MONDAY

653 Synergistic suppression of T cell-induced eosinophilia by glucocorticoid and CTLA4-Ig

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RATIONALE: To control therapy-resistant eosinophilia, synergistic effects of CTLA4-Ig and glucocorticoid was investigated on T cell-induced asthma model.

METHODS: Ovalbumin (OVA) specific murine helper T cell (Th) clones were established from splenocytes of DO11.10 transgenic mice expressing T cell receptor specific for OVA/H-2d. To analyze steroid responsiveness in vitro, Th clones were cultured with antigen presenting cells and OVA in the presence of various concentration of dexamethasone (DEX). Proliferative responses were measured by incorporation of either 3H-thymidine or BrdU. For in vivo analysis, unprimed Balb/c mice were transferred with Th clones, challenged with OVA, and administered with DEX subcutaneously. CTLA4-Ig was administered either intravenously or intranasally. Bronchoalveolar lavage fluid (BALF) was obtained 48 hours after the challenge, and the number of infiltrating cells was differentially counted.

RESULTS: Steroid-sensitive (SS) and -resistant (SR) clones were selected based on the effect of DEX on the proliferative responses of antigen-stimulated Th clones. Airway infiltration of eosinophils of mice transferred with SS clones were effectively inhibited by the administration of DEX. In contrast, those of mice transferred with SR clones were not significantly inhibited by DEX. Addition of CTLA4-Ig into the culture significantly suppressed the proliferation of DEX-treated SR clones in vitro. Administration of CTLA4-Ig significantly suppressed eosinophil infiltration of SR asthma model transferred with SR clones in vivo. CTLA4-Ig and DEX synergistically suppressed in vitro proliferation of SS clones and in vivo BALF eosinophilia of mice transferred with SS clones.

CONCLUSIONS: Blocking costimulatory signal mediated through CD28 and/or CD80/CD86 is a promising target to treat therapy-resistant eosinophilia.

654 Evaluation of Cough Triggers Among Responders and Non-Responders of Treatment with MK-7264, a P2X3 Receptor Antagonist

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RATIONALE: To control therapy-resistant cough, synergistic effects of MK-7264 treatment response.

METHODS: We performed house dust mite (HDM) stimulation in BEAS-2B and U937 cell line with and without dexamethasone or against CD93 siRNA treatment. We investigated CD93 expression and level in HDM-induced asthma mouse model. In addition, we conducted post-hoc analysis for the predictive power of CD93 for asthma using 96 human subjects who were previously studied.

RESULTS: BEAS-2B cell stimulated by HDM extract (100 mg) for one hour showed increased mRNA expression of TSLP, IL-33, and CD93. CD93 level in culture supernatants steadily increased for 24 hours after HDM stimulation. Dexamethasone and siRNA (targeting CD93) treatment significantly suppressed it. The siRNA treatment led to increase of IL-6 and TSLP level in culture supernatants, whereas it did not affect IL-33 level. In asthma mouse model, CD93 level decreased in bronchial epithelial cell and lung homogenates; whereas it increased in serum. In human, serum CD93 level in asthmatic patients was significantly higher than that in healthy control. When adjusted with age and sex, higher level of serum CD93 predicts asthma diagnosis with moderate sensitivity (71.4%) and specificity (82.4%) (AUC = 0.787, P < 0.001).

CONCLUSIONS: The level of CD93 significantly increased after HDM stimulation in vitro and in vivo. We demonstrated potential role of sCD93 as a novel biomarker in allergic asthma.

655 Potential Role of Soluble CD93 in Allergic Asthma

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RATIONALE: CD93 has been studied as a novel biomarker for various inflammatory and immune associated diseases, even in asthma recently. We aimed to evaluate the potential role of soluble form of CD93 (sCD93) for allergic asthma.

METHODS: We performed in vitro stimulation with Potent Cough Triggers Among Responders and Non-Responders of Treatment with MK-7264

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CONCLUSIONS: The level of sCD93 significantly increased after HDM stimulation in vitro and in vivo. We demonstrated potential role of sCD93 as a novel biomarker in allergic asthma.

Cough Frequency [ACF] > 30% at Week 12) according to the ‘Yes’ or ‘No’ cough trigger categories.

RESULTS: Of 253 randomized patients, 252 reported triggers. The most common questionnaire items leading to a ‘Yes’ as cough triggers were ‘My cough is unpredictable’ (79%), ‘A tickle in my throat’ (73%), and ‘An irritation in my throat’ (73%). ‘Poor Air Quality’ (50%) and ‘A change in air temperature’ (43%) both non-responders and responders reported a high/similar rate (>80%) of ‘Yes’ to cough triggers of ‘Unpredictable’, ‘Tickle’, and ‘Throat Irritation’; a slightly higher rate of non-responders vs. responders reported ‘Yes’ to ‘Poor Air Quality’ (88% vs. 65%) and ‘Temperature Change’ (76% vs. 70%).

CONCLUSIONS: Identification of specific triggers appears not to be associated with MK-7264 treatment response.
**656** Bronchial hyperresponsiveness observed in the children with post-infectious bronchiolitis obliterans: a long-term follow-up study

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**RATIONALE:** Post-infectious bronchiolitis obliterans (PIBO) is an irreversible form of chronic obstructive lung disease secondary to severe lower respiratory infection (LRI). The children who had PIBO during infancy usually show recurrent wheezing and frequent exacerbations due to respiratory infection. We followed them and examined their clinical characteristics, airway hyperresponsiveness, and lung function parameters.

**METHODS:** Forty-one patients diagnosed with PIBO before 3 years of age were enrolled. Diagnosis of PIBO was made according to the previously described criteria: 1) history of acute LRI in previously healthy children 2) unresolved respiratory symptoms associated with airway obstruction (cough, shortness of breath on exertion and/or abnormal breath sounds) that last for more than 6 weeks after the initial episode despite treatment 3) mosaic perfusion with air trapping, bronchiectasis, or atelectasis on pulmonary HRCT. Spirometry and methacholine challenge test were performed in these children at 6 years of age and lung function parameters were compared with age-matched control values using Z score.

**RESULTS:** Mean onset age of PIBO was 21.8 months. Mean follow-up period was 61.1 months. PIBO patients showed significantly lower FEV1 and FEF25-75% Z scores compared with age-matched control values. Bronchial hyperresponsiveness was observed in more than 40% of PIBO patients and it was not related with the atopic status of the patients.

**CONCLUSIONS:** In our study, the children who had PIBO during infancy had reduced lung function parameters and many of them showed bronchial hyperresponsiveness. Our study suggests that PIBO during early infancy might cause persistent lung function impairment.

**657** Bronchoalveolar Lavage Findings In Patients With Asthma, Wheezing Or Chronic Pneumopathy At A Pediatric Referral Center In Colombia

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**RATIONALE:** Chronic lower airway respiratory conditions in children are a diagnostic challenge as common conditions like asthma, as well as other respiratory, anatomical, genetic, infectious, immunological and systemic diseases may have a similar presentation. Bronchoscopy with bronchoalveolar lavage (FBC+BAL) is a diagnostic aid, especially in those patients with poor response to treatment. Accordingly, in our study, we used FBC+BAL to characterize underlying lung abnormalities in children with lower airway symptoms unresponsive to conventional treatments.

**METHODS:** We conducted a retrospective case review of 45 children who underwent FBC+BAL due to unresponsive lower respiratory airway symptoms during 2017 in a tertiary pediatric center in Colombia.

