaussian modelling of EQ-5D utilities< 1. The utility during each grass pollen season was calculated as area under the curve.

RESULTS: A total of 16,690 weekly and 137,792 daily EQ-5D observations were recorded over the trial period. The binomial model showed the daily RSS and RMS to be the two most important predictors of “perfect health” (RSS: OR=0.729; p< 0.001; RMS: OR=0.841; p< 0.001). The Gaussian model of subjects with “imperfect health” confirmed this correlation. Based on relationship the average annual utility was estimated to 2.2 QALD.

CONCLUSIONS: In a clinical trial including subjects with grass pollen induced rhinoconjunctivitis, the daily RSS and RMS were found to be suitable predictors of the EQ-5D health utility. The findings confirm the beneficial impact of the SQ-standardised Timothy grass allergy immunotherapy tablet (75,000 SQ-T/2,800 BAU, ALK) on health utilities with a clinical relevant QALY gain.
**770 Ex-Vivo Allergen Stimulation In Whole Blood: A Novel Approach For Evaluating Mechanisms Of Action Of Synthetic Peptide Immuno-Regulatory Epitopes**

*Dr. Pascal L.C. Hickey, BPharm PhD1, Dr. Mark Larché, PhD2, Dr. Rod Hafner, PhD3, Ms. Kristen Armstrong, MSc4, Ms. Eileen Lee, BA (Hons)5, Dr. Elaine Lee, PhD5, Dr. Stephen A. Killeffer, PhD5, Adiga Life Sciences, Hamilton, Canada, 2McMaster University, Hamilton, ON, Canada, 3Circassia Ltd, Oxford, United Kingdom, 4Adiga Life Sciences Inc., Hamilton, ON, Canada, 5Aeitec Limited, Newcastle upon Tyne, United Kingdom.*

**RATIONALE:** Novel immunotherapies such as Synthetic Peptide Immuno-Regulatory Epitopes (SPIREs) act on a very small subset of the immune cell population to produce immune tolerance. The biochemical signature of these effects is extremely difficult to detect in readily sampled tissues. *Ex-vivo* allergen stimulation of whole blood, coupled with modern analytical techniques and computational tools may overcome these challenges.

**METHODS:** A subgroup of 13 ragweed-allergic subjects from a phase II clinical study of Ragweed-SPIRE provided heparinised blood samples for biomarker research prior to, during and up to 3 months following treatment. An *ex-vivo* allergen challenge involving incubation with ragweed allergen or vehicle control for 1, 6 and 24 hours at 37°C was performed. Concentrations of 45 immune-inflammatory markers were determined using a customised Luminex™ multiplex immunoassay.

**RESULTS:** The following markers demonstrated a significant *ex-vivo* elevation in response to ragweed allergen (>100% of control; p<0.05): TNFα, MIP-1β and IL-5 at 1 to 6 hours; IL-1β, MCP-1, MIP-1α, MIP-1β, IL-5 and IL-8 at 6 to 24 hours; TARC, IP-10, osteopontin, eotaxins 2 and 3 at 24 hours only. Furthermore, changes in baseline cytokine concentrations were also observed over the course of the study.

**CONCLUSIONS:** This study identified clear, allergen-induced changes in the plasma concentrations of a range of cytokines during *ex-vivo* allergen challenge in blood samples from clinical trial subjects. These responses could relate to mechanisms underlying *in-vivo* early and late phase responses to allergens and may provide a tool for the assessment of mechanism of action of novel immunotherapies such as SPIREs.

**771 Efficacy Of 300IR 5-Grass Pollen Sublingual Tablets In Grass Pollen-Induced Allergic Rhinoconjunctivitis: Pooled Analysis By Age**

*Dr. Robert K. Zeldin, MD1, Prof. Ulrich Wahn, Prof Dr Med2, Prof. Alain Didier, MD, PhD3, Mrs. Armelle Montagnet4, Dr. Marie-Pierre Furrer, PhD5, 1Stallergenes S.A., Antony, France, 2Charite, Berlin, Germany, 3Laarly Hospital, CHU, Toulouse, France.*

**RATIONALE:** The efficacy of 300IR 5-grass pollen sublingual tablet administered 4 months pre-seasonally and co-seasonally has been demonstrated. Here, we present the results of a pooled efficacy analysis by age group.

**METHODS:** Adults, adolescents and children (>5 years old) were enrolled in one of four double-blind, placebo-controlled, natural field studies and randomized to receive placebo or 300IR 5-grass pollen sublingual tablet daily beginning 4 months (4M) prior to the grass pollen season and continuing for its duration. The severity of each of six rhinoconjunctivitis symptoms (0-3 scale) and the use of rescue medication were recorded daily. Derived scores were the rhinoconjunctivitis total symptom score (RTSS, scale 0-18) and the rescue medication score (RMS, scale 0-3). In the pooled database, the daily Combined Score [daily CS = (RTSS/6 + RMS)/2] was analyzed using a repeated measures linear mixed model.

**RESULTS:** Data from 1,113 adults (placebo: n=581; 300IR (4M): n=532) and 266 adolescents/children (placebo: n=135; 300IR (4M): n=131) were analyzed. Significant differences in daily CS between the 300IR (4M) and placebo groups were observed in both age groups (point estimate: -0.15 CI 95% [-0.19; -0.11] in adults, p<0.0005 and -0.19 CI 95% [-0.29; -0.08] in adolescents/children). The daily CS relative LS mean difference vs. placebo was -30.1% in adolescents/children and -26.3% in adults.

**CONCLUSIONS:** Treatment with the 300IR 5-grass pollen extract sublingual tablet was similarly effective in adults and adolescents/children with grass pollen-induced allergic rhinoconjunctivitis.

**772 Characterization Of Allergic Rhinitis Symptomatology Induced By A Nasal Allergen Challenge (NAC) Titration In A Dust Mite Sensitive Population**

*Mr. Paul Gomes1, Endri Angjeli2, Mr. Keith Lane2, Dr. Paul H. Ratner, MD, FAAAAI3, 1ORA, Inc, Andover, MA, 2Ora, Inc, Andover, MA, 3Sylvania Research, San Antonio, TX.*

**RATIONALE:** Allergic rhinitis signs and symptoms can be safely and precisely evaluated using nasal allergen challenge (NAC) titration.

**METHODS:** Eligible skin test positive dust mite subjects underwent NAC titration. Challenge titration began with bilateral instillation of 100uL of saline. Increasingly concentrated doses of dust mite allergen were instilled until a positive reaction was elicited. Primary endpoint was Total Nasal Symptom Score (TNSS, 0 to 12 scale) the sum of nasal itching, congestion, rhinorrhea, and sneezing (0 to 3 scales). A positive NAC was defined as TNSS > 8 within 15 minutes of instillation. Secondary measures included investigator evaluated inflammation (0 to 4 scale).

**RESULTS:** Twenty-one (21) subjects were screened and 13 successfully completed NAC titration. Baseline TNSS scores were 0.38±0.87 increasing to 9.2±1.2 following the qualifying challenge. Individual post-NAC scores were: itching, 2.0±0.8; congestion, 2.5±0.5; rhinorrhea, 2.4±0.5; and sneezing, 2.1±0.5. The dose of allergen needed for qualification varied from 2 to 8 concentrations. Twenty-five percent of subjects demonstrated negative correlation between signs and symptoms R = -0.85.

**CONCLUSIONS:** NAC titration is a useful tool for characterizing the rhinitis response of a study subject to a particular allergen. Additionally, the NIR may be useful as an enrichment tool for clinical trials.

**773 Atopic and Non-Atopic Individuals Manifest Partly Concordant Clinical and Leukocyte Responses Following Exposure To House Dust Mite In An Antigen Challenge Chamber (ACC)**

*Weijing He, MD1, 2, Nathan Harper, BS1, 2, Andrew Carrillo, BS1, 2, Charles Andrews, MD3, Cynthia Rather, CCRC4, Daniel Ramirez, MD4, Robert L. Jacobs, MD5, Sunil K. Ahuja, MD5, 2, Department of Medicine, University of Texas Health Science Center, San Antonio, TX, 3Veterans Administration Center for Personalized Medicine, South Texas Veterans Health Care System, San Antonio, TX, 4Biogenics Research Chamber, San Antonio, TX.*

**RATIONALE:** While inter-subject differences in the responsiveness to seasonal allergens in an ACC have been demonstrated much less is known about heterogeneity in responses to perennial allergens such as house dust mite.

**METHODS:** Twenty-three dust mite sensitive and 15 normal controls were enrolled to undergo 3 hour chamber exposures on 4 consecutive days to a milled, purified mite body preparation of Dermatophagoides pteronyssinus. Total symptom scores (TSS) were monitored at baseline and 30 minute intervals. Complete blood cell counts (CBC) were measured immediately prior to and immediately after the exposures on the first and fourth day.

**RESULTS:** 65% of the atopy develop TSS ≥ 15 (out of 28) while the majority of the non-atopics had TSS ≤ 4. The increases in lymphocyte, monocyte and eosinophil cell counts were concordant between atopics and non-atopics, but eosinophilia was greater in the atopics compared with non-atopics. Hierarchical clustering of TSS identified five clinical endophenotypes in the atopics: 4 differed primarily with respect to severity of TSS, with one group remaining non-responsive; the fifth endophenotype was characterized by a progressive decrease in TSS with each ACC exposure and a distinct CBC signature.

**CONCLUSIONS:** While atopics exhibit wide heterogeneity in severity of symptom responses following dust mite exposure in an ACC, non-atopics are non-responsive. Despite this, non-atopics and atopics share a partly concordant leukocyte response. Identifying the basis for non-responsive-ness despite leukocyte responses following exposure to dust mites in an ACC could potentially uncover the basis for resistance to dust mite allergy.
774 The Effects Of Pollen Season On Reactions To Subcutaneous Immunotherapy

Dr. Devi Jhaveri, DO1, Dr. Julie Abraham, MD2, Megan Betteley, BS1, Dr. Mary Ann O’Riordan, PhD1, Dr. Theodore H. Sheer, MD, FAAAAI1, Dr. Robert W. Hostoffer, DO1, Dr. Haig Tcheurekdjian, MD, FAAAAI1; 1University Hospitals, South Euclid, OH, 2Case Western Reserve University School of Medicine, Cleveland, OH, 3Case Western Reserve University School of Medicine, Cleveland, OH, 4Allergy/Immunology Associates, Inc., South Euclid, OH.

RATIONALE: It is common practice to hold build-up dosing of subcutaneous allergen immunotherapy (SCIT) during pollen season. We hypothesized that build-up dosing during pollen season, as compared to held dosing, would not increase the rate of adverse reactions to SCIT.

METHODS: A prospective, blinded, randomized study was conducted over four months in northeast Ohio. Subjects ≥5 years old on build-up phase of SCIT for tree and/or grass pollens were randomized to one of two groups: build-up SCIT dosing (Group 1) or held SCIT dosing (Group 2) through the pollen seasons. Each SCIT visit was analyzed for immediate and delayed reactions via patient questionnaire.

RESULTS: 47 patients were randomized; 36 had 108 visits during tree season and 37 had 100 visits during grass season. Group 1 and 2 had no differences in age, sex, or asthma history. Tree season immediate reaction rate was 48% (all local) vs. 50% (5% of which were systemic) for group 1 and 2, respectively (p=0.59). All were local. Grass season delayed reaction rate was 10% (all local) vs. 8% (3% of which were systemic) for group 1 and 2, respectively (p=0.76). Grass season immediate reaction rate was 34% vs. 39% for group 1 and 2, respectively (p=0.59). All were local. Grass season delayed reaction rate was 7% vs. 5% for group 1 and 2 respectively (p=1). All were local.

CONCLUSIONS: There is no significant difference in the rate of reactions in build up versus held dosing of SCIT in tree/grass pollen season.

775 Protease Inhibitor Reduces Airway Response and Inflammation In Mouse Model Of Cockroach Allergy

Mr. Sanjay Saw, MSc, Dr. Naveen Arora, PhD; CSIR Institute of Genomics and Integrative Biology, New Delhi, India.

RATIONALE: Serine protease(s) are potent inducer of airway resistance and inflammation and the allergic response may be modified by proteases inhibitors. In the present study, effect of serine protease inhibitor in cockroach allergen induced airway resistance and inflammation was determined in mouse model.

METHODS: Mice were immunized with cockroach extract (CE) or Per a 10 and treated with 4-(2-Aminoethyl) benzenesulfonyl fluoride (AEBSF) 1 h before challenge. AHR was measured, one day after the last challenge and mice were euthanized to get BALF, blood and lung to evaluate airway resistance and oxidative stress.

RESULTS: AEBSF treatment to mice reduced more than 90% AHR in CE and in Per a 10 challenged mice (p<0.05). EPO, IgE, IL-4, IL-5 and IL-13 levels were significantly (p<0.05) reduced in AEBSF treated mice as compared to untreated group. The treatment lowered the total cell, eosinophil and neutrophil count in BALF to 90, 80 and 83 % in CE and 100, 62 and 90 % in Per a 10 challenged mice (p<0.05), respectively. Lung histology revealed that AEBSF treated mice had reduced inflammation and low mucus production in airways. Furthermore, the treatment had significantly reduced 8-isoprostane and ROS level to 88 and 86 in CE and 82 and 83 % in per a 10 challenged mice in comparison to untreated group (p<0.05).

CONCLUSIONS: AEBSF reduces allergen induced airway resistance and inflammation indicating that it might be used in “add-on” therapy for respiratory diseases. The therapeutic effect of inhibitor is independent of protease activity of allergen.

776 Aryl Hydrocarbon Receptor (AhR) Modulates Cockroach Allergen Induced TGF Beta 1 Secretion In Fibroblasts

Sarah Mirza1, 2, Yufeng Zhou, MD, PhD1, Priya Tripathi, PhD1, Liang Yuan1, Beverly Plunkett, MS1, Allen Myers, PhD1, Peisong Gao, MD, PhD1, 1Division of Allergy & Clinical Immunology, Johns Hopkins University School of Medicine, Baltimore, MD, 2Sher-I-Kashmir Institute of Medical Sciences, Jammu and Kashmir, India.

RATIONALE: Aryl hydrocarbon Receptor (AhR) is a multifunctional regulator that senses and responds to environmental stimuli and plays a critical role in linking environmental exposure to the development of allergic diseases. We sought to investigate whether AhR plays a role in mediating cockroach allergen induced immune responses.

METHODS: AhR expression in fibroblasts of human airway from asthmatic and healthy individuals was examined by immune-staining. FITC-labeled Bla-g 2 uptake by fibroblasts was also tested. Differential levels of Transforming growth factor β1 (TGFβ1) and IL6 were measured when fibroblasts were treated with cockroach extract (CRE) in the presence or absence of AhR agonist, TCDD and antagonist CH122319, or using fibroblasts with AhR knock-down. α-SMA, MMP2, and ADAM33 expression were also examined in AhR knock-down fibroblasts. Similar observation will be made in lung fibroblasts from wild type (WT) and knock-out (AhR-/mice).

RESULTS: Airway tissues from patients with asthma have more fibroblasts in the basement membrane as compared to those from healthy controls. AhR expression was higher in airway fibroblasts from asthmatic subjects. TGFβ1 production was significantly increased in CRE-treated fibroblasts, and further enhanced by TCDD, but inhibited by CH122319 and AhR knock-down. Furthermore, α-SMA, MMP2, and ADAM33 expression was reduced in AhR knock-down fibroblasts. Validation for these findings is ongoing in the lung fibroblasts that we have recently cultured from WT and AhR-/ mice.

CONCLUSIONS: These results provide evidence supporting a role of AhR in mediating cockroach allergen induced allergic immune responses, cell differentiation, and possibly airway remodeling in asthma.

777 Effect Of Peanut Allergens On Intestinal Barrier Permeability and Tight Junction Localisation In Caco-2 Cell Cultures

Prof. Cenk Suphioglu, PhD1, Ms. Dwan Price, BSc Hons1, Prof. Leigh Ackland, PhD2, A. Wesley Burks, MD, FAAAAI1, Dr. Matthew Knight, PhD2, 1Deakin University, Australia, 2Deakin University, Australia, 1University of North Carolina, Chapel Hill, NC, 4Department of Primary Industries, Australia.

RATIONALE: To investigate allergen-epithelial interactions of peanut allergens with the human intestinal epithelium.

METHODS: We investigated the intestinal epithelial transport of peanut extract using the human Caco-2 cell culture model, exposed to varying concentrations of crude peanut extract. Western and immunofluorescence analysis were used to identify the cellular and molecular changes of peanut extract on the intestinal epithelium.

RESULTS: Following exposure of Caco-2 cells to 1 or 3mg/mL peanut extract, strong binding of the peanut allergens Ara h 1 and Ara h 2 to the apical cellular membrane was observed. These allergens were also observed to cross the Caco-2 monolayers. Treatment with peanut extract resulted in a decrease in transepithelial electrical resistance, indicating compromised barrier integrity, but not to the extent to allow increased flux of Lucifer Yellow. Total cellular protein levels of the tight junction proteins occludin, junctional adhesion molecule-A (JAM-A), claudin-1 and Zonula occludin-1 (ZO-1) remained unchanged. However, co-localisation of the transmembrane tight junction proteins occludin, JAM-A and claudin-1, with the intracellular adhesion protein ZO-1, were significantly altered.

CONCLUSIONS: The disruption of Caco-2 barrier integrity through disrupted tight junctions may enable movement of peanut proteins across the intestinal epithelium without M cell involvement. This may account for peanut’s increased allergenicity, compared to other food allergens, and provide an explanation for the potency of peanut allergens in eliciting an immune response. Indeed, this may be similar to that of immune adjuvants that alter barrier integrity to obtain artificial immune stimulation.
Synergistic Effect Of Dermatophagoides Pteronyssinus Allergens and Dexamethasone On Expression Of CD163 By Peripheral Blood Mononuclear Cells Of Allergic Asthma Patients

Prof. Krzysztof Kowal, MD, PhD1, Pawel Bernatowicz, MD, PhD2, Prof. Lech Chyczewski, MD, PhD2, Prof. Anna Bodzenta-Lukaszyk, MD, PhD1; 1Medical University of Białystok, Białystok, Poland, 2Medical University of Białystok, Poland.

RATIONALE: CD163 is a marker of anti-inflammatory monocytes/macrophages. We evaluated in vitro the effect of Dermatophagoides pteronyssinus (Dp) allergens and dexamethasone (Dx) on expression of CD163 by peripheral blood mononuclear cells (PBMC) of allergic asthma patients (APs).

METHODS: PBMC from 14 mild-moderate and 6 severe Dp-APs, and 10 healthy controls (HCs) were cultured with Dp (2500 SBE/ml, Allergopharma, Germany), Dx (10^-6M), Dp+Dx or without any stimulation for up to 144 hours (T144). Concentration of soluble CD163 (sCD163, sCD163, interleukin- (IL-)6 and -10 mRNA expression were evaluated using real-time PCR.

RESULTS: At T144, the mean concentration of sCD163 in Dp (5.14±3.46 ng/ml) was greater than in HCs (2.73±1.78 ng/ml; p=0.049). Stimulation with Dp resulted in increase of sCD163 concentration in HCs (4.66±2.7; p=0.003), but not in APs (8.34±11.3; p=0.07). Stimulation with Dx, resulted in increase of sCD163 concentration both in APs (17.14±16.3 pg/ml; p=0.002) and in HCs (8.64±5.1 pg/ml; p=0.001). The effect was attenuated in severe asthmatics (58±47 pg/ml; p=0.04). The synergistic effect of Dp+Dx on CD163 mRNA expression was seen at T35 and T48 but not at T7, Dp decreased Dp induced secretion of IL-6 but did not affect Dp induced production of IL-10.


IgE Antibodies and FcεRI Are Critical For Acquired Resistance Against Honeybee Venom In Mice

Dr. Philipp Starki, PhD1, Dr. Thomas Marichal, DVM PhD1, Dr. Laurent L. Reber, PhD1, Dr. Janet Kalesnikoff, PhD1, Dr. Hans C. Oettgen, MD, PhD1; 1Stanford University School of Medicine, Stanford, CA, 2Boston Children's Hospital, Boston, MA, 3Charite Campus Mitte, Berlin, Germany.

RATIONALE: Except for evidence that IgE antibodies can contribute to immune responses against certain parasites, the physiologic function of IgE is unclear. We have shown that type 2 immune responses induced by injection of sub-lethal amounts of honeybee venom (BV) can increase the resistance of mice to challenge with potentially lethal amounts of BV. Considering the important contribution of mast cells to innate resistance to BV (M. Metz et al. Science. 313:526-30, 2006) and the ability of IgE to enable antigen-specific mast cell activation, we investigated whether IgE and FcεRI contributed to acquired protection against BV.

METHODS: We studied wild-type C57BL/6 and BALB/c mice and mice of either background lacking IgE, FceRIγ, or FcεRIα. Knock-out and respective control mice were either actively immunized by sub-cutaneous injection of BV (or PBS as a control) or received serum derived from BV- or PBS-mock-immunized mice. We measured body temperature and survival to assess responses to BV challenge.

RESULTS: Wild type mice acquired increased resistance to BV challenge either by active immunization with a sub-lethal amount of BV or by passive immunization with serum from BV-immunized mice, unless IgE function in the serum had been neutralized (by treatment with anti-IgE or heating at 56°C for 1 hour) before transfer. IgE^-/- mice did not acquire increased resistance by active immunization. We could transfer protection passively to IgE^-/^- mice, but not to FcεRIγ- or FcεRIα-deficient mice.

CONCLUSIONS: We conclude that IgE antibodies and FcεRI-expressing effector cells are critical for acquired resistance to BV in mice.
**AB226 Abstracts**

**MONDAY**

**782** Balsam Of Peru, a Common Contact Dermatitis Allergen, Is a CD1a Antigen

Sarah Nicolai, MD1,2, Tan-Yun Cheng, PhD1,2, Elvire A. Bourgeois, PhD1,2, Annemieke de Jong, PhD1, D. Branch Moody, MD3,2, 2Brigham and Women’s Hospital, Division of Rheumatology, Immunology and Allergy, Boston, MA, 2Harvard Medical School, Boston, MA, 3Columbia University Medical Center, Department of Dermatology, New York, NY.

**RATIONALE:** CD1 proteins activate T cells using a mechanism that is similar to MHC proteins, but involves lipid instead of peptide antigens. CD1a is prominently expressed on epidermal Langerhans cells in the skin. We hypothesized that common contact dermatitis allergens bind to CD1a and activate T cells.

**METHODS:** As a screen of antigenicity, T.R.U.E. Test individual allergen patches were incubated with CD1a-antigen presenting cells and a CD1a-dependent T cell line (BC2). Activation was measured with IFN-gamma ELISA and CD1a dependence was documented with plate-binding assays and gene transfection.

**RESULTS:** Balsam of Peru coated patches activated T cells, leading to further tests that documented a CD1a dependent response to pure Balsam of Peru. Balsam of Peru Oil and one of its major chemically defined components Benzyl Cinnamate. Non-oil contact sensitizers such as Nickel and Potassium Dichromate did not activate CD1a-restricted T cells.

**CONCLUSIONS:** Our results indicate that Balsam of Peru – a common contact allergen – and one of its major components Benzyl Cinnamate are presented by CD1a to T cells. Oils have long been known as contact sensitizers, and T cells participate in the response, but any specific molecular mechanism for T cell activation by oils is currently unknown. Our results provide proof of concept that an oil-based allergen can be directly presented by the CD1a system and recognized by CD1a T cells.

**783** Cellular Infiltrate Induced By Bites From The Tick Amblyomma Americanum In Subjects With Or Without IgE To Galactose-Alpha-1,3-Galactose (Alpha-gal)

Dr. Nikhila Schroeder, MD1, Mr. Jake Eccles2, Erin J. Klaflky, MD, PhD1, Thomas A. E. Plattes-Mills, MD, PhD, FAAAAI1, 1Division of Asthma, Allergy & Immunology, University of Virginia Health System, 2University of Virginia School of Medicine.

**RATIONALE:** Bites from A. americanum cause severe pruritis and are considered to be the main cause of sensitization to alpha-gal. We hypothesized that local inflammation at the tick bite site plays a significant role in stimulation of the IgE response.

**METHODS:** Naturally occurring bites of larval or adult ticks were biopsied 1 day (n=2), 2 days (n=1), or 4 days (n=1) post bite. Two subjects had previous positive IgE to alpha-gal and one was negative. The samples were either frozen and sectioned, or formalin-fixed and paraffin-embedded. H&E staining and immunohistochemistry for evaluation of eosinophils, basophils, dendritic cells, T cells, and TSLP was compared between alpha-gal positive and negative subjects and to normal skin.

**RESULTS:** Biopsies of lesional skin demonstrated numerous clusters of dendritic cells (Anti-CD11c, Anti-HLADR) and T cells (Anti-CD3), and an increase in TSLP expression (Anti-TSLP) in the stratum granulosum. Those with IgE to alpha-gal showed eosinophils (Anti-MBP) and basophils (Anti-ENPP3, Anti-2D7) as well as T cells throughout the dermis. The biopsy specimen from the subject without IgE to alpha-gal showed numerous neutrophils surrounding the tick mouthparts. These results were distinct from normal skin.