**RESULTS:** Patients were aged 4-179 months (median age 36.5 months) and there was no sex predominance (24 males). Initial diagnosis included asthma (46.7%), recurrent wheezing (33.3%) and chronic cough (17.8%). Common imaging findings prior to FBC+BAL included consolidations (44.2%), atelectasis (42%), mosaic attenuation (21%). Bronchoscopy findings included: airway anatomical abnormalities (n = 3), tuberculosis (n = 2), BAL lipophagous index >86 suggesting chronic aspiration (n = 14), positive BAL culture for common bacteria (n = 9) and atypical microorganisms (Cytomegalovirus = 11, candida dublinensis = 1) in 12 patients.

**CONCLUSIONS:** Pulmonary infections by mycobacteria and atypical microorganisms, anatomical abnormalities and chronic aspiration underlay wheezing and lower airway respiratory symptoms in 68% of patients in our study. Bronchoscopy proved definitive for the appropriate diagnosis and treatment of these conditions. Early recognition of cases in need for bronchoscopic evaluation of the airway is required for all physicians treating children with lower airway respiratory symptoms.

**658** Alda-1 Attenuates Hyperoxia-Induced Acute Lung Injury in Mice

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**RATIONALE:** Acute lung injury (ALI) is a critical lung disorder where the inefficient oxygen uptake causes acute hypoxemia and Acute Respiratory Distress Syndrome (ARDS). There are nearly 200,000 annual cases of ALI in the United States alone, and the incidence rate is increasing. At the molecular level, hyperoxic exposure causes an increase in reactive oxygen species, leading to an accumulation of 4-Hydroxy-2-nonenal (4HNE), a lipid peroxidation product causes protein adducts and inhibits the activity of the mitochondrial enzyme Aldh2 (Aldehyde dehydrogenase), which is involved in metabolism of alcohol. Currently, it is well-known that the use of compound Alda-1 enhances Aldh2 activity. Therefore, use of Alda-1 may reduce the effect of acute lung injury.

**METHODS:** DMSO or Alda-1 (20 mM), then they were exposed to 100% oxygen 48 hours. The lung samples, as well as Bronchial Alveolar Lavage Fluid, were collected for the evaluation of infiltration of cytokines, inflammation, autophagy, and apoptosis by Diff Kwik staining, H&E staining, and western blot.

**RESULTS:** The Mice treated with DMSO in hyperoxia showed more cytokine and neutrophil infiltration and elevated inflammation than mice treated with Alda-1 in hyperoxia. The western blot analysis of Alda-1 treated mice showed reduced cytochrome C release, reduced LC3B, and reduced NF-kB, while also showing a decrease in oxidative stress, inflammation and autophagy.

**CONCLUSIONS:** The findings imply that Alda-1, an Aldh2 activator is a potential therapeutic drug for the treatment of acute lung injury.
659 Characterization of cell proliferation in idiopathic pulmonary fibrosis

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RATIONALE: Dysregulated cell proliferation in the lung is one of the key hallmarks in idiopathic pulmonary fibrosis (IPF). Proliferation of type II alveolar epithelial cells (AECs) and fibroblasts is a particularly important event in IPF development. However, it is not understood how such proliferation leads to an advanced stage of fibrosis. Therefore, it is very important to characterize the proliferation of type II AECs in IPF lungs with different histological appearances.

METHODS: Lung samples were removed from the whole lung explants of patients with IPF and patients with pulmonary arterial hypertension (PAH, control subjects) undergoing lung transplantation at Tampa General Hospital (IRB protocol Pro00032158). Paraffin-embedded lung sections were immunohistochemically labeled for Ki67 (proliferation marker) and pro-SPC (a lineage marker for type II AEC).

RESULTS: In normal looking alveoli of PAH and IPF lungs, Ki67 signals were sparsely colocalized with pro-SPC. In mildly affected alveoli with thickened interstitium in IPF lungs, Ki67 signals are noted with higher density than normal alveoli of PAH and IPF. Intriguingly, most of them are either weakly positive or negative for pro-SPC. In severely fibrotic regions in IPF lungs, most of the Ki67 positive cells are negative for pro-SPC.

CONCLUSIONS: The results indicate that type II AEC proliferation is a key event in IPF. The results also suggest that type II AEC proliferation gradually shifts to proliferation of different cell types as the lung becomes more fibrotic. These cells are presumably dedifferentiated type II AECs that have lost pro-SPC expression or other progenitor cell types.

660 Enumeration of IL-17A/F Producing Innate Lymphoid Cells in Subjects with COPD

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RATIONALE: Chronic obstructive pulmonary disease (COPD) is characterized by inflammation and progressive airway obstruction caused by smoking and/or air pollution. Interleukin (IL)-17 mediated neutrophilia is associated with COPD exacerbations. Type 3 innate lymphoid cell (ILC3) are functionally similar cells to Th17 lymphocytes, and increased ILC3s have been detected in the bronchial mucosa of COPD subjects. More recent studies shown that type 2 ILCs (ILC2) from mice express IL-17 as well. This study investigated the expression of IL-17 by CD4+ T cells, ILC2 and ILC3 in COPD subjects.

METHODS: We included 11 mild to moderate COPD subjects (FEV1/FVC<70%, predicted FEV1<50% and smoking history>10 pack years) who were stable 4 weeks prior to the study and were not using inhaled or oral corticosteroid therapy at time of sampling. Blood and sputum extracted cells were subject to immunofluorescence staining for flow cytometric acquisition and analyses. All data were analyzed using non-parametric methods.

RESULTS: Absolute numbers of IL-17A/F+ CD4+ T cells (Lin-CD45+CD4+) in blood and sputum were significantly greater than ILC2s (Lin-CD45+CD127+CRTH2+) and ILC3s (Lin-CD45+CD127+CRTH2+CD117+). However, there was a significantly higher proportion of IL-17A/F+ ILC3s compared to IL-17A/F+ CD4+ T cells and IL-17A/F+
662 Protective Role Of Catalase In RSV Bronchiolitis

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RATIONALE: Respiratory syncytial virus (RSV) is the primary cause of lower respiratory tract infections (LRTI) in infants. We have previously shown that RSV-mediated disease is characterized by enhanced reactive oxygen species (ROS) generation and decreased expression of antioxidant enzymes (AOE). Moreover, exogenous administration of antioxidant mimetics or catalase reduced inflammatory chemokines and improved disease in RSV-infected cells and mice, respectively. In this study, we determined if the severity of clinical disease in children with RSV LRTI correlated with catalase activity and/or increased pro-inflammatory chemokines in the airways.

METHODS: Hospitalized children <24 months with RSV LRTI were enrolled and samples of nasopharyngeal secretions (NPS) were collected for analysis of catalase activity by a bioassay, and catalase concentration by Bio-Plex 27-targets array. Clinical data was analyzed and disease severity scored based on oxygen requirements and need for ICU admission.

RESULTS: Of the enrolled patients, 23% had mild disease (<12 hours of oxygen support), 51% were moderate (>12 hours oxygen), and 26% were severe (i.e. ICU admission). Catalase activity in NPS correlated inversely with severity of RSV disease. In addition, IL-8 (p < 0.05), MIP-1α (p < 0.01), and MCP-1 (p < 0.01) were increased in patients with more severe disease.

CONCLUSIONS: Severe episodes of RSV LRTI were associated with lower catalase levels and increased levels of pro-inflammatory chemokines, suggesting a critical role of the oxidative balance in the pathogenesis of RSV infections.