**CONCLUSIONS:** Tick bites induce local inflammation, which can last for days to weeks. The histology in patients with alpha-gal sensitivity showed dendritic cells, T cells, eosinophils, basophils, and increased TSLP expression. The alpha-gal negative subject demonstrated dendritic cell and T cell clustering within the bite lesion. The results are compatible with a significant role of skin infiltrate in dictating the nature of the antibody response to alpha-gal.

**784** Duox2 and Mitochondria-Induced Antiviral Innate Immune Response After Influenza A Virus Infection In Human Nasal Epithelium

Prof. Hyun Jik Kim1,2, Prof. Chang-Hoon Kim3,4, Dr. Sung-Shik Kim5, Prof. Joo-Heon Yoon5,6, 1Chung-Ang University College of Medicine, Seoul, South Korea, 2Airway Mucus Institute, Seoul, South Korea, 3Department of Otorhinolaryngology, Yonsei University College of Medicine, Seoul, South Korea, 4The Airway Mucus Institute, Yonsei University College of Medicine, Seoul, South Korea, 5Koenko Nose Institute, Seongnam, South Korea, 6Research Center for Human Natural Defense System, Yonsei University College of Medicine, Seoul, South Korea.

**RATIONALE:** The interferon (IFN) signaling system is perhaps the most critical pathway for antiviral defense and protective actions of IFNs rely on signaling through IFN receptors, transcription factors (Stat) and IFN-stimulating genes or antiviral cytokines requiring for degradation of virus and suppression of viral transcription or translation. Our goal is to explore the role of IFN signaling in nasal epithelium, especially Stat and IFN-stimulating genes and to investigate the molecules for regulating IFN-signaling after influenza A virus (IAV) infection.

**METHODS:** We performed endonasal brushing and ALI culturing human nasal epithelial cells (NEC) from normal volunteers.

**RESULTS:** Microarray results showed that mRNA levels of Stat1, Stat2 and IFN-stimulating genes, such as Mx1, OAS1, IFIT1 and CXCL10 were highly induced after IAV infection. We found that mRNA levels of Mx1, OAS1, IFIT1 and CXCL10 were higher in NEC until 3 days post of infection (PI). Similarly, phosphorylation of Stat1 and Stat2 increased after PI 1 day. Interestingly, IFN signaling was down-regulated in case of scavenging ROS generated by Duox2 and mitochondria. Both Stat1 and Stat2 phosphorylation were significantly decreased after inhibition of mitochondria respiratory chain reaction and was also suppressed after knock-down of Duox2 gene expression. Inhibition of mitochondrial and Duox2-induced ROS generation attenuated mRNA levels of Mx1, OAS1, IFIT1 and CXCL10, resulting in increasing viral titer highly.

**CONCLUSIONS:** Our findings suggest that IFN-signaling be primarily responsible for controlling IAV infection and both mitochondria and Duox2 might be important molecules for regulating antiviral innate immune response in nasal epithelium.
785 Persistent Endothelial Damage After Intravenous Immunoglobulin Therapy In Kawasaki Disease
Dr. Yoshihiko Sakurai1,2, Dr. Hideo Takatsuka1, Dr. Mutsuzo Takada1, Dr. Masato Nishino1,1,1Nara Prefectural Minimo Hospital, Sango, Japan, 2Matsubara Tokushukai Hospital, Matsubara, Japan.
RATIONALE: Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology. Endothelial cell damage associated with vasculitis lead to hypercoagulability, which might be involved in coronary artery disease. However, the alteration of coagulability after intravenous immunoglobulin therapy (IVIG) has been less well investigated. We hypothesized that inflammation-coagulation axis would affect endothelial function and IVIG would prevent endothelial damage through suppression of inflammation.
METHODS: To test the hypothesis, we assessed the markers of inflammation, coagulation, and endothelial damage before and after IVIG. We retrospectively reviewed the medical records of pediatric patients with KD who met the following criteria. They were admitted to our hospital between May 2010 and April 2012 and were treated with IVIG. In 26 patients who met the inclusion criteria (mean age 6.1 years ± 5.1 years), PT, APTT, FDP, and D-dimer were assessed as coagulation markers; serum amyloid A, procalcitonin, and ferritin as inflammation markers; factor VIII activity (FVIII:C) and von Willebrand factor antigen (VWF:Ag) as endothelial damage.
RESULTS: IVIG was effective in all patients. Prolonged PT and APTT before IVIG were significantly shortened after IVIG, and elevated levels of FDP and D-dimer were significantly decreased. Furthermore, elevated levels of inflammation markers were significantly decreased after IVIG. However, elevated levels of FVIII:C and VWF:Ag remained high even after IVIG.
CONCLUSIONS: IVIG ameliorated inflammation as previously reported, which might ameliorate hypercoagulable state as well. Nevertheless, our results suggest that endothelial damage might be prolonged in IVIG effective patients. Control of endothelial damage might be critical in KD.

786 Prevalence Of Toxocariasis In General Population Based On Serologic Test
Prof. Byung-Jae Lee, MD1, Dr. Jin-Young Lee, MD1, Dr. Mi-Jung Oh, MD2, Prof. Dong-Chull Choe, MD1,1Samsung Medical Center, 2Bundang Jesaeng General Hospital.
RATIONALE: Toxocariasis is known to be the most common cause of peripheral blood eosinophilia and provokes eosinophilic infiltration in various organs including lung. However, the prevalence of toxocariasis in general population is rarely reported.
METHODS: We evaluated the serum specific IgG antibody to Toxocara larval antigen among healthy people who underwent routine-checkups including blood tests and low dose chest CT scan at Samsung Medical Center, South Korea.
RESULTS: From March 2011 to August 2013, total 488 people (291 men, 197 women) were recruited. Among them, 230 (47.1%) showed positivity.
CONCLUSIONS: The prevalence of Toxocara infection in general population is high, even though a large portion of them are asymptomatic.

787 Vitamin D Levels and Sensitization To Indoor Inhalant Allergens In Korea
Dr. Kyung-Hwan Lim1,2, Dr. Min-Gyu Kang1,2, Dr. Han-Ki Park1, Prof. So-Hee Lee1, Prof. Min-Suk Yang1,2, Prof. Woo-Jung Song, MD1, Prof. Hye-Ryun Kang1, Prof. Heung-Woo Park, MD, PhD1, Prof. Sun-Sin Kim1, Prof. Yoon-Seok Chang1,2, Prof. Sang Heon Cho, MD, PhD1, Prof. Kyung-Up Min, MD, PhD1, Prof. Sue-Hoon Kim1,2, 1Department of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea, 2Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea, SMG-SNU Boramae Medical Center, Seoul, South Korea.
RATIONALE: Recently, many studies have suggested possible effects of vitamin D on the manifestations of allergic diseases. However, it is still unclear whether vitamin D level is linked to a sensitization to indoor inhalant allergens. We sought to investigate the association between serum vitamin D and sensitization to indoor inhalant allergens using data of the Fifth Korea National Health and Nutrition Examination Surveys (KNHANES V) conducted in 2010.
METHODS: We analyzed the relationship between serum 25 hydroxyvitamin D (25(OH)D) levels and total IgE in a nationally representative samples of 2342 participants over 10 years old. The association of 25(OH)D level with specific IgE levels of 3 different indoor inhalant allergens (Dermatophagoides farinae, cockroach, and dog hair) was assessed after adjusting possible confounders by using logistic regression models.
RESULTS: There was a significant positive correlation between 25(OH)D level and log-transformed total IgE level. Logistic regression revealed an inverse association between low levels of 25(OH)D and sensitization to Dermatophagoides farinae (p<0.01) and cockroach (p<0.01), whereas there was no significant association between 25(OH)D level and the sensitization to dog hair.
CONCLUSIONS: This study suggests that elevated serum vitamin D level is associated with high total IgE and sensitization to Dermatophagoides farinae and cockroach in Koreans. Further research is required to confirm these findings.

788 Measuring Vascular Leak During Respiratory Viral Infections
Dr. Brian T. Kelly, MD, Mrs. Desire Hunter, Dr. Mitchell H. Grayson, MD, FAACAAI, Medical College of Wisconsin, Milwaukee, WI.
RATIONALE: Respiratory viruses are associated with increased risk of asthma in children. Viral pulmonary infection results in the production of viral specific IgE; we hypothesize that during viral infections this IgE leads to increased vascular leak in the lungs. This study was designed to quantify the level of vascular leak in the lungs during a severe respiratory viral infection.
METHODS: Uninfected and C57BL/6 mice inoculated with Sendai Virus (SeV) or UV inactivated SeV (UV-SeV) were sacrificed on 6, 8, and 10 days post inoculation. One hour prior to euthanasia, mice were injected with 20mg/kg Evan’s Blue Dye (EBD), a commonly used marker for vascular leak. Lungs were harvested, photographed, and homogenized to extract the EBD. Spectrophotometric analysis was used to determine the concentration of EBD in the lung tissue. Non-parametric unpaired t-tests were used in data analysis.
RESULTS: SeV infection led to greater EBD (i.e., vascular leak) at all three time points tested when compared to uninfected mice (p<0.044, 0.025, and 0.047, for days 6, 8, and 10, respectively, n>3). Lung EBD was greatest at day 8 post SeV, although the difference between days did not reach statistically significance. As expected, vascular leak was significantly greater in SeV compared to UV-SeV inoculated mice (p<0.03; n>3). No difference in vascular leak was noted between UV-SeV inoculated and uninfected mice (p>0.154, n=3).
CONCLUSIONS: Severe viral infection is associated with a measurable increase in vascular leak early in the infection. Whether this leak is dependent upon anti-viral IgE will be examined in future studies.
789 Effects Of Rhinovirus (RV) 39 Infection On Airway Hypersensitivity (AHR) To Histamine and Carbachol In Human Airways
Joshua L. Kennedy, MD¹, Stacie M. Jones, MD²,3, Ms. Megan Kurten¹,3, Ms. Suzanne House¹,3, Richard Kurten, PhD¹,3, ¹Arkansas Children’s Hospital Research Institute, Little Rock, AR, ²University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Little Rock, AR, ³University of Arkansas for Medical Sciences, Little Rock, AR.

RATIONALE: RV infection is associated with asthma exacerbations. We hypothesized that airway infection with RV39 would induce AHR, a diagnostic feature of asthma, in lung tissue derived from deceased organ donors with and without a history of asthma.

METHODS: Precision cut lung slices (PCLS) were prepared from cadaver lungs and cultured ex-vivo. Airway viability was confirmed microscopically by ciliary motility, by bronchoconstriction with carbachol, and subsequent bronchodilation with isoproterenol. Cumulative dose response curves for carbachol- and histamine-induced contractility (as a biomarker for AHR) were measured using slices derived from asthmatic (n=4) and non-asthmatic donors (n=1) before and after infection with RV39.

RESULTS: Overall, RV39 infection of PCLS from donors with a history of asthma failed to stimulate enhanced AHR within 48h. In one donor, RV39 induced histamine-specific AHR (EC50 was reduced from 109 nM to 30nM after 48h; p<0.01) with little change in responsiveness to carbachol (EC50, 81nM to 109nM p=NS). By contrast, RV39-infected PCLS derived from a donor without a history of asthma were less responsive to histamine (EC50: 40nM to 200nM) with no change in response to carbachol (EC50:200nM to 180nM).

CONCLUSIONS: RV39 induced AHR in human PCLS airways derived from 1 of 4 donors previously diagnosed with asthma. AHR to histamine, but not to carbachol in a subset of ‘asthmatic’ airway provides insights into a potential mechanism by which viral infections and atopy could synergize to induce asthma exacerbations. Human PCLS provide an outstanding platform with which to dissect these interactions.

790 Poor Asthma Control In Older Adults Is Associated With Reduced Adherence To Controller Therapies and Inability To Afford Medications
Dr. Jessica Tan, MPH¹, Dr. David I. Bernstein, MD, FAAAAI², Ms. Cheryl Koff Bernstein, RN, BSN, CCRC³, Dr. Patrick Ryan, PhD³, Dr. Jonathan A. Bernstein, MD, FAAAAI¹, Ms. Banu Kesavalu¹, Dr. Manuel S. Villareal, MD, FAAAAI¹, Dr. Andrew M. Smith, MD, FAAAAI⁴, Dr. Peter Lenz², Dr. Tolly Epstein, MD, MS¹⁵, ¹University of Cincinnati Medical Center, Cincinnati, OH, ²Bernstein Allergy Group, Cincinnati, OH, ³Bernstein Clinical Research Center, LLC, Cincinnati, OH, ⁴Cincinnati Children’s Hospital Medical Center, Cincinnati, OH, ⁵University of Cincinnati, Cincinnati, OH, ⁶Division of Immunology Allergy & Rheumatology, University of Cincinnati Medical Center, Cincinnati, OH, ⁷University of Cincinnati, Cincinnati, OH, ⁸3255 Eden Ave., HPB 350, University of Cincinnati Medical Center, Cincinnati, OH, ⁹The University of Cincinnati Medical Center, ¹⁰Allergy Partners of Central Indiana, Indianapolis, IN

RATIONALE: Nonadherence to asthma medications may contribute significantly to higher morbidity and mortality from asthma in adults age 65 years and older. Standardized measures to evaluate nonadherence in this population are lacking.

METHODS: Adults age 65 years and older with an objective diagnosis of asthma (n=175) were recruited from Allergy and Pulmonary clinics. They were administered a standardized survey with Likert scale responses, consisting of questions regarding asthma medication use and reasons for nonadherence in the previous month. Demographic data, medical history, including emergency department (ED) visits in the past year, and the validated asthma control questionnaire (ACQ) and asthma control test (ACT) were completed. Composite medication use scores (CMUS) were determined by summing responses. Logistic regression was used to compare asthma outcomes (ACT, ACQ, ED visits) to composite scores and individual questions, and to evaluate predictors of adherence.

RESULTS: The mean CMUS was 7.1±2.9 (range 5-25; 5=perfect adherence); ACQ≥1.5 8.5, ACQ <1.5 6.7. Subjects with ACQ ≥1.5 and/or ACT<20 (poor asthma control) and/or any ED visits were less likely to be adherent (OR 0.37, [95% CI 0.19-0.72], p<0.05; 0.44 [0.24-0.79], p<0.05; 0.19 [0.07-0.50], p<0.001, respectively). Individuals with ACQ≥1.5 were less likely to report continued asthma medication use despite symptom improvement (OR 0.29, [0.13-0.65], p<0.005), and less able to afford medications (OR 0.23 [0.08-0.71], p<0.05). Findings were similar for ED visits.

CONCLUSIONS: Discontinuation of medications and the inability to afford medications were significant predictors of poor asthma control in older adults.

791 Texting Medication Reminders For Better Asthma Control In Children and Teens
Dr. Humaa M. Bhatti, DO¹, Ms. Wafa Alame, RN¹, Mr. Joseph Adams², Dr. Jenny M. Montejo, MD¹, Dr. Milind V. Pansare, MD, FAAAAI¹, Dr. Pavadee Poowuttikul, MD¹, Dr. Elizabeth A. Secord, MD, FAAAAI², ¹Children’s Hospital of Michigan, Detroit, MI, ²Wayne State University, Detroit, MI.

RATIONALE: Non-adherence to medication regimens continues to be a persistent problem among patients with asthma. Technology makes communication with our patients between visits easier and more meaningful for all parties. We examine the effects on asthma control of sending medication reminders and allowing patients to communicate with staff via text messaging.

METHODS: 22 participants (up to age 18 years) enrolled, with ongoing enrollment for future addition to the study population. Written assent obtained from teenage participants and informed consent obtained from all parents. Text reminders were sent twice daily by a research assistant to the parents and/or teenage patients with understanding that patients should receive medication at receipt of reminders. Retrospective chart review was completed to examine frequency of steroid bursts, ER visits, and hospitalizations for asthma occurring in the year prior to starting the study, and number of these occurring since starting.

RESULTS: 18/22 participants completed 2-5 months of the study to date, four dropped out. In the 12 months prior to the study, 14/18 patients had two or more steroid bursts, all 18 patients had at least one urgent visit, and 14/18 had been admitted. Since starting the study, 14/18 patients had no steroid bursts, ER visits, or hospitalizations since starting the study. Extrapolating the results for each participant since starting the study to 12 months, this represents a significant reduction in the above unfavorable outcomes.

CONCLUSIONS: Our results suggest that communicating with our patients via text reminders is effecting positive change on control of their asthma.
**792** Adherence To Prescribed Controller Therapy and Effects On Asthma Control In The Hispanic Population Of A Pediatric Disease Management Program

**Dr. Lyne G. Scott, MD**1, Tricia Morphew2, Marilyn Li1, Dr. Salima A. Thobani, MD1,1University of Southern California, 2Morphew Consulting, LLC, CA.

**RATIONALE:** Guidelines suggest asthma controller therapy based on baseline severity and asthma control. Adherence to therapy is associated with improved asthma control. This study evaluated the effect of controller therapy (mono vs. combination) prescribed and used on time to achieve well-controlled asthma (TWCA) and maintenance of well-controlled asthma (MWCA) for patients receiving specialty-based care in Los Angeles mobile asthma clinics (LAC-USC Breathmobile Program).

**METHODS:** Data was collected for 233 Hispanic asthmatic patients at 1261 visits, ages 3-18, with program enrollment during 2011 and return for follow-up within six months over two-year potential. Data for TWCA, MWCA, and factors (therapy prescribed, adherence, age, gender, BMI, allergic rhinitis, ED visits, School days missed, season, and visit interval) associated with well-controlled asthma were evaluated.

**RESULTS:** Effect of controller medication use >5 vs. <5days/week on TWCA varied by baseline severity: Mild HR=1.59 (95%CI 3-3, p=.186); Moderate mono-therapy HR=2.73 (95% CI 10-7.2, p=.023); Moderate combination-therapy HR=2.94 (95%CI 1.4-63, p=.005); and Severe-no differences. Effect of controller medication use >5 vs. <5days/week on MWCA varied by baseline severity: Mild OR=4.88 (95%CI 1.7-141, p=.003); Moderate mono-therapy-no differences; Moderate combination-therapy OR=4.85 (95%CI 1.4-16.6, p=.012); and Severe-no differences. Diagnosis of allergic rhinitis was significant in TWCA for all baseline severities but not in MWCA. A proportion of patients with intermittent baseline severity did require controller therapy to maintain well-controlled asthma.

**CONCLUSIONS:** Results suggest importance of controller adherence >5 vs. <5days/week. Fluctuations in therapy prescribed to achieve and maintain well-controlled asthma reinforce dynamic nature of asthma symptoms and need to reassess asthma control at each visit.

**793** Correlation Between Emergency Department Visits For Asthma Exacerbation and No Show Visits To Primary Care Provider In a Pediatric Population

**Dr. Margaret Redmond, MD**1, David R. Stukus, MD, FAAAAI; Nationwide Children’s Hospital, Columbus, OH.

**RATIONALE:** Poor asthma control secondary to non-adherence is a known contributing factor for Emergency Department (ED) visits and Inpatient Hospitalizations (IP) in the pediatric population. The relationship between missed scheduled physician visits and subsequent ED/IP encounters has not previously been reported.

**METHODS:** A retrospective review of the electronic medical record (EMR) was performed for all patients ages 2-18 with a primary diagnosis of 493.xx (asthma) who utilized the Primary Care Network (PCN) at a tertiary care pediatric academic center between 2010-12. EMR was also reviewed during same time period for all ED/IP visits with primary diagnosis 493.xx. PCN no show visits/cancellation (NS) records were cross referenced with the two databases.

**RESULTS:** We identified 3101 ED and 749 IP total visits for asthma. Unique individuals accounted for 1877(1.65/patient) ED and 550(1.36/patient) IP encounters. There were 8179 total NS, with 1665 unique patients(4.9 NS/patient). 69%(1297/1877) of all ED patients had NS in prior 12 months, 14%(N=256)<30 days, 29%(N=542)<60 days, 63%(346/550) of all IP patients had NS in prior 12 months, 11%(N=63)<30 days, and 25%(N=137)<60 days. Of all NS patients, 54%(N=902) had ED encounter; 46%(N=763) of all NS patients did not utilize ED for asthma.

**CONCLUSIONS:** This data suggests a strong association between NS visits at PCN and subsequent ED/IP encounters for asthma. More than 25% of patients had NS visit within 60 days of asthma exacerbation and more than 50% of patients with NS visit utilized ED for asthma exacerbation. Tracking NS visits may offer a useful tool to adopt intervention strategies identifying at risk asthma patients and preventing ED/IP encounters.

**794** Choosing Wisely: Adherence By Allergists To Recommended Use Of Spirometry In The Diagnosis and Management Of Adult Asthma

**Dr. Kristin C. Sokol, MD, MPH**1, Dr. Gregg Wilkinson, PhD, Ms, Karen Pierson, MA, Dr. Randall M. Goldblum, MD; University of Texas Medical Branch, Galveston, TX.

**RATIONALE:** The American Board of Internal Medicine foundation initiative “Choosing Wisely” suggests that allergists should use spirometry in diagnosing and managing asthma. The NHLBI and ATS provide similar guidelines. However, prior studies outside the USA suggest that pulmonary function testing is underutilized. The goal of this study was to assess the utilization of spirometry in privately insured, adult asthma patients in the US.

**METHODS:** A United Health Care claims database was reviewed to identify a cohort of patients newly diagnosed with asthma during the years 2002 to 2011. The proportion of these patients in which spirometry was performed was scored by age, region of country, and type of treating physician.

**RESULTS:** 219,966 patients were found to have a diagnosis of asthma. Patients were excluded who had any comorbid pulmonary condition. 92,216 (41.92%) patients had spirometry performed. Interestingly, our results revealed a pattern of declining use of spirometry with a significant decrease in years 2009-2011. Spirometry was more likely to be used in diagnosing rather than managing asthma. Allergists were significantly more likely to order spirometry than primary care physicians (50% vs. 29%).

**CONCLUSIONS:** This study demonstrates that many physicians are not using spirometry as recommended. This might negatively impact clinical outcomes or cost of care for adults with asthma. This data set will allow us to determine whether use of spirometry truly improves quality of care, as indicated by frequency of ED visits and hospitalizations for asthma exacerbations. In addition, we will determine whether the use of spirometry alters cost of asthma care.
795 Protein-Coupled Receptor Kinase-3 (GRK-3) In Bone Marrow Niche Interactions and Transplantation

Jaimie M. Brozowski1,2, Roman Timoshchenko2, Jessica Koontz3, Janet Rubin1,2, Matthew Billard2, Teresa K. Tarrant2,3, 1Department of Microbiology and Immunology, University of North Carolina School of Medicine, Chapel Hill, NC 27599, USA, 2Thurston Arthritis Research Center and Department of Medicine, Division of Rheumatology, Allergy, and Immunology, University of North Carolina, Chapel Hill, NC 27599, USA, 3School of Medicine, University of North Carolina, Chapel Hill, NC 27599, USA.

RATIONALE: Hematopoietic stem cell transplantation (HCT) is performed as an approach to address multiple forms of cancer and hereditary diseases including immune deficiency, though patient outcome of immune reconstitution is variable. Our study explores the effect of G protein-coupled receptor kinase-3 (GRK-3) on hematopoietic (HSCs) and mesenchymal stem cells (MSCs) in the bone marrow (BM) niche. We hypothesize when GRK-3 regulation is absent it may enhance leukocyte engraftment in HCT through functional effects on proliferation, differentiation, and homing that are in part mediated through the CXCL12/CXCR4 signaling axis.

METHODS: MSCs were isolated from C57BL/6 and GRK-3 deficient (-/-) mice and supplemented with adipogenic or osteogenic media for differentiation analysis. MSC proliferation was determined by absorbance after addition of CCK-8, and HSC proliferation was determined by colony forming unit (CFU-GM) assay in the absence and presence of CXCL12. In vivo CFU-spleen (CFU-S) assay quantitatively assessed primitive BM cells by colony formation counts on day 8.

RESULTS: Our studies show GRK-3(-/-) mice have increased HSCs and total leukocytes in the BM and blood. GRK-3(-/-) HSCs have increased proliferation, which is enhanced in the presence of CXCL12. GRK-3(-/-) MSCs have an increased proliferation and differentiate into osteogenic progenitor cells more readily. In vivo CFU-S data revealed enhanced colony formations on the explanted spleen with utilization of either GRK-3(-/-) donor marrow or GRK-3(-/-) recipients, with an additive effect of GRK-3(-/-) donor marrow into GRK-3(-/-) recipients.

CONCLUSIONS: These data indicate a positive effect of GRK-3 deficiency on HCT and hematopoiesis with regards to both MSC and HSC function.

796 Allogeneic Hematopoietic Stem Cell Transplantation For Immune Dysregulation, Polyendocrinopathy, X-Linked (IPEX) Syndrome Resolves Enteropathy and Autoimmunity: A Single Institution Experience

Dr. Zeynep Yesim Yesim Kucuk, MD, Dr. Jack J. H. Blessing, MD, PhD, Dr. Rebecca A. Marsh, MD, Dr. Kejian Zhang, MD, Dr. Stella Davies, MBBS, PhD, Dr. Alexandra H. Filipovich, MD, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

BACKGROUND: Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is a rare, life-threatening systemic autoimmune disease caused by mutations in the FOXP3 gene resulting in failure to develop functional T regulatory (Tregs) lymphocytes. Patients usually present in infancy with a clinical triad of intractable diarrhea, diabetes, eczema and require lifelong immunosuppression. However, immunosuppression does not adequately control all symptoms nor prevent premature mortality. Hematopoietic stem cell transplantation offers a viable option leading to prolonged survival and improved quality of life.