664 PARKIN overexpression in hyperoxia-induced lung injury

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RATIONALE: PARKIN is a protein component of the multiprotein E3 ubiquitin ligase complex. Previous studies have identified PARKIN to play a crucial role in clearance of ROS and mitophagy. No studies have identified the function of PARKIN in lung tissue, or in response to hyperoxia-induced lung injury. PARKIN-associated mitophagy has been previously linked with ALDH2 activation in liver. We hypothesized that PARKIN is overexpressed during hyperoxia-induced lung injury in ALDH2 Knock-In mice.

METHODS: ALDH2 Knock-In mice and their littermates (C57BL/6 background, 7-9 wk of age) were exposed to room air or 100% O2 (hyperoxia) for 48 hours. Protein was extracted from lung tissue and fractionated. Whole cell and mitochondrial protein lysates were analyzed by Western blotting. Antibodies to PARKIN, PINK1, and β-actin were used.

RESULTS: Levels of PARKIN were overexpressed in ALDH2 Knock-In mouse lungs following exposure to hyperoxia for 48 hours.

CONCLUSIONS: Hyperoxia-induced lung injury in ALDH2 Knock-In mice is associated with overexpression of PARKIN in lung tissue. This may implicate PARKIN-associated mitophagy as a novel pathway in the pathogenesis hyperoxia-induced lung injury.

665 Decreased mononcytic TNF-α, IL-6 and IL-b after 72 hours of injury lead to positive outcome in severely injured trauma patients

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RATIONALE: Trauma is one of the leading causes of mortality worldwide with infections as important causes of death. Therefore, the present study was designed to monitor the peripheral blood mononcytic activity to produce cytokines (TNF-α, IL-6 & IL-1β) during the acute post-traumatic period and to correlate with clinical outcome of these patients.

METHODS: Trauma patients who presented to the hospital casualty department within 24 hours of injury with Injury Severity Score ranging from 25 to 45, further admitted to the surgical Intensive care unit were enrolled in this study. Surface staining and intracellular staining of the mononcytic-cytokines after 4 hours stimulation with LPS was done by flow cytometry.

RESULTS: A total of 28 severely injured trauma patients were included in the study. Of these, 4 (14%) had posttraumatic complications like Multi-Organ Dysfunction Syndrome, Ventilator Associated Pneumonia, Septicemia, and Acute Respiratory Distress Syndrome. There were 4 (14%) fatalities. Levels of mononcytic TNF-α, IL-1β, IL-6 were significantly decreased in the initial 72 hours of injury and increase later to similar levels as of the healthy controls. The levels of these cytokines were significantly low in fatal patients as compared to healthy controls.

CONCLUSIONS: Initial fall in the mononcytic TNF-α, IL-6 & IL-1β and revival after 72 hours post-injury correlate with a positive outcome, whereas a consistent depression of mononcytic activity to produce these cytokines indicate poor prognosis in severely injured trauma patients.
**CONCLUSIONS:** Chronic cough in the primary care setting is generally primarily caused by gastroesophageal reflux or rhinosinusitis. Primary care respondents indicated that their patients with chronic cough typically (n = 5,919) were aged 30-50 years, and 55% were aged >50 years. Respondents indicated that the majority of the cough had been present for 2-6 months (n = 18 respondents), 6-12 months (n = 10), or more than 1 year (n = 1) and the primary cause was gastroesophageal reflux (n = 23), rhinosinusitis (n = 21), asthma (n = 9), “other” (n = 5), COPD (n = 4), or idiopathic (n = 2). The majority of respondents indicated they referred their patients with chronic cough to pulmonologists (n = 33) and allergists (n = 26). Respondents indicated that their patients with chronic cough typically experienced decreased quality of life (n = 35), loss of sleep (n = 31), embarrassment (n = 27), absence from work/school (n = 14), and depression (n = 4).

**CONCLUSIONS:** Chronic cough in the primary care setting is generally primarily caused by gastroesophageal reflux or rhinosinusitis. Primary care providers typically refer patients with chronic cough to pulmonologists and allergists. Chronic cough negatively affects patients’ quality of life and sleep, and is a source of embarrassment.

**EVERY BREATH YOU TAKE – IMPROVING ASTHMA WELLNESS**

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**RATIONALE:** Good control of asthma reduces related deaths and costs. The CDC recommends pneumococcal vaccination for patients with asthma, aged 18-64 years. Guidelines recommend assessment and documentation of asthma severity at each clinic visit. Objectives were to determine whether specific interventions would improve rates of pneumococcal vaccination and asthma severity documentation in asthma patients.

**METHODS:** IRB exempt. Electronic records were used to identify patients above the age of 18 years with a diagnosis of asthma seen at the Family Health Center Clinic during a period designated as “2017”. Interventions implemented included individualized EMR alerts placed on patient charts; verbal reminders to residents during weekly pre-visit team huddles; pocket cards provided to residents; asthma severity forms and two educational sessions. An analysis of pneumococcal vaccination and asthma severity documentation was performed after the implementation of interventions during a period designated as “2018”.

**RESULTS:** 52 patients were identified in the 2017 period and data was compared to the 2018 period. Prior to the interventions, 24 patients had received the pneumococcal vaccination (46%). Analysis of data was performed using one-tailed non-parametric tests. Results revealed that after the intervention, 29 patients had received the pneumococcal vaccination (56%, p = 0.0032). Prior to the intervention, 23 patients had documentation of asthma severity (44%). After the intervention, 35 patients had documentation of asthma severity (67%, p < 0.0001).

**CONCLUSIONS:** Our results suggest that optimal resident education, EMR alerts and pre-visit team huddles were effective at improving the rates of pneumococcal vaccination.

**MONTELUKAST DOES NOT INCREASE THE RISK OF NEUROPSYCHIATRIC DISEASE IN CHILDREN WITH ASTHMA: A NATIONWIDE POPULATION-BASED COHORT STUDY**

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**RATIONALE:** Montelukast, a leukotriene receptor antagonist, is one of the most common medication used in childhood asthma. Since March 2008, there have been concerns about a possible risk of neuropsychiatric disease during Montelukast use. However, former conflicting evidence bothered both clinicians and parents of children with asthma. We thought to examine whether Montelukast intervention in asthmatic children is associated with an increased risk of neuropsychiatric disease.

**METHODS:** Children aged less than 18 years old with newly diagnosed as having asthma during 2004 to 2008 were retrieved from a nationwide population-based database. A Montelukast cohort (n = 14668) and a non-Montelukast cohort (n = 8489) were conducted and matched using propensity score.

We compared the incidence of hazard ratios of subsequent neuropsychiatric diseases. The maximal follow-up time was 9 years.

**RESULTS:** The incidence of overall neuropsychiatric (NP) disorder in Montelukast cohort was not significantly higher than that in non-Montelukast cohort (adjusted hazard ratio (aHR) = 0.91, 95% confidence interval = 0.81-1.01). Boys in Montelukast cohort had lower risk NP disease (aHR = 0.83, 95% CI = 0.69-0.97). Compared with non-Montelukast cohort, children took Montelukast for less than 101 days had lower risk for NP disease (aHR = 0.66, 95% CI = 0.40-0.96). In both Montelukast and non-Montelukast cohort, the risks for NP disease increased in those with not well-controlled asthma (aHR = 0.92, 95% CI = 12.79-74.76 and aHR = 0.92, 95% CI = 0.92-0.99, respectively).

**CONCLUSIONS:** Our population-based cohort study showed that the risk of neuropsychiatric disease in asthmatic children is not elevated by Montelukast usage whereas increased in those without adequate control.

**ASSOCIATION OF ASTHMA WITH OSTEOPENIA, OSTEOPOROSIS, OSTEOALACIA AND PATHOLOGICAL FRACTURES UNITED STATES ADULTS**

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**RATIONALE:** Previous studies examining the relationship between asthma, osteoporosis, and pathological fractures found conflicting results. We sought to determine whether asthma is associated with osteoporosis and fractures in US adults.

**METHODS:** We analyzed data for 198,102,435 children and adults, including 10,127,807 with asthma from the 2006–2012 National Emergency Department Sample, including a 20% cross-sectional sample of emergency care visits throughout the US.

**RESULTS:** In pooled analysis across all 7 years, patients with asthma had significantly higher odds of osteopenia (multivariable logistic regression; adjusted odds ratio [95% confidence intervals]: 1.454 [1.406-1.504]), osteoporosis (1.849 [1.817-1.881]), osteomalacia (1.997 [1.605-2.485]), ankylosing spondylitis (1.487 [1.377-1.606]), and pathological fractures (1.238 [1.204-1.273]). Similarly, asthma was associated with higher odds of osteoporosis (P < 0.0001 for all), osteopenia (P < 0.0001 for all), and ankylosing spondylitis (P < 0.02 for all) in all 7 years, and osteomalacia in 6 of 7 years (P < 0.02 for 2007-2012). There was significant sex- and age-related differences of the associations of asthma with these comorbidities.

**CONCLUSIONS:** Asthma was associated with osteopenia, osteoporosis, osteomalacia, ankylosing spondylitis and pathologic fractures.
670 Evaluation of an Indigenous Community Possibly Protected Against Sensitivity to Mites in the Andean Region

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RATIONALE: Mites species are present throughout the world, the sensitization to these oscillate according to the region. However, little has been clarified in some ethnic. Intraepidermal tests and specific immunoglobulins for mites are lower in indigenous people compared to other predominant ethnic groups in the region.

METHODS: An analytical study was carried out to compare ethnic groups in an Andean region of South America. The indigenous group selected with the Respondent-Driven Sampling technique (RDS) and the mestizos group was from a capital city, paired by sex and age group. Prick tests with extracts, with concentrations of 300 µg/mL for B. tropicalis, 300 µg/mL for D. pteronyssinus, and 400 µg/mL for D. farinae, as well as an allergen-specific immunoglobulin E (IgE) measurement, were tested on individuals with allergic disease history. We used correlational effect sizes for comparing two groups using the Point-Biserial correlation.

RESULTS: Diameters of the wheals showed large size effect, with lower diametral values in the indigenous group compared with the values of the mestizo group B. tropicalis (r = 0.50, 95% CI: -0.68 to -0.21), D. pteronyssinus (r = 0.54, 95% CI: -0.71 to -0.26) and D. farinae (r = 0.47, 95% CI: -0.66 to -0.17). The IgE reported medium effect sizes, with lower values in the indigenous ethnic group B. tropicalis (r = 0.29), D. pteronyssinus (r = 0.35) and D. farinae (r = 0.33, 95%).

CONCLUSIONS: The environmental aspects and social determinants could be modifiable factors for the reaction of the indigenous population against Blomia tropicalis, Dermatophagoides pteronyssinus and Dermatophagoides farinae mites.

671 Can Social Media Reliably Predict Trends in Pediatric Asthma-related Emergency Department Visits?

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RATIONALE: Prior research examining fluctuations in asthma-related ED visits has focused on factors such as food trends and environmental activity; however, less is known about the predictive potential of using social media data. Our objective was to examine the correlation of asthma-related search terms using Google Trends (GT) with pediatric asthma-related ED visits. We can provide asthma surveillance information quicker than traditional Center of Disease Control methods. EPA particulate data may also play a correlative role in the influx of ED visits.

METHODS: Using Pediatric Health Information System data from pediatric free-standing hospitals, weekly counts of asthma-related ED visits from 2010-2015 were compared to weekly GT SVI (search volume index). In addition, EPA data was generated from the most complete data and focused on 5 particulates, including Ozone, CO, NOx, SO2, and PM10 Speciation. Correlations with GT SVI, EPA, and ED visits were calculated using yearly aggregated data.

RESULTS: Data from 11 metropolitan areas were included. Comparisons between ED visit data and EPA data frequently showed positive correlation in 6 cities across years investigated.

CONCLUSIONS: There is evidence that the fluctuation of pediatric asthma-related ED visits may be related to social media data. GT SVI data may be a valuable new source for predicting influxes of asthma-related ED visits.

672 Knowledge Gaps On Asthma Diagnosis Among General Physicians And Specialists In Contrast With Evidence-Based Clinical Guideline Recommendations: Results From A National Survey

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RATIONALE: This study sought to identify how knowledge concerning some aspects of asthma diagnosis may vary according to the treating physician’s medical specialty.

METHODS: We conducted an online national survey among 860 Mexican board-certified practitioners who routinely evaluate patients with asthma to assess their knowledge about several aspects of asthma diagnosis. Their replies were contrasted with evidence-based recommendations of the Mexican Asthma Guidelines (GUMA).

RESULTS: 34 otolaryngologists, 62 general practitioners (GPs), 161 pulmonologists, 239 pediatricians and 364 allergists completed the survey. Although the overall application of diagnostic clinical criteria agreed with most GUMA recommendations in all groups (up to 85%), several specialties-related knowledge gaps were also documented. Up to 30% of non-pulmonologists didn’t recognize chest discomfort as a clue symptom of asthma, and all except pulmonologists incorrectly listed FEV1 as the best parameter to confirm expiratory flow obstruction. Almost 75% of all physicians were not aware of the morning-evening PEF measurement as an alternative tool to demonstrate variable airflow obstruction, and almost half erroneously believed wheeze-associated viral illnesses in non-atopic children predispose to asthma. The GUMA recommendation to restrict allergy testing and only perform when allergy is suspected was not shared by >50% of GPs, pediatricians and allergists, as they would perform these tests in all asthma cases.

CONCLUSIONS: There are considerable specialties-related variations in physicians’ knowledge about predisposing factors, phenotyping, diagnostic criteria and classification of asthma in contrast to GUMA recommendations. Recognition of such discrepancies could encourage specialty-specific learning tools and stimulate further activities of guidelines’ dissemination.
673 Increased Recruitment and Retention of Pediatric Research Participants after Implementation of Novel Recruitment Strategies in Inner City Asthma Consortium Site.

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RATIONALE: High risk population groups can be difficult to recruit for clinical research participation. We studied the impact of increasing recruitment efforts by leveraging electronic medical record (EMR) notifications, community outreach and communication with primary care providers in order to meet study recruitment goals for the NIAID-sponsored Inner City Asthma Consortium (ICAC).

METHODS: Recruitment tactics were implemented including EMR notifications of new emergency room visits of potentially eligible participants. The team also worked to expand community involvement through 2 health fairs with goals to educate, improve self-efficacy, and increase participation in research. Primary care practitioners (PCPs) were informed about research studies through document sent in the EMR and informal presentations. A follow-up survey assessed the value of this communication to PCPs.

RESULTS: ICAC staff received 442 EMR notifications from one hospital in 9 months. Of these, 171 were asthma related. Eighty-six lead to recruitment calls, which resulted in 33 participants enrolled. Eighty potential participants were contacted through community health fairs. Anonymous surveys were sent to 37 PCPs regarding research participants. One hundred percent of providers reported communication was valuable and reported this communication improved their willingness to recommend and refer patients for clinical research trials. Six months after implementation of these strategies, the Cincinnati Children’s site was 89% above the ICAC target enrollment goal.