RATIONALE: To report long term outcomes of 7 patients with IPEX syndrome following hematopoietic stem cell transplantation (HSCT).

METHODS: Retrospective analysis of 7 patients with IPEX who underwent HSCT between 2000-2012 at a single institution.

RESULTS: Seven patients with IPEX underwent allogeneic HSCT. Myeloablative conditioning was used in three patients and reduced intensity conditioning in four patients. Four patients are currently alive without immunosuppressive drugs, surviving 4 to 7 years post transplant. The overall survival was 80% in last decade. The earlier age at transplantation resulted in long-term survival. All survivors experienced reconstitution of Tregs with resolution of enteropathy and autoimmunity.

CONCLUSIONS: HSCT results in development of functional Tregs with reversal of autoimmune enteropathy.

797 Natural Killer Cell Immunoglobulin Like Receptor (KIR) Genetic Profile Is a Strong Predictor Of Allogeneic Hematopoietic Cell Transplant Outcomes

Dr. Rehan M. Faridi, PhD1, Taylor Kemp1, Dr. Poonam Dharmani, PhD2, Dr. Victor Lewis, MD3, Dr. Nouredine Berka, PhD3, Dr. Jan Storek, MD, PhD3, Dr. Faisal Khan, PhD3, 1University of Calgary, Calgary, AB, Canada, 2Alberta Children’s Hospital, Calgary, AB, Canada, 3Calgary Laboratory Services, Calgary, AB, Canada.

RATIONALE: In spite of high resolution HLA matching and optimal care, complications of allogeneic hematopoietic cell transplantation (allo-HCT), including graft versus host disease (GVHD), relapse of the underlying disease and reactivation of otherwise latent viral infections are substantial. Recently, natural killer (NK) cell genetic system, regulated by activating and inhibitory Killer Immunoglobulin-like Receptors (KIR) has garnered substantial research interest as a modifier of HCT outcomes. Here we set out to determine the influence of KIR gene repertoire of HCT pairs on allo-HCT complications including GVHD, relapse, posttransplant lymphoproliferative disorder (PTLD) and cytomegalovirus (CMV) reactivation.

METHODS: KIR typing was obtained for 92 and 111 (discover and validation cohorts) HLA- matched antithymocyte globulin (ATG) conditioned allo-HCT pairs and 50 healthy individuals by Luminex-based rSSO method. Effect of KIR genotypes on HCT outcomes was analyzed using binomial regression and Kaplan-Meier tests. PBMCs from healthy volunteers were stimulated against different targets to enumerate KIR-dependent target-specific NK cell response.

RESULTS: Significant protection against GVHD was observed in donor-recipient pairs matched for the KIR-AA and B/x genotypes (HR = 2.224; p = 0.01) without any effect on disease relapse (HR = 1.098; p = 0.934). Donor KIR-centromeric linkage group was strongly associated with the incidence of PTLD (p = 0.01). Higher activating donor-KIR conferred protection against CMV reactivation (p = 0.02). A unique target-induced functional response with higher number of herpes-virus induced functional NK cells in individuals lacking KIR-centromeric linkage group was observed.

CONCLUSIONS: NK cell responsiveness, a function of KIR gene repertoire modified the risk of GVHD, PTLD and CMV reactivation indicating relevance of KIR gene profiling for predicting HCT outcomes.
**A Systematic Analysis Of Pollen Transcriptomes From Plant Allergens Reveals Conserved Targets Of Immune Responses**

**Dr. Bjorn Peters**, 1 Dr. Jason Greenbaum, 1 Dr. Veronique M. Schulten, 1 Dr. Denise Baker, 1 Dr. April Frazier, 1 Dr. Alessandro Sette, 2 Dr. Biol. Sci., 1 Dr. Michael Wullner, 3 Ms. Heidi Hofer, 3 “La Jolla Institute for Allergy and Immunology, La Jolla, CA, 2University of Salzburg, Salzburg, Austria.

**RATIONALE:** We have recently identified a set of novel antigens in Timothy grass (TG) pollen using an integrated transcriptomic and proteomic analysis, and have shown that these antigens are prominent targets of T cell responses. Here we determined the degree of conservation of these antigens in multiple plant species, as conserved antigens could be targets of cross-reactive T cells, which would make them potential candidates for pan-pollen immunotherapy approaches.

**METHODS:** RNA was extracted and sequenced from nine plant allergens (4-grass, 2-weed, and 3-tree pollens). For each pollen, >600 million paired 100 nt reads were generated and assembled into >50,000 transcripts. Peptides from TG were examined for conservation across these pollens using sequence alignments. We also conducted pan-pollen immunotherapy approaches.

**RESULTS:** We find that conservation of a peptide across pollen increases the likelihood that it will elicit Th2 responses in allergic donors. At the protein level, several major plant protein allergens were found to be conserved in all examined pollens, including pollens from species for which only a limited number of allergen proteins have been identified (e.g., Western ragweed). In addition, several of the novel TG proteins that we identified were conserved across all pollens, including some for which strong Th2 cytokine production was detected without significant IgE responses.

**CONCLUSIONS:** We have identified a set of antigens targeted by T- and B-cell immune responses that are significantly conserved across multiple plant allergen species. This raises the possibility that these antigens could be used in diagnostic or immunomodulatory applications that simultaneously target a broad range of pollen allergies.
801 Urinary Polycyclic Aromatic Hydrocarbon Metabolites and Th2 Immunity In Children

Kunjal M. Hew, PhD1, Annett I. Walker, MD1, Arunima Kohtli1, Aleena Syed1, Cameron McDonald-Hyman1, Zheng Li, PhD, MPH2, Andreas Sjodin, PhD2, Dr. Kari C. Nadeau, MD, PhD, FAAAAI3, 1Department of Pediatric Allergy and Immunology, Stanford University, Stanford, CA, 2Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, 3Pediatric Allergy Immunology, Stanford University, Stanford, CA.

RATIONALE: Exposure to polycyclic aromatic hydrocarbons (PAH), a major component of ambient air pollution, has been linked with increased asthma morbidity in children. However the precise mechanisms as to the cellular pathways leading to the immunological impairment remain unknown. Metabolites of PAH are measurable in urine and can be used as biomarkers of personal exposure. We hypothesized that higher ambient PAH exposure would lead to an increased Th2 associated immune response in children. Furthermore, using urinary PAH metabolites we will be able to associate ambient PAH exposure with Th2 associated immune markers.

METHODS: Levels of mono-hydroxylated metabolites (1-naphthol, 2-naphthol, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene and 1-hydroxypyrene) from 4 parent PAHs (naphthalene, fluorene, phenanthrene and pyrene) were determined by gas chromatography mass spectrometry in urine samples from children (10-21 years, n=49 asthmatics, n=97 non-asthmatics). Expression of IL-4, IL-13 and CCR8 in CD4+CD25hi T cells in PBMCs was measured using flow cytometry. Asthma diagnosis was determined by NHLBI criteria.

RESULTS: Our data show that IL-4, IL-13 and CCR8 expression in CD4+CD25hi T cells are significantly associated with 5 of the 9 urinary PAH metabolites measured across all subjects. Asthmatic children showed significant association with pyrene based PAH metabolites and Th2 associated immune markers. In contrast, non-asthmatic children showed significant associations with naphthalene, fluorene, and phenanthrene derived PAH metabolites and Th2 associated immune markers.

CONCLUSIONS: Urinary PAH metabolites from children exposed to high levels of ambient air pollution are linked with Th2 associated immune markers. IL-4, IL-13 and CCR8 with differential impact on asthmatic children.

802 Impact Of BMI On Ozone-Induced IL-1β In The Airways Of Human Volunteers

Dr. Michelle L. Hernandez, MD1, Dr. Krista Todoric, MD1, Ms. Katherine Mills, BA2, Dr. Haibo Zhou, PhD3, Dr. David B. Peden, MD, MS, FAAAAI1, 1University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, 2University of North Carolina Chapel Hill School of Medicine, Chapel Hill, NC, 3University of North Carolina at Chapel Hill, School of Public Health, 4Office #544, Campus Box 7310, University of North Carolina at Chapel Hill School Medicine, NC.

RATIONALE: BMI has been previously found to explain the impact of increased BMI on ozone-induced decrements in spirometry.

RESULTS: BMI was significantly correlated with %change in IL-1β after ozone (r=0.4, p<0.004), but not with %change in IL-6 or IL-8. For each 1 unit increase in BMI, there was a significant increase of 20 ng/ml in IL-1β after ozone (p=0.02). There were no significant BMI effects on changes in IL-6 and IL-8. Gender, age, ethnicity, and asthma status did not significantly impact the relationship between BMI and change in IL-1β.

CONCLUSIONS: Increased BMI exaggerates the IL-1β airway inflammatory response after ozone exposure. IL-1β has been previously found to play a role in airway hyper-responsiveness. This BMI effect on IL-1β may explain the impact of increased BMI on ozone-induced decrements in spirometry.

803 Group-2 Innate Lymphoid Cells Promote Air-Pollutant Induced Airway Inflammation and Hyperresponsiveness (AHR)

Dr. Qi Yang, PhD, Moyar Q. Ge, Blerina Kokalari, Imre G. Reda, Xinxin Wang, Dr. Avinash Bhandoola, MBBS, PhD, Dr. Angela Haczku, MD, PhD, FAAAAI, University of Pennsylvania, Philadelphia, PA.

RATIONALE: Exposure to ozone evokes airway inflammation and triggers exacerbation of chronic asthma. We previously found that Balb/c mice respond to ozone by IL-5 release into the airsaws associated with exacerbation of allergen-induced airway inflammation. ILC2 are recently described innate lymphocytes with a potential to mediate ozone generated airway inflammation.

METHODS: To investigate the specific role of ILC2, Balb/c mice were exposed to ozone (2ppm, 2h) and studied at different time points. Pulmonary ILC2 were isolated by FACS sorting. ILC2 were depleted by anti-Thy1.2 mAb and replaced using Thy1.1+ ILC2 adoptive transfer (106/mouse) intratracheally. Airway inflammation, AHR to methacholine (FlexiVent) and ILC2 responses (IL-5 and IL-13 mRNA qPCR) were examined 12h after ozone exposure.

RESULTS: Ozone inhalation induced a time-dependent release of IL-33 (a known ILC2 activator), AHR, increased numbers of neutrophils, Siglec F+ cells (eosinophils) and IL-5 expression in the lung. Isolated pulmonary ILC2 (but not Th2 or NK cells) had markedly elevated IL-5 and IL-13 mRNA expression from ozone exposed mice in comparison with air exposed mice (p<0.01, n=8). Depletion of ILC2 by anti-Thy1.2 treatment abolished AHR and eosinophil infiltration and reduced the neutrophil number in ozone exposed lungs compared with control antibody treatment. ILC2 add-back restored ozone induced airway inflammation and dramatically enhanced ozone induced AHR (p<0.001, n=6).

CONCLUSIONS: Ozone exposure rapidly activated resident ILC2 in the lungs. Our data suggest that these cells were responsible for mediating ozone induced airway inflammation and AHR in Balb/c mice. This is a previously unrecognized role of lung resident ILC2.
804 Peanut T Cell Epitope Discovery: Ara h1 and Ara h3
Dr. Manish Ramesh, MD, PhD1, Madhan Masilamani, PhD2, Dr. George N. Konstantinou, MD, PhD, MS1, 2, Jay A. Lieberman, MD1, Hugh A. Sampson, MD, FAAAAI1, Dr. Madhundra Sivakumar1, Dr. Araya Yuengyowvit, MD1, Dr. Mariona Pascal, PhD1, 3 Mount Sinai School of Medicine, New York, NY, 4Icahn School of Medicine at Mount Sinai, New York, NY, 5Icahn School of Medicine and Mount Sinai, New York, NY, 624 General Military Training Hospital, Thessaloniki, Greece, 7First Pediatric Department, Aristotle University of Thessaloniki, Hippokration General Hospital, Thessaloniki, Greece, 8University of Tennessee, Memphis, TN. 9Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, 7Prince of Songkla University, Songkhla, Thailand, 6Serv”du Immunologie, Centre de Diagnostic Biomedic, Hospital Clinic., Barcelona, Spain.

RATIONALE: Peptide-based immunotherapy is a viable modality that circumvents IgE-mediated adverse reactions. Here we identify candidate peptides of Ara h1 and that display promiscuous binding to MHC class II and induce TH2 cytokine production by T cells.