CONCLUSIONS: A multifaceted approach led to increased research participation of a high risk population group. Further, bidirectional communication channels have been established with the community PCPs who largely manage the target population.

674 Clinicians perspective of the new pregnancy and lactation labeling final rule (PLL): results from a FDA/AAAAI survey

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RATIONALE: In 2015, the FDA removed the letter category system (A,B,C,D or X) from the product label of all prescription drugs. The letter category system first established in 1979 was regarded as overly simplistic and misinterpreted as a grading system. A new PLLR format was created to better aid in presenting the available safety data. In an attempt to assess awareness, understanding and value of the new PLLR, a survey formed in collaboration between the AAAAI and the FDA was distributed among the membership of the AAAAI.

METHODS: An online survey was sent to a random sample of the US membership of the AAAAI. The survey content consisted of questions addressing the following: demographics, awareness and use of the PLLR, understanding of the new PLLR format in example form, and the value of the new PLLR format.

RESULTS: Of 1500 members who received an email survey, 184 (12%) completed the survey. Less than half of responders were aware that the pregnancy letter categories were replaced with a narrative summary. Most of the responders did not feel the new PLLR format was clear or concise, and almost all responders continued to use the pregnancy letter category system (A,B,C,D or X) to make prescribing decisions.

CONCLUSIONS: Inadequate management of chronic medical conditions during pregnancy can have profound effects on maternal and fetal health. This survey shows that most clinicians find the new label does not meet their needs in obtaining critical information for patient care.

675 Screening With Serology Testing Children With Asthma Could Contribute To Substantial Cost Savings To US Payors: A Population-Based Simulation Study

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RATIONALE: 8.3% of American children was affected by asthma in 2016 [CDC]. Sensitization to mites can occur in 30.6% of asthmatic children, with a linear dose-response curve between sIgE and asthma morbidity [Wang-2016].

Exacerbation prevention strategies can include allergy testing and the usage of mite-impermeable encasings [Murray-2017]. Asthma exacerbations is one of the main causes of hospital-admissions, with 37.3% of asthmatic children admitted to hospital every year [Berry-2013] ($3,782/year/child [Barrett-2014]); dust mites can increase this risk [Wang-2009].

This study estimates the potential cost savings to US payors, should serology testing be performed in the total population of asthmatic children, and should interventions to reduce exposure to mites be in place for 5 years.

METHODS: In 2016, there were 6,132,000 asthmatic children [CDC-data] and 1,876,392 mite-sensitized-asthmatics. The model simulated an intervention where all asthmatic children were screened with serology ($154 for 25 tests [CMS-data]), encasings were assigned to mite-sensitized individuals (not included in the cost calculations), with a 27% reduction in hospitalizations after prevention [Murray-2017]. The output, from payors perspective, were exacerbation-related hospital-admission costs with and without intervention.

RESULTS: Without intervention, mite-related hospital-admission costs were $15,951,152,031 in 5 years. Screening with serology all prevalent and incident (almost 500,000 incident cases per year [Winer-2012]) asthmatic children once costed $1,270,390,384, leading to total savings to payors equal to $ 2,875,600,859 in 5 years.

CONCLUSIONS: The proposed simulated intervention, screening with serology testing all asthmatic children and assigning beddings to the mite-sensitized ones, could hypothetically lead to substantial cost savings to US payors due to reduced hospital-admissions.
All abstracts are strictly embargoed until the date of presentation at the 2019 Annual Meeting.

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676 Emergency Department Use for Non-emergent Asthma-related Symptoms

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RATIONALE: While many ED visits for asthma or wheezing are for true exacerbations, patients who do not seek emergency services often do, unnecessarily increasing asthma-related healthcare costs. We sought to identify patients utilizing the ED for asthma-related care when not necessary.

METHODS: This retrospective chart review during fiscal year 2016 looked at patients who were (a) triaged at level 4 or 5 (lowest level of acuity) and (b) had an established primary care provider (PCP) within one mile from the ED; those who only required a single MDI or nebulizer treatment qualified. Factors such as time of day, day of the week, age, whether treatments were done at home and what interventions were done in the ED were recorded. Children older than 5 are automatically triaged at level 3 or higher and therefore were not included.

RESULTS: Out of 59 chart reviews, 31 (53%) patients met all criteria. The average age was 2.4 years. 65% of visits were during normal business hours; 42% did not attempt any treatments at home within 4 hours of ED arrival; 42% received a single MDI or nebulizer treatment; 58% required no treatment. All patients had a diagnosis of asthma later in life.

CONCLUSIONS: This pilot study identified a group of patients who presented to the ED for mild respiratory symptoms during business hours of their easily accessible PCP. Further studies might identify factors associated with unnecessary ED usage and focus on cost-saving interventions to encourage and educate families on the appropriate location when seeking asthma care.

677 Does an Inpatient "High Risk Asthma Protocol" Impact Outpatient Follow-up?

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RATIONALE: Our children’s hospital created a "high-risk asthma protocol" (HRAP) to ensure that patients who meet criteria receive a cohesive package of evidence-based interventions. A goal of this effort was to bridge the gap from inpatient to outpatient care. The purpose of this investigation was to assess the impact of each HRAP intervention on outpatient follow-up.

METHODS: Records of asthma-related admissions since HRAP initiation were reviewed from 10/27/14 to 10/27/17. Enrollment criteria was defined as ≥4 acute care visits in the previous year or one PICU admission. HRAP included an inpatient asthma class, environmental phone consult, social work assessment, optional inpatient specialist consult and scheduling follow-up. Each intervention in the protocol was examined to assess its impact on the patient’s likelihood to attend the follow-up.

RESULTS: Of the 518 patients enrolled in HRAP, 414 (80%) were scheduled with follow-up; 261 (63%) attended within 90 days. Chi-square analysis of patients receiving the intervention (versus not) and impact of attending follow-up showed: inpatient asthma class (4%; P=0.61); environmental phone consult (1%; P=0.78); social work assessment (-3%; P=0.75); and optional inpatient specialist consult (-6%; P=0.16).

CONCLUSIONS: This study could not demonstrate statistical significance for any single intervention’s impact on attending follow-up. Further investigation is required to ascertain if a combination of interventions could change overall outcomes for this high risk population. The psychosocial and socioeconomic barriers of this population may be inherent to why this “high risk” cycle is so difficult to break.

678 Association of Prescription Opioid Use for Chronic Pain Syndromes with Asthma and Allergy

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RATIONALE: Opioids have, in addition to analgesic properties, immune altering effects including upregulation of Th2 responses. Whether this has clinical expression in altering asthma and allergic responses has not been determined. We hypothesize that in patients with chronic pain conditions, there is an increased prevalence of asthma and allergy when prescribed opioid medications.

METHODS: EMR review of opioid prescription for chronic pain conditions and the prevalence of allergic rhinitis and allergic conjunctivitis was conducted (n=3502). ICD coding from inpatient, emergency room and ambulatory surgery settings at Kings County Hospital in Brooklyn, NY from 2013-2017 was obtained for the following conditions: chronic pain syndrome, osteoarthritis, joint disorder, fibromyalgia, back pain, myalgia and myositis, asthma, allergic rhinitis and allergic conjunctivitis. We sought record of minimum one prescription for opioid medication.

RESULTS: Prevalence of asthma was 8.7% (178/2049) in patients without opioid prescription versus 15.1% (220/1453) in patients with opioid prescription (OR=1.92, 95% CI [1.56, 2.40], p<0.001). Prevalence of allergic rhinitis and/or allergic conjunctivitis was 5.1% (119/2049) in patients without opioid prescription versus 10.9% (158/1453) in patients with opioid prescription (OR=1.94, 95% CI [1.51, 2.51], P<0.001).

CONCLUSIONS: Among patients with chronic pain conditions, prescription opioid use was associated with asthma and allergy.
**AB224 Abstracts**

**679** Asthma as a comorbidity in adult patients receiving treatment in an emergency department, ambulatory surgery and inpatient for back pain in a large, inner city, municipal New York hospital.

Nneoma Obiejemb, MD1, Obinna Obiejenma, DrPH2, Sairaman Nagarajan, MD, MPH1, Roslani Naik, MD1, and Rauno Joks, MD3,1; 1Center for Allergy and Asthma Research at SUNY Downstate Medical Center, Brooklyn, NY, 2Morgan State University, Baltimore, MD, 3Kings County Hospital Center, Brooklyn, NY.

**RATIONALE:** As pain can exacerbate asthma, we hypothesize that people with back pain and asthma experience exacerbation of asthma during flare of back pain. Men and women equally suffer from back pain. Whether sex and age influence the co-occurrence of asthma and back pain has not been determined.

**METHODS:** A cross sectional data analysis was performed using secondary data of adults (n=20,588) treated at Kings County Hospital Center (inpatient, Emergency Department, Ambulatory Surgery) between Oct 2015 and March 2017 with ICD 10 code for back pain (M54.) and/or asthma (J45.). Logistic regression was used to determine the likelihood of presentation.

**RESULTS:** The mean age of the study population was 46 yrs ± 15 while the median age was 47 years. Females made up 12,189 (59%) of the study sample and males 8,399 (41%). The occurrence of asthma with back pain was 404 (2%); of this, 274 (68%) were females and 130 (32%) were males (P <0.001). Age was not significantly associated with the co-occurrence of asthma and back pain. Males were 36% less likely to present with asthma and back pain when compared to females after adjusting for location of treatment and age (OR 0.64 (95% CI: 0.51 to 0.79), P<0.001.

**CONCLUSIONS:** Females were more likely to present with a co-occurrence of asthma and back pain than males in acute care hospital settings.

**680** High Rates of Abnormal Lung Function and Lower Airway Inflammation in Non-Asthmatic Children Residing Near Point Sources of Outdoor Air Pollution

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**RATIONALE:** Our group recently reported a high prevalence of asthma and poor disease control among a large cohort of school aged children residing near point sources of outdoor air pollution (OAP) in Pittsburgh. The purpose of this follow-up investigation was to determine if exposure to OAP impacts on lung function and lower airway inflammation in school children without asthma.

**METHODS:** Participants were recruited from schools near OAP point sources. Asthma diagnosis was assessed using a validated risk survey. Lung function was assessed by spirometry and abnormal lung function was defined as a forced expiratory volume in one second (FEV1) of ≤80% predicted. Lower airway inflammation was assessed by exhaled nitric oxide (FeNO) levels and elevated levels were defined as >35 ppb.

**RESULTS:** 267 fifth graders participated (52.4% male; 37.5% African American and 44.2% with public health insurance). 159 (59.6%) were identified as not having asthma. 30% of those without asthma had FEV1 ≤80%. 12% of those without asthma had FeNO >35 ppb.

**CONCLUSIONS:** These results demonstrate elevated rates of abnormal lung function and lower airway inflammation in school aged children without a diagnosis of asthma who reside near point sources of OAP. Future studies are needed to determine if these lung abnormalities are a precursor for the later development of asthma or other chronic lung diseases.

**681** Home Visits: An Overlooked Yet Acceptable Intervention for Asthma Management in Low Income and Minority Adults

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**RATIONALE:** Uncontrolled asthma has worse outcomes in low income and minority adults partly because of difficulties in accessing and engaging with healthcare. Home visits (HVs) by community health workers (CHWs), used in children, might improve care coordination and access in adults. We present a qualitative analysis of the acceptability of the HVs using responses to an open-ended survey.

**METHODS:** Adults with uncontrolled asthma (history of hospitalization, ED visit, or need of prednisone in the past year) from low-income neighborhoods, participating in a larger study of the patient portal, had up to 4 home visits. CHWs conducted a needs assessment, checked inhaler technique and the presence of medications, drafted an action plan for approval by the asthma clinician, and demonstrated the patient portal. The Home Visit Satisfaction Survey, administered after 12 months of study participation, evaluated patient engagement and experience with the home visitor. Responses were evaluated with qualitative coding and a Grounded Theory analytical approach.

**RESULTS:** 74 patients completed the questionnaire: median age 52 (range 21-77), 90% female, 81% Black/African-American, 14% Hispanic, 56% permanently disabled, 18% unemployed, with poorly controlled asthma (mean asthma control score 2.4 ± 1.1). Perceptions of HVs and CHWs were uniformly positive. Patients reported increased understanding of the severity of their asthma, motivation for adherence, access to knowledge, and preparation for medical visits; better recognition of treatment methods and of asthma-related triggers.

**CONCLUSIONS:** HVs by CHWs were feasible and acceptable and should be further explored for improving access to care for low-income and minority urban adults with asthma.
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Rationale: Mouse allergen reduction is associated with improvements in asthma among sensitized and exposed children, but whether age modifies responsiveness to mouse allergen reduction is unclear.

Methods: 350 mouse-sensitized and exposed asthmatic children (5-17y) were enrolled in a clinical trial of integrated pest management+education versus education alone. Symptoms (days/2 weeks), acute visits, and mouse allergen exposure were assessed every three months. Groups were combined for analyses because there were no differences in exposure or clinical outcomes. Analyses of relationships between mouse allergen and asthma outcomes were stratified at the median age (older vs. younger (>9y)). Mixed-effects generalized linear models were adjusted for gender, age, race, insurance, and included interaction terms (age*mouse allergen level).

Results: Participants were predominantly low-income and minority (78% Black; 22% Hispanic), and had uncontrolled asthma. Among older participants, each 50% reduction in mouse allergen was associated with fewer symptom-days (IRR [95% CI]: maximal symptoms: 0.96 [0.94-0.99], cough wheeze/chest tightness: 0.96 [0.93-0.99], running symptoms: 0.88 [0.85-0.91], cough: 0.92 [0.88-0.96], and rescue medication use 0.97 [0.95-0.99]). There was little effect of mouse allergen reduction on symptoms among younger participants (p-values >0.05). P-values for age*mouse allergen interactions were: maximal symptoms: 0.92, cough/wheeze/chest tightness: 0.17, running symptoms: <0.001, cough: 0.001, and rescue medication use: 0.001. Mouse allergen reduction was not associated with acute visits, stratified by age.

Conclusions: Mouse allergen reduction was associated with greater improvement in some symptoms, but not acute visits, among older mouse-sensitized and exposed asthmatic children, suggesting that the effectiveness of allergen reduction on symptoms may vary by age.

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Rationale: Evidence-based guidelines support the use of asthma action plans (AAPs) for asthma self-management and education despite ongoing controversy on improving outcomes. We sought to evaluate the patient and provider characteristics associated with having an AAP.