METHODS: A two-step peptide screening process was employed. In silico MHC class II binding prediction was performed using NetMHCIIpan 2.0 (peptide length 15, 1-mer offset) using the most abundant class II alleles in our population. Promimmune Reveals (in vitro MHC class II peptide reporter) assay was performed using synthesized 15-mer peptide offsets by 5-mer spanning the protein. One hundred patients with an unequivocal history of peanut allergy or IgE level >95% predictive of peanut allergy were enrolled, PBMCs collected, and 3H-Thymidine T-cell stimulation assay used to assess reactivity.

RESULTS: Comparison of in vitro and in silico results showed good concordance for both Ara h1 and Ara h3. A pool of 36 Ara h1 peptides was selected for T-cell stimulation assays and confirmed these results. In silico analysis predicted promiscuous binding to different HLA types by several peptides. This was also seen in ex vivo T-cell stimulation assays. In combination with cytokines secreted in T-cell assays, we have identified 4 vaccine candidate Ara h1 peptides. Using a similar approach, we have also identified 4 Ara h3 vaccine candidate peptides.

CONCLUSIONS: Pre-selection of peptides in combination with conventional methods was an effective strategy for identifying peanut T-cell vaccine candidates.

805 Microparticles Encapsulated With Antigen Protect Against Sensitization and Reduce Anaphylactic Reactivity In a Food Allergy Model
Dr. Karen B. Chien, PhD1, Dr. Paul Bryce, PhD2, 1Northwestern University, Chicago, IL, 2Division of Allergy-Immunology, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL.

RATIONALE: Treatment of food allergy through oral immunotherapy has shown promise, but patients exhibit a high frequency of adverse reactions. Desensitization, rather than tolerance, also appears to be the likely mechanism. We previously demonstrated that chemical-coupling of antigen to spleenocytes promoted tolerance and inhibited experimental food allergy; however, this method has limitations for therapy. Therefore, we developed biodegradable microparticles as antigen carriers and examined their use in allergic models.

METHODS: Poly(lactic-co-glycolic acid) (PLGA) microparticles encapsulated with ovalbumin (OVA) were fabricated using double emulsion techniques and characterized for antigen release. Their effects on immune sensitization were determined by prophylactic treatment prior to intraperitoneal OVA/alum, while their ability to inhibit food allergy responses was assessed using a cholera toxin-driven model with treatment at established reactivity.

RESULTS: PLGA microparticles encapsulating OVA were homogeneous in size (1-20 microns) and exhibited a sustained release of antigen over several weeks. Pretreatment of animals with different microparticle doses prevented increases in OVA-specific IgE and TH2-associated cytokine responses. Administration to fully sensitized mice, especially by anaphylaxis upon challenge, triggered no immediate reactions and prevented anaphylactic symptoms and body temperature changes on challenge after only 1 week. Further studies are ongoing to investigate the mechanisms and efficacy of this therapeutic approach to anaphylaxis.

CONCLUSIONS: We have fabricated biodegradable microparticle carriers as an antigen delivery system. Our data suggests that these microparticles are capable of preventing sensitization and can be administered into sensitized animals safely. Since these microparticles ablate subsequent anaphylactic reactions to antigen exposure, they may be a novel approach to treating food allergy.

806 Over-The-Counter Dietary Supplements Genistein and Ipriflavone Suppress Peanut Allergy Symptoms
Ms. Lisa Chang, BS1, Ms. Mohanapriya Kamalakannan, MS1, Mr. Matthew Stadler1, Hugh A. Sampson, MD, FAAAAI, Madhan Masilamani, PhD1, 1Icahn School of Medicine at Mount Sinai, New York, NY, 2Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY.

RATIONALE: Genistein and Ipriflavone are popular dietary supplements used for the treatment of post-menopausal disorders. Both genistein and ipriflavone belong to a group of anti-inflammatory compounds called isoflavonoids. Ipriflavone is an anabolic synthetic daidzein-derivative. We tested the effect of these molecules on peanut allergic mouse models and in vivo basophil degranulation in food allergic subjects.

METHODS: 6-8 week old female C3H/HeJ mice were fed a soy-free diet (n = 28), diet containing 1500 ppm each of genistein (n = 14), ipriflavone (n = 17) or genistein+ipriflavone (n = 11). Mice were sensitized, boosted and challenged orally with peanut extract. The allergic symptoms (anaphylaxis scores and body temperature) were recorded after 60 min of challenge at week 10. Whole blood from 6 peanut- and 6 milk allergic subjects was pre-incubated with 100μM genistein, ipriflavone or genistein+ipriflavone for 30 min. Basophil degranulation assays were performed in the presence of allergenic extracts and isoflavonoids.

RESULTS: Dietary genistein+ipriflavone significantly suppressed peanut-induced anaphylaxis in mice compared to soy-free diet (mean scores: 0.18 vs 1.13, p < 0.001; mean temperature change: 0.6 vs -1.6, p < 0.001). Switching from soy-free diet to genistein+ipriflavone diet in “peanut-allergic” mice reduced the allergic symptoms. Ipriflavone+genistein dose-dependently suppressed anti-IgE mediated basophil degranulation and suppressed allergen-induced degranulation in food allergic subjects (mean fold change compared to control stimulation: 11 vs 18 for peanut, p < 0.01 and 6 vs 11 for milk, p < 0.001).

CONCLUSIONS: Unlike soy-derived isoflavone mixtures, synthetic genistein and ipriflavone are well documented to be safe for humans and allergic-free. We are currently investigating whether dietary Ipriflavone and genistein supplementation can be used therapeutically for food allergy.
**AB234 Abstracts**

**807 Analyzing Casein-Specific IL-4 and IL-13 Secreting T-Cells: A Reliable Tool for Diagnosis Of Cow’s Milk Allergy**

Dr. Benedicte Michaud, MD, PhD1,2, Dr. Joseph Aroulondom, MD3, Mrs. Nour Baiz, PhD3, Dr. Flore Amat, MD3, Dr. Ralhé Gourvis-Echraghi, MD1, Dr. Sophie Candon, MD, PhD2,3, Mr. Renny Couderc, PhD, PharmD2, Prof. Jean-Francois Bach, MD, PhD2,3, Prof. Lucienne Chatenoud, MD, PhD2,3, Prof. Jocelyne Just, MD, PhD3,4, 1Université Paris Descartes, Sorbonne Paris Cité, France, 2Institut national de la santé et de la recherche médicale, Unité U1013, Paris, France, 3Allergology department, Trouseau hospital AP-HP–UPMC Paris 6, France, 4Epidemiology of Allergic and Respiratory diseases (EPAR) Department, UMR-S 707 INSERM, UPMC Paris 6, France, 5Service de Biochimie et Biologie Moléculaire, Trouseau hospital AP-HP, Paris, France.

**RATIONALE:** Cow’s milk allergy (CMA) is a frequent food allergy in young children. The oral food challenge is the gold standard for diagnosis and there is currently no biological test. Our aim was to evaluate as a diagnostic tool a functional assay assessing allergen-specific Th2-cell response in CMA children.

**METHODS:** 29 children aged 2.8 to 10.5 years underwent a double blind placebo control food challenge (DBPCFC) to cow’s milk. Blood samples were collected before performing the DBPCFC and peripheral blood mononuclear cells were cultured in an 18 hours ELISPOT assay with casein, α-lactalbumin or β-lactoglobulin. The number of antigen-specific IL-4 and IL-13 secreting T-cells was assessed. Serum specific IgE, IgG4 and total IgE levels were measured. ROC curves were generated.

**RESULTS:** 17 (59%) children reacted to cow’s milk and were considered as cow’s milk allergic (CMA). The mean number of casein-specific IL-4 and IL-13 secreting T-cells was higher in CMA than in non-CMA children (p = 0.009, p = 0.004 respectively). Moreover, it was inversely correlated to the cow’s milk tolerated cumulative dose (p = 0.003, p = 0.009 respectively). Receiver-operating characteristic (ROC) curve of combined IL-4 and IL-13 analysis was generated. AUC was 0.98 (95% CI 0.90-1.06). For a cut-off of 10 IL-4- and 12 IL-13 secreting T-cells, sensitivity and negative predictive value were 100%.

**CONCLUSIONS:** Analyzing the number of casein-specific IL-4 and IL-13 secreting T-cells is a suitable tool to diagnose cow’s milk allergy in children and if confirmed in a larger study, could avoid performing oral food challenges.

**808 Growth Of Children Aged 2-17 With Cow’s Milk, Peanut, and Egg Allergy In NHANES**

Dr. Karen Robbins, MD, Robert A. Wood, MD, FAAAAI2, Corinne Keet, MD, MS2; Johns Hopkins University School of Medicine, 2Johns Hopkins University Medical Center, Baltimore, MD.

**RATIONALE:** Although food allergy has the potential to impact nutrition and growth, population wide studies on these issues are limited.

**METHODS:** Nationally representative data from NHANES 2007-2010 were used to analyze anthropometric measurements and nutrient intake in 6117 children aged 2-17. Milk allergy was defined as the combination of self-report of cow’s milk allergy and avoidance of uncooked cow’s milk; peanut and egg allergy were defined as self-report alone. Differences in height-, weight-, and BMI-for-age percentiles, and nutrient intake (total calories, protein, fat, vitamin D, and calcium calculated from 24 hour recall) by food allergy status were analyzed by linear and logistic regression.

**RESULTS:** Milk allergy was a risk factor for lower weight-for-age (mean percentile difference 22, 95%CI:13-31%, p<0.001), height-for-age (mean percentile difference 22, 95%CI:13-31%, p<0.001), and BMI-for-age (mean percentile difference 17, 95%CI:3-32%, p=0.02), as well as an increased risk of weight and BMI <85th percentile (OR 5.32, 95%CI: 1.9-14%, p=0.002 and OR 3.61 95%CI: 1.2-11, p=0.03, respectively). No significant differences in daily total calorie, protein, or fat intake were detected for children with reported milk allergy (p>0.12 for all) though they did have significantly decreased daily calcium (mean mg difference: 309, 95%CI:142-476, p=0.001) and Vitamin D intake (mean mcg difference: 3.1 mcg, 95%CI:2.5-3.7, p<0.001). Reported allergy to peanut or egg was not associated with significant differences in any growth parameter (p>0.12 for all).

**CONCLUSIONS:** Children with self-reported cow’s milk allergy are at significant risk for poor growth and decreased calcium and Vitamin D intake.

**809 Allergic Causes Of Death In The United States**

Dr. Susan J. Kim, MD1, Dr. Jordan C. Brooks, PhD, MPH2, 1Kaiser Permanente Southern California, Los Angeles, CA, 2Life Expectancy Project, San Francisco, CA.

**RATIONALE:** United States death certificates contain physician-recorded information on underlying causes of death using International Classification of Disease (ICD-10) codes. The objectives were to document the number of United States deaths in which allergic reaction played a causal role during the period 1999-2010, and to test whether there have been secular trends in the incidence of such deaths.

**METHODS:** The Center for Disease Control’s Multiple Cause of Death compressed mortality file was accessed online and queried for ICD-10 classifications relating to asthma, urticaria, angioedema, and anaphylaxis. Age-adjusted death rates and 95% confidence intervals were calculated using the 2000 U.S. census standard population for the periods 1999-2004 and 2005-2010.

**RESULTS:** There were 113,778 deaths in which asthma of any type was noted as a contributing cause. The age-adjusted death rate from asthma declined from 3.38 (95% CI 3.35-3.41) per 100,000 to 2.95 (95% CI 2.92-2.97) per 100,000 from the early (1999-2004) to late (2005-2010) periods. There were 908 total deaths in which angioedema played a contributory role. The age-adjusted death rate from angioedema significantly increased from 0.0157 (0.0136-0.0178) per 100,000 in the early period to 0.0289 (0.0262-0.0317) per 100,000 in the late period. There were no significant trends in deaths from urticaria or from anaphylaxis.

**CONCLUSIONS:** The age-adjusted death rate from asthma has experienced a modest but statistically significant decline in the past decade. Interestingly, there was a significant increase in the age-adjusted death rate due to angioedema.

**810 Death From Anaphylaxis Is a Reassuringly Unusual Outcome**

Dr. Larry Borish, MD, FAAAAI1, Dr. Theodore Danoff, MD, PhD2, Dr. Liyuan (Larry) Ma, PhD2, 1Asthma and Allergic Disease Center, Carter Center for Immunology Research, University of Virginia, Charlottesville, VA, 2Endo Pharmaceuticals Inc.

**RATIONALE:** Anaphylaxis is a serious, life-threatening allergic reaction; however, the actual risk of death is unclear. The current study estimated the fatality rate among hospitalizations or emergency department (ED) presentations for anaphylaxis and the mortality rate associated with anaphylaxis for the general population.