Methods: We examined data from 28,508 de-identified patients documented in the Asthma IQ database to determine current AAP use in relationship to provider type (primary care vs. asthma specialist), patient characteristics (age, race, smoking history) and comorbid conditions (rhinosinusitis, GERD, depression and obesity). Descriptive statistics were performed and Chi-square tests used to examine associations. We determined odds ratios of current AAP use for each characteristic/comorbidity.

Results: 36% of children and 34% of adults with persistent asthma had a current AAP. Patients seen by an asthma specialist were more likely to have an AAP compared to those seen by a primary care physician (Child OR: 1.7, 95% CI:1.3-2.1; Adult OR: 1.8, 95% CI: 1.5-2.4). Children with rhinosinusitis (OR: 1.3; 95% CI: 1.1-1.7; p<0.05) and African American children (OR: 1.5; 95% CI 1.1, 2.0; p<0.05) were more likely to have a current AAP. Adults that were younger (OR: 0.99; 95% CI: 0.98-0.99; p<0.05), obese (OR: 1.6; 95% CI: 1.2-2.1; p<0.05) or had depression (OR: 2.1; 95% CI: 1.3-3.6; p<0.05) were more likely to have a current AAP.

Conclusions: AAPs were more commonly used by asthma specialists and prescribed to patients with characteristics that have been previously shown to be associated with poor asthma outcomes. Programs such as Asthma IQ might facilitate the appropriate use of AAP in higher risk patients.
684 Impact of Multi-Disciplinary School-Based Health Care Delivery Model on Asthma Outcomes

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RATIONALE: The objective of this study was to assess the impact of a multi-disciplinary school-based health care delivery model on outcomes in elementary school subjects with asthma.

METHODS: Subjects with physician diagnosed asthma were recruited from two local school districts. In-school visits occurred at baseline and at 2, 4, 8 and 12 weeks. At each visit, the allergy/asthma specialist conducted a medical assessment and adjusted drug therapy according to NHLBI-EP3 and the study pharmacist provided disease related and medication specific education. Asthma severity/control, knowledge and compliance were assessed at each visit.

RESULTS: Fifty subjects enrolled (mean age 8.9±1.7 years, 52% male, 62% minority) and 23 had persistent asthma. 92.0% of subjects were compliant with ≥80% of visits (P=0.011). In those with persistent asthma, use of controller therapy increased from 21.4% to 78.5% before and after baseline, respectively (P<0.001). 6.1% and 60.0% of subjects had complete knowledge at baseline and final visits, respectively (P<0.001). 37.8% and 65.7% of caregivers had complete knowledge at baseline and final visits, respectively (P=0.011). Asthma control test scores improved from 20.0±3.6 to 22.9±3.4 before and after baseline, respectively (P<0.001).

CONCLUSIONS: In summary, compliance with school-based visits was very high and asthma knowledge and disease control improved significantly. Future studies need to examine the impact of this specific multi-disciplinary school based intervention on morbidity outcomes such as disease exacerbations, acute visits and hospitalizations.

685 Lower socioeconomic status predicts lower pneumococcal antibody titers among young adults with asthma

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RATIONALE: Despite the significantly increased risk of invasive pneumococcal disease among patients with asthma, the association of socio-economic status (SES) with antibody titers is not known. We conducted a prospective study to assess the association of pneumococcal titers and immune response to PPSV23 to SES.

METHODS: We prospectively enrolled 50 asthmatics between 19-21 years old that did not have a history of PPSV23 from Mayo Clinic primary care practice. One person in 50 had PCV-7 while none had PCV-13 immunization in childhood. Pneumococcal titers for 23 serotypes were assessed at each visit. The allergy/asthma specialist conducted a medical assessment and adjusted drug therapy according to NHLBI-EP3 and the study pharmacist provided disease and medication specific education. Asthma severity/control, knowledge at baseline and final visits, respectively (P<0.001). 6.1% and 60.0% of subjects had complete knowledge at baseline and final visits, respectively (P<0.001). Asthma control test scores improved from 20.0±3.6 to 22.9±3.4 before and after baseline, respectively (P<0.001).

CONCLUSIONS: In summary, compliance with school-based visits was very high and asthma knowledge and disease control improved significantly. Future studies need to examine the impact of this specific multi-disciplinary school based intervention on morbidity outcomes such as disease exacerbations, acute visits and hospitalizations.

686 Vaccination against yellow fever in patients with IgA deficiency

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RATIONALE: Yellow fever is a serious infectious disease caused by an arbovirus. Caution is recommended in its indication and is contraindicated in the vast majority of primary immunodeficiencies. The objective of the present study was to evaluate the presence of adverse events and serious side effects after vaccination against yellow fever in individuals with a history of IgA deficiency.

METHODS: Retrospective and descriptive study carried out with a review of records of patients diagnosed with IgA deficiency and who received the vaccine against yellow fever in the last eleven years, being followed up at a tertiary hospital in São Paulo, Brazil.

RESULTS: Twenty-five patients with IgA deficiency were included in the study. They all received the vaccine against yellow fever. No patient had severe adverse events. Seventeen patients (68%) did not have any type of reaction, one (4%) presented local reaction (hyperemia and pruritus at the vaccine site) and three (12%) systemic events such as coryza, headache, fever, nausea and asthenia. The mean of CD4+ T lymphocytes was 915 mm³ and total lymphocytes 2,000 mm³.

CONCLUSIONS: In Brazil, most of the territory is considered an endemic area or a risk zone for yellow fever. We have to be cautious to contraindicate vaccination because the disease has high lethality and for which there is no specific treatment. We note from this study that vaccination in patients with IgA deficiency is possibly safe, contradicting current studies. Vaccination remains the most effective form of protection against disease.
687 Sputum and serum immunoglobulins in patients with asthma and recurrent neutrophilic bronchitis

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RATIONALE: Some patients with severe asthma on high-dose inhaled/systemic corticosteroid, with normal serum immunoglobulins, are prone to recurrent respiratory infections. We hypothesized that they may have reduced airway immunoglobulins (Ig). The objectives of this study are to: 1) compare Ig levels in serum and sputum in such patients compared to normal healthy controls and 2) to compare the effects of subcutaneous (SC) and intravenous (IV) Ig replacement on sputum and serum Ig levels and clinical outcomes.

METHODS: All Ig classes were measured by Multiplex assay (Eve Technologies, Alberta) in serum and cell-free sputum supernatants in severe asthmatics with ≥2 prior episodes of neutrophilic/infective bronchitis (total sputum cell count >25×10⁶ cells/g and neutrophils >79% and pathogens identified on bacterial culture) (n=25), and in healthy controls (n=6). Measurements were repeated in a subset of patients 3 months after IV or SC Ig therapy.

RESULTS: Overall, Ig levels (across all classes) were higher in serum than in sputum. Igs were not lower in sputum in the neutrophilic bronchitis patients compared to controls. In fact, IgG₃ (3.67×10⁶ vs 1.21×10⁶ ng/mL, p<0.03) and IgG₄ (83.86 vs 13.90 ng/mL, p<0.05) levels were higher than in healthy controls. Greater improvements in sputum IgG₃ (p=0.06) and sputum IgA (p=0.01) were seen following IVIg compared to SCIg (n=9), associated with less episodes of infective bronchitis during the 6-month follow-up (2.3 vs 0.8, P<0.03, paired t-test).

CONCLUSIONS: Ig replacement by IV may be more effective than SC in patients with recurrent neutrophilic bronchitis. A larger randomized clinical trial is warranted.