**METHODS:** This was a population-based epidemiologic study using 3 national databases: Nationwide Inpatient Sample (NIS, 1999-2009), Nationwide ED Sample (NEDS, 2006-2009), and Multiple Cause of Death Data (MCDD, 1999-2009). Sources for these databases are hospital, ED discharge records and death certificates, respectively.

**RESULTS:** Case fatality rates were between 0.25% and 0.33% among hospitalizations or ED presentations with anaphylaxis as the principal diagnosis. These rates represent between 63 and 99 deaths per year in the US, ~7% of which occurred in hospitalized patients. Population mortality rates ranged from 0.63 to 0.76 per million person-years based on death certificates (186 to 225 deaths per year). Despite an increased incidence of anaphylaxis, mortality rates have been stable in the last decade, as were age-adjusted mortality rates.

**CONCLUSIONS:** The overwhelming majority of hospitalizations or ED presentations for anaphylaxis do not result in death, with an average case fatality rate of 0.3%. Despite the increase of anaphylaxis incidence, it is reassuring that mortality rates associated with anaphylaxis have remained stable in the last decade and were well under 1 per million person-years. Although anaphylactic reactions are potentially life threatening, the probability of dying is very low for those cases that require ED or hospital attention, and is likely much lower when all anaphylactic reactions are considered.
811 Allergic Rhinitis, Asthma and Cardiovascular Disease

Dr. Angelina M. Crans Yoon, MD1, Dr. Anne M. Staveren, MD2, Dr. Michael S. Kaplan, MD, FAAAAI3, Dr. Javed Sheikh, MD, FAAAAI4, Dr. Bruce J. Goldberg, MD, PhD, FAAAAI5, 1Kaiser Permanente, Los Angeles, CA, 2Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA.

RATIONALE: Several studies have suggested an association between eosinophilia, positive skin tests, total IgE, daily pollen burden, asthma and cardiovascular disease. The relationship between cardiovascular disease and allergic rhinitis is largely unknown.

METHODS: We assembled a cohort of allergic rhinitis patients (N=109,229) and a cohort of asthma patients (N=92,775) matched 1:1 by age, sex, and ethnicity to reference cohorts and compared the incidence of cardiovascular and cerebrovascular events and all-cause mortality from 1/1/1995 to 12/31/2012 using the Kaiser Permanente Southern California regional database and ICD-9 codes. Hazard ratios (HR) were calculated using survival analysis with a fully adjusted COX proportional model.

RESULTS: Patients with allergic rhinitis had significantly lower risk for acute myocardial infarction (MI) (HR 0.75, 95% CI [0.71, 0.80]) and cerebrovascular disease (HR 0.81, 95% CI [0.77, 0.84]), and all-cause mortality (HR 0.51, 95% CI [0.49, 0.53]). However, their risk of all cardiovascular events was equivalent to the control cohort (HR 0.97, 95% CI [0.94, 1.00]). Patients with asthma had significantly higher risk of all cardiovascular disease (HR 1.36, 95% CI [1.32, 1.40]), however had no increased risk of cerebrovascular disease (HR 0.81, 95% CI [0.77, 0.84]) or all-cause mortality (HR 1.00, 95% CI [0.97, 1.03]).

CONCLUSIONS: Our study results supported other studies that patients with asthma have increased cardiovascular events. However patients with allergic rhinitis have decreased acute MI, cerebrovascular disease, and all-cause mortality. This suggests atopy may not be contributing to the increased cardiovascular events seen in patients with asthma.

812 Pre-Natal and Early Life Predictors Of Atopy In Canadian Children: Results Of The Family Study

Tahira Batool, MBBS, FRCPCC1, Michael M. Cyr, MD, FRCPCC, FAAAAI1, Ms. Karleen Schulze, MMath2, Sonia Anand, MD, FRCPCC, Koon Teo, MD, FRCPCC, Family Investigators2; 1Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, ON, Canada, 2Population Health Research Institute, Department of Medicine, McMaster University, ON, Canada.

RATIONALE: Multiple epidemiologic and immunologic studies have pointed to the roles of pre-natal and early life environmental exposures in the development of atopy and allergic disease.

METHODS: The Family Atherosclerosis Monitoring In Early Life (FAMILY) Study prospectively evaluated 21 pre-natal and 31 early life traits in 901 babies, 857 mothers and 530 fathers in a general population birth cohort. The influences of preexisting allergic disease in parents, maternal diet, antibiotics, tobacco, pet ownership and exposure to farm animals were evaluated through questionnaires during antenatal and one year follow up visits. The effects of breastfeeding, infant food intake, medications, smoking exposure, and vaccination on development of atopy and allergic disease in the infant were evaluated through questionnaires and allergy skin prick testing at one year of age.

RESULTS: Key allergic outcomes included: any food allergy (15%); cow’s milk allergy (2.1%); wheeze (12%); atopy (14%) and, eczema (9.2%). Paternal history of allergic disease; exposure to rodents and birds; use of antibiotics in first year of life; and, introduction of cow’s milk and soy before 6 months of age, were all significant predictors of atopy in infants. Factors associated with decrease in atopy included: exposure to pet dogs during pregnancy and the first year of life; breast feeding in the first 17 weeks of life; and, infant use of acetaminophen.

CONCLUSIONS: The FAMILY study demonstrated high rates of food allergy, atopy, wheeze and eczema. Several previously reported, as well as novel prenatal and postnatal exposures were associated with the development of atopy and allergic disease.
The Clinical Significance Of Specific Antibody Deficiency (SAD) Severity In Chronic Rhinosinusitis (CRS)

Dr. Anjeni Keswani, MD1, Neha Mehrotra, MD2, Dr. Angelica Manzur1, Dr. Raksh Chandra, MD3, Dr. David Conley, MD3, Dr. Bruce K. Tan, MD3, Dr. Leslie C. Grammer, MD, FAAAAI4, Dr. Robert C. Kern, MD5, Dr. Robert P. Schleimer, PhD, FAAAAI6, Dr. Anju T. Peters, MD, FAAAAI1, 1Department of Medicine, Division of Allergy-Immunology, Northwestern University Feinberg School of Medicine, Chicago, IL, 2University of Chicago, IL, 3Department of Medicine, Northwestern University Feinberg School of Medicine, 4Northwestern University, Chicago, IL, 5Department of Otalaryngology, Northwestern University Feinberg School of Medicine, 6Division of Allergy-Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL.

RATIONALE: Despite the increased identification of SAD in CRS patients, little is known about the relationship of SAD severity, as classified by recent guidelines, and severity of CRS.

METHODS: Electronic health record data from the Northwestern Medicine Enterprise Data Warehouse was utilized to identify patients with CRS evaluated for humoral immunodeficiency with quantitative immunoglobulins and Streptococcus pneumoniae antibody titers pre- and post-pneumococcal vaccine. Patients with SAD were classified by severity by the working group guidelines with severe defined as ≥2 protective post-vaccination titers and moderate defined as 3 to 6 protective post-vaccination titers of the 14 serotypes tested. Lund-MackKay scoring system was used to stage radiographic severity of CRS.

RESULTS: Of the 595 CRS patients evaluated for immunodeficiency, 24.2% (n=144) had SAD, 5.9% (n=35) had common variable immunodeficiency, 2.7% (n=16) had IgA deficiency and 67.2% (n=402) demonstrated normal immune function. Of the 144 SAD patients, 17.4% (n=25) were classified as severe and 82.9% (n=119) were considered moderate. 63.2% (n=91) of the SAD patients had asthma and 22.9% (n=33) had nasal polyps. Patients with severe SAD were less likely than patients with moderate SAD to have nasal polyps (p=0.05) and asthma (p=0.03). Patients with severe SAD had lower Lund-MacKay scores than moderate SAD patients, even when controlled for nasal polyps (p=0.03).

CONCLUSIONS: SAD severity as defined by recent guidelines does not reflect severity of CRS. Despite widespread prevalence of this disease originating in the mucosa of upper airways, currently afflicting close to 10% of the US population. Despite widespread prevalence of this disease and an ever-growing volume of gene expression data, there is a surprising lack of consensus across studies on which genes could serve as biomarkers of the disease or give further insights into disease pathology.

METHODS: We collated and analyzed raw microarray data from three independent sources and conducted a secondary bioinformatics analysis to identify genes exhibiting expression behavior in CRS. Multivariate statistics and pathway analysis were used to model biological processes consistent with altered gene expression and polyp tissue formation in patients with CRS. We further confirmed gene expression levels of seven newly identified biomarkers by qPCR of mucosal samples from an independent cohort of CRS patients at Northwestern.

RESULTS: Among 66 consensus genes with biomarker potential, POSTN and chemokines CCL13 and CCL18 showed the highest upregulation in pre-polypous and polyp tissue from CRS patients relative to controls. Numerous genes belonging to families of molecules involved in innate defense and basal barrier maintenance were significantly downregulated. Pathway analysis of common CRS gene expression profiles emphasized changes in epithelial junctions and alterations in WNT, growth factor and nuclear hormonal signaling. All seven genes tested by qPCR confirmed the consensus array findings.

CONCLUSIONS: Results of our analysis suggest that genes with consistent expression patterns across three microarray studies are indicative of epithelial barrier remodeling associated with deficiency in mucosal defense and polyp tissue formation in patients with chronic rhinosinusitis.

Meta-Analysis Of Gene Expression Microarrays Reveals Novel Biomarkers Consistent With Altered Functionality Of Mucosal Barrier In Patients With Chronic Rhinosinusitis

Dr. Sergejs Berdnikovs, PhD1, Dr. Atsushi Kato, PhD2, Mr. James Norton, MS3, Ms. Lydia Suh, BSc4, Dr. Robert C. Kern, MD2, Dr. David Conley, MD3, Dr. Raksh Chandra, MD4, Dr. Anju T. Peters, MD, FAAAAI5, Dr. Leslie C. Grammer, MD, FAAAAI6, Ms. Kathleen E. Harris, BSc2, Dr. Michael Platt, MD3, Dr. Ralph Metson, MD6, Dr. Robert P. Schleimer, PhD, FAAAAI2, 1Division of Allergy-Immunology, Northwestern University Feinberg School of Medicine, Chicago, IL, 2Department of Medicine, Division of Allergy-Immunology, Northwestern University Feinberg School of Medicine, Chicago, IL, 3Department of Otalaryngology, Northwestern University Feinberg School of Medicine, Chicago, IL, 4Northwestern University, Chicago, IL, 5Department of Allergy-Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL.

RATIONALE: Chronic rhinosinusitis (CRS) is an inflammatory disease originating in the mucosa of upper airways, currently afflicting close to 10% of the US population. Despite widespread prevalence of this disease and an ever-growing volume of gene expression data, there is a surprising lack of consensus across studies on which genes could serve as biomarkers of the disease or give further insights into disease pathology.

METHODS: We collated and analyzed raw microarray data from three independent sources and conducted a secondary bioinformatics analysis to identify genes exhibiting expression behavior in CRS. Multivariate statistics and pathway analysis were used to model biological processes consistent with altered gene expression and polyp tissue formation in patients with CRS. We further confirmed gene expression levels of seven newly identified biomarkers by qPCR of mucosal samples from an independent cohort of CRS patients at Northwestern.

RESULTS: Among 66 consensus genes with biomarker potential, POSTN and chemokines CCL13 and CCL18 showed the highest upregulation in pre-polypous and polyp tissue from CRS patients relative to controls. Numerous genes belonging to families of molecules involved in innate defense and basal barrier maintenance were significantly downregulated. Pathway analysis of common CRS gene expression profiles emphasized changes in epithelial junctions and alterations in WNT, growth factor and nuclear hormonal signaling. All seven genes tested by qPCR confirmed the consensus array findings.

CONCLUSIONS: Results of our analysis suggest that genes with consistent expression patterns across three microarray studies are indicative of epithelial barrier remodeling associated with deficiency in mucosal defense and polyp tissue formation in patients with chronic rhinosinusitis.
**Oncostatin M Is Elevated In Chronic Rhinosinusitis and Decreases Barrier Function In Human Airway Epithelium**

Ms. Kathryn L. Pothevën1,2, Mr. James Norton, MS, Dr. Christopher Ocampo, MD, PhD3, Ms. Lydia Suh, BS3, Mr. Roderick Carter, BS2, Dr. Kathryn E. Hulse, PhD1, Dr. Sudarshan Seshadri, PhD2, Dr. Brian K. Tan, MD2, Dr. Rakesh Chandra, MD3, Dr. Anju T. Peters, MD, FAAAAI3, Ms. Kathleen E. Harris, BS2, Dr. David Conley, MD4, Dr. Leslie C. Grammer, MD, FAAAAI5, Dr. Robert C. Kern, MD5, Dr. Robert P. Schleimer, PhD, FAAAAI5, 1Driskill Graduate Program, Northwestern University, Chicago, Illinois, 2Department of Medicine, Division of Allergy-Immunology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, 3Northwestern University, Chicago, Illinois, 4Department of Otolaryngology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, 5Division of Allergy-Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

**RATIONALE:** Dysfunctional sinonasal epithelial barrier is thought to play a role in chronic rhinosinusitis (CRS). Activators of STAT3 such as Oncostatin M (OSM) are known to modulate epithelial function. We tested the hypothesis that OSM may play a role in epithelial dysfunction in CRS.

**METHODS:** RNA and protein were isolated from uncinate tissue (UT) and nasal polyps (NP) from controls and CRS patients. Normal human bronchial epithelial (NHBE) cells and nasal epithelial cells (NEC) were grown at air liquid interface (ALI) conditions until fully differentiated and either left unstimulated, or stimulated with OSM. Barrier function was assessed using transepithelial electrical resistance (TEER), dextran flux, and tight junction staining.

**RESULTS:** Analysis of CRS samples showed increased levels of OSM mRNA (28.3 fold, p < 0.01, n = 12) and protein (4.4 fold, p < 0.05, n = 12-19) in NP compared to control UT by RT-PCR and luminex assay. OSM stimulation reduced barrier function measured by transepithelial electrical resistance (TEER) in NHBE cells (63% reduction, p < 0.0001, n = 11) and NEC cultures (43% reduction, p < 0.0001, n = 7), and increased dextran flux in NHBE cells (2.45 fold increase, p < 0.05, n = 5). OSM did not kill epithelial cells and permeability increases induced by OSM were reversible. Staining for junction proteins, occludin and E-cadherin, showed that junctional staining was disrupted in OSM stimulated NHBE and NEC, while the junctions remained intact in unstimulated cells (n = 5).

**CONCLUSIONS:** OSM profoundly increased barrier permeability, and elevated levels of OSM found in nasal tissue from patients with CRS may play a role in the known loss of barrier function in this important disease.

**Immunologic Changes During Chronic Rhinosinusitis Exacerbations Compared To Controls**

Dr. Shefali Samant, MD1, Dr. Matthew A. Rank, MD, FAAAAI2, Dr. John B. Hagan, MD, FAAAAI2, Dr. Erin O’Brien1, Dr. Devyani Lai1, Hirohito Kitai, MD1, 1Mayo Clinic, Rochester, MN, 2Mayo Clinic, Scottsdale, AZ, 3Mayo Clinic, Phoenix, AZ.

**RATIONALE:** The immunologic pattern of airway inflammation during exacerbations of chronic rhinosinusitis (CRS) is not well understood.

**METHODS:** We prospectively collected nasal secretions and washes from subjects with CRS with nasal polyps or control subjects with no history of CRS at baseline and during periods of worsening upper respiratory symptoms (“exacerbation”). Specimens were analyzed for the levels of IL-5, IL-6 and major basic protein (MBP). We compared the immunological parameters between subjects with CRS and controls using the rank sum test. The study was approved by the IRB.

**RESULTS:** Ten control subjects and 9 CRS subjects had an exacerbation during the study period (among 22 control and 23 CRS enrolled subjects). Median (interquartile) concentration of IL-6 (pg/ml) in nasal washes at baseline were 14.3 (7.0-36.4) for controls versus 99.3 (40-248) for CRS subjects (p = 0.007), for IL-5 (pg/ml) in nasal washes were 7.9 (3.0-32.7) versus 17.5 (8.3-43.8), (p = 0.14), and for MBP (ng/ml) in nasal secretions were 3.4 (3.4-6.3) versus 51.5 (3.4-237), (p = 0.06). When comparing control subjects to CRS subjects at the exacerbation visit, median (interquartile) concentrations were significantly higher during exacerbation for all 3 of the selected measures: IL-6 17.5 (7.6-32.3) versus 160 (27.3-1,678), p = 0.02; IL-5 8.1 (5.2-20.9) versus 38.3 (8.5-91.4), p = 0.03; and MBP 3.4 (3.4-7.0) versus 234 (21.1-706), p = 0.02.

**CONCLUSIONS:** Nasal levels of IL-6 are elevated in CRS both at baseline and during exacerbation while IL-5 and MBP were increased during exacerbation compared to controls. Enhanced inflammatory responses during disease exacerbation as compared to normal subjects may explain the pathophysiology of CRS.
**820 Asthma Susceptibility Due To Environmental Programming Of Innate Immunity In Utero**
Sarah Manners, BS1, Rafeul Alam, MD, PhD, FAAAAI1, David A. Schwartz, MD2, Magdalena M. Gorska, MD, PhD3, 1National Jewish Health, Denver, CO; 2University of Colorado Denver School of Medicine, Aurora, CO.

**RATIONALE:** Most asthma begins in first years of life. This early onset cannot be merely attributed to genetic defects as asthma prevalence is increasing. Instead, epidemiological studies suggest the role of prenatal and early childhood environmental exposures, including exposure to diesel exhaust. Despite compelling epidemiological evidence, limited progress has been made to understand mechanisms. The key obstacle is paucity of animal models. Animal models are essential as intentional prenatal exposures of humans are unethical. The goal of this study was to establish a mouse model of asthma susceptibility through prenatal diesel exhaust exposure.

**METHODS:** Pregnant C57BL/6 females repeatedly received intranasal applications of diesel exhaust particles (DEP) or phosphate-buffered saline (PBS). Offspring underwent suboptimal immunization and challenge with ovalbumin (OVA) or received PBS. Pups were examined for features of asthma and transcription from DEP-sensitive loci.

**RESULTS:** Maternal DEP exposure made offspring hypersensitive to OVA. These pups demonstrated airway inflammation and hyperresponsiveness, elevated serum OVA-specific IgE and increased pulmonary and systemic Th2/Th17-type cytokines. These cytokines were primarily produced by natural killer (NK) cells. Antibody-mediated depletion of NK cells prevented airway inflammation. Asthma susceptibility was associated with augmented levels of the aryl hydrocarbon receptor (AhR) signature transcripts and transcripts characteristic of the oxidative stress response. Features of asthma were either marginal or absent in OVA-treated pups of transcripts and transcripts characteristic of the oxidative stress response.

**CONCLUSIONS:** Features of asthma were either marginal or absent in OVA-treated pups of transcripts and transcripts characteristic of the oxidative stress response. Reduced levels of the aryl hydrocarbon receptor (AhR) signature were observed in NK cells. Antibody-mediated depletion of NK cells prevented airway inflammation. Asthma susceptibility was associated with augmented levels of the aryl hydrocarbon receptor (AhR) signature transcripts and transcripts characteristic of the oxidative stress response. Features of asthma were either marginal or absent in OVA-treated pups of transcripts and transcripts characteristic of the oxidative stress response.

**822 Der p 3 Allergen Activated Ano-1 Channel On Afferent Airway Nerves Regulates Th2 Cell Responses**
Mr. Mayur Patil, MS1, Dr. Edward G. Brooks, MD2, Dr. Michael Henry, DDS, PhD3, Dr. Armen Akopian, PhD3, 1UTHSCSA, san antonio, TX, 2Univ. Texas Health Science Center San Antonio, San Antonio, TX, 3UTHSCSA, San Antonio, TX.

**RATIONALE:** Allergic airway nerves could contribute to the initiation, development and maintenance of airway inflammation, a characteristic of many pulmonary diseases. This “axon reflex” theory implies that allergic airway nerves recognize environmental cues, including allergens, and trigger maladaptive transformation of the respiratory immune system. The aims of this study were to identify channel(s) activated by Der p 3 allergen, and examine its role in Der p 3 and HDM-induced asthma.

**METHODS:** We used pharmacological approach coupled with electrophysiology and Ca²⁺-imaging to identify the channels mediating Der p 3 responses in airway neurons of nodose/jugular ganglia. Channel-specific antagonists were employed to evaluate the channels role in development of Der p 3 and HDM-induced asthma in mouse models. Th2 responses were evaluated by total and differential immune cell counts from BALF, measuring cytokine release in BALF and examining lung pathology. Data were analyzed using one-way or two-way ANOVA.

**RESULTS:** We demonstrate that Ano-1, a Ca²⁺-dependent CI-channel, mediates Der p 3, but not HDM responses in airway neurons. Ano-1 also controls allergen-evoked neuropoetide release in bronchi. Administration of Ano-1 antagonists during the sensitization and challenge steps by Der p 3 resulted in a significant reduction in eosinophilia and certain cytokines. Ano-1 did not alter the HDM asthma model phenotypes.

**CONCLUSIONS:** Ano-1 mediates Der p 3 responses in airway nerves and contributes to development of Th2 response by Der p 3, but not HDM in mouse asthma models. Our observation provides novel therapeutic opportunities for the treatment of asthma induced by certain allergens.

**821 Rhinovirus Challenge Augments Allergen Responsiveness In Basophils Of Atopic Asthmatics**
Rachana Agrawal, PhD, Thomas A. E. Platts-Mills, MD, PhD, FAAAAI, Peter W. Heymann, MD, Judith A. Woodfolk, MBChB, PhD, FAAAAI; University of Virginia, Charlottesville, VA.

**RATIONALE:** Rhinovirus infections result in asthma exacerbations in atopic asthmatics; however, the mechanisms for this remain unclear. Binding of allergen to IgE receptor on the surface of basophils and dendritic cells (DCs) plays a pivotal role in driving Th2 responses in atopic asthma. We sought to test how in vivo rhinovirus exposure impacts the IgE pathway.

**METHODS:** PBMCs from atopic asthmatics and non-atopic controls were cultured for 24 hours with allergen, and markers downstream of IgE receptor (Syk and TSLP receptor) were then analyzed in DCs and basophils by flow cytometry. A subset of asthmatics were challenged intranasally with human rhinovirus 16 and cell phenotypes analyzed in PBMC cultures established immediately before challenge, and at days 4 and 21 post-challenge.

**RESULTS:** Basophils and DCs from atopic asthmatics (geometric mean total IgE = 553 IU/ml [361-848 IU/ml]) showed a propensity to markedly upregulate TSLP receptor on their surface in response to IgE receptor ligation. In rhinovirus infected asthmatics, this effect was augmented in basophils, but not DCs, and was only observed 21 days post-challenge. Fluxes in intracellular Syk levels were observed 4 days post-infection in both basophils and DCs, and levels were restored at day 21. No changes in surface levels of IgE receptor or serum levels of total IgE or allergen-specific IgE antibodies occurred.

**CONCLUSIONS:** Rhinovirus infection influences intracellular Syk levels and promotes the IgE/TSLP receptor axis in basophils. These findings provide new insight into how rhinovirus and IgE might interact during the acute and chronic phase of rhinovirus infection in atopic asthmatics.

**823 Increased Serum Soluble ST2 In Asthmatic Children And Recurrent Early Wheezers**
Prof. Hai Lee Chung, MD, PhD, Dr. Eun Joo Lee; Catholic University of Taegu, Taegu, South Korea.

**RATIONALE:** Soluble ST2 (sST2) has been reported to regulate Th2 response. In this study, serum levels of sST2, Th1, and Th2 cytokines were measured in recurrent early wheezers and asthmatic children. We aimed to investigate if there is any difference or similarities in immune responses between those two patient groups.

**METHODS:** Fifty-nine patients admitted with exacerbation of wheezing or asthma were enrolled. Two patient groups were defined: children with atopic asthma (≥2 yrs, N = 21) and recurrent early wheezers (≤2 yrs, N = 38). Recurrent early wheezers were divided based on their atopic status: 19 were atopic and 19 were non-atopic. sST2, IL-33, IL-5, and IFN-γ were measured in serum samples from two patient groups. sST2 and cytokine levels in both patient groups were compared with their age-matched controls. Their relationships with blood eosinophil, serum IgE levels, and severity of symptom were also evaluated.

**RESULTS:** sST2 and IL-5 were significantly increased both in asthmatic children (P = 0.02, P = 0.004) and recurrent early wheezers (P = 0.01, P = 0.001) compared to their age-matched controls. IL-5 was significantly higher in atopic wheezers compared with non-atopic wheezers (P = 0.04). Severity score showed a positive correlation with sST2 and IFN-γ in asthmatic children, but only with IFN-γ in early wheezers. There was an inverse correlation between sST2 and blood eosinophil counts both in asthmatic children and atopic recurrent wheezers.

**CONCLUSIONS:** Our study suggests that sST2 might regulate allergic inflammation by suppressing eosinophilia and play an important role in pathophysiology of acute exacerbation of wheezing or asthma both in asthmatic children and early wheezers.