689 Regulation of allergic airway inflammation through CD4 T cell plasticity

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RATIONALE: LPS acts as a potent adjuvant in the airway to promote Th2 and Th17 immune responses to inhaled allergens. We investigated whether the airway neutrophilia triggered by inhaled LPS contributes to its adjuvant activity.

METHODS: Mice were treated with a neutrophil-depleting antibody (1A8) or with an isotype control (IC) antibody, then sensitized to ovalbumin (OVA) using small amounts of LPS as the adjuvant. Allergic airway inflammation was subsequently elicited by exposing the mice to aerosolized OVA on either one occasion, or on five consecutive days. Some mice received adoptive transfer of naïve, OVA-specific, IL-17 fate mapping CD4 T cells prior to allergic sensitization. Flow cytometry was used to sort progeny of these cells post-allergen challenge for RNA extraction and gene profiling.

RESULTS: Levels of TGF-beta in the airway during allergic sensitization were reduced by prior neutrophil depletion. IL-17 in regional lymph nodes and allergic responses to single subsequent challenge were unaffected by neutrophil depletion. However, this treatment was associated with increased allergic inflammation following multiple OVA challenges. Analysis of fate mapped Th17 cells revealed that after several OVA challenges, Th17 cells acquired a more regulatory phenotype, and that this shift was less apparent in mice that had undergone neutrophil depletion prior to sensitization.

CONCLUSIONS: LPS-induced neutrophils produce TGF-beta that enhances the transition of Th17 cells to a more regulatory phenotype upon continued allergen exposure. These findings suggest that modulating the plasticity of Th17 cells might be an effective strategy to control allergic asthma.

688 Off-label use of omalizumab in pediatric anaphylaxis

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RATIONALE: Off-label uses of drugs require a careful assessment of benefit-risk ratio. Omalizumab indications include severe asthma and chronic urticaria in patients older than 6 years.

METHODS: We describe a group of children receiving omalizumab as an off-label use for anaphylaxis and their clinical response.

RESULTS: Five children (4 boys/1 girl), median age: 5 years (Interquartile range [IQR]: 3-15). Indications were: 1° case: Enzyme replacement therapy (ERT) induced anaphylaxis, after failed desensitization attempts; 2°: Recurrent anaphylaxis due to combined milk, egg and nut allergies; 3°: Traces-induced milk allergy as specific oral tolerance induction (SOTI) premedication; 4°: Failed SOTI attempts with milk and egg, respectively. Median anaphylaxis episodes before omalizumab: 4 (IQR: 1-6). Total IgE values: 602 KU/L (IQR: 15-2000). Weight: 24 kg (IQR: 11-49). Patients received (median dose) 300 mg/monthly (IQR: 75-600 mg) for (median) 18 months (IQR: 4-36). Afterwards, a patient developed 2 anaphylaxis (1 during SOTI induction and the other during maintenance phase). ERT has been administered for 18 months so far and the SOTI has been tolerated by the other 3 patients. Omalizumab doses/frequency have been diminished in 2 out of 5 patients, and increased in another one.

CONCLUSIONS: Omalizumab addition allowed continuing SOTI/desensitization procedures in high risk patients, reducing the number of anaphylaxis episodes. Despite its administration protective measures such as anaphylaxis management plans, cofactors avoidance and rescue medication are to be maintained in such patients. As our sample includes very young children, we must be aware there is no knowledge about our choice’s future consequences.
690 Inactivated influenza vaccine induces IgE antibody to the vaccine in preschool children

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RATIONALE: We previously reported highly increased levels of specific IgE antibodies (sIgE) to vaccine component in children with influenza vaccine-induced anaphylaxis (J Allergy Clin Immunol 2016). We investigated whether inactivated influenza vaccine induces vaccine-specific IgE antibody in general population and sought risk factors of sensitization.

METHODS: Subjects were children/adolescent (0 to 18 years old) who participated in a clinical trial to compare immunogenicity of trivalent and quadrivalent inactivated influenza vaccines. Serum samples were obtained before and 3-4 weeks after 1st and 2nd dose of vaccination. The subjects >13 years old received only 1 dose. Influenza vaccine-sIgE (IV-sIgE) was measured with ImmunoCAP® assay system. ImmunoCAP titer<0.1 U/ml was regarded as positive.

RESULTS: A total of 393 subjects were enrolled in the study, consisting of 4 age-groups; 0-2-year-old (N=95), 3-5-year-old (n=101), 6-12-year-old (n=100) and 13-18-year-old (n=97). No systemic adverse events occurred. Local reactions were observed in 30% of the subjects. Prevalence of sensitization to the vaccine before vaccination was 30%, 72%, 62% and 50 % in 0-2, 3-5, 6-12, and 13-18-year-old groups, respectively. IV-sIgE titers were significantly elevated after 1st dose in 0-2 and 3-5-year-old groups, no further elevation after 2nd dose. The titers in age groups of 6 years and older did not change after vaccination. Elevation of sIgE was associated with the local reactions. Multi-variate logistic analysis revealed that history of asthma and young age were significant risk factors for sensitization.

CONCLUSIONS: Influenza vaccine induces IgE sensitization in young children, which may predispose vaccine-induced anaphylaxis.

691 Yellow Fever Vaccine (YFV) for Patients with Egg Allergy: Protocol Proposal

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RATIONALE: The current yellow fever epidemic in Brazil has already 1,266 confirmed cases and 415 deaths by 2018-July. Vaccination is the most effective measure of protection against this disease. However, YFV shows ovalbumin levels (>2μg/ml) not considered safe for patients with egg allergy (EA). Our objective was to describe the vaccination protocol using the Brazilian YFV in EA patients attended in a Reference Allergy Center and to relate the YFV skin tests (ST) to the clinical manifestations reported.

METHODS: Patients with EA were submitted to a standardized interview and Brazilian YFV-ST (skin prick test [SPT] and or intradermal skin test [IDST]). Patients with positive YFV-SPT or IDST (after negative SPT) underwent desensitization; and those with negative SPT and IDST were vaccinated under medical supervision. Desensitization was based on the Brazilian Association of Allergy and Immunology’s Protocol - 4 applications every 30 minutes (Adapted by Munóz-Cano).

RESULTS: 79 patients with EA were vaccinated, 52 (65.8%) by the usual way and 27 (15 positive SPT and 12 positive IDST) underwent desensitization (no adverse reactions during and mild hives in 4 patients 24-72h after the procedure). Described egg reactions in those with positive YFV-ST were considered moderate-severe in 16 (59.2%) and mild in 11 (40.8%) patients (P<0.01). One negative YFV-ST patient presented anaphylaxis (grade 2) during the observation period following usual vaccination.

CONCLUSIONS: Vaccination protocol with Brazilian YFV proved to be safe and allowed to vaccinate patients with egg allergy, always under medical supervision. Moderate/severe egg-related reactions showed substantial concordance (K = 0.70) with ST performed with YFV.

692 Gender differences in dendritic cell population in nasal and oral cavity between allergic and non-allergic subjects.

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RATIONALE: It is well documented that male and female immune systems differ physiologically, leading to different responses against invading pathogens. It stands to reason that the different responses are reflected in the populations of immune cells. As dendritic cells (DC) are integral participants of both innate and adaptive immune responses, it is possible that males and females vary in the concentration of tissue-resident DCs, such as in the nasal and oral mucosa.

METHODS: A public-available dataset (https://doi.org/10.5281/zenodo.50228) with DC counts obtained from biopsies of the epithelium and lamina propria of both the nasal and oral mucosa was analyzed using a two sample t-test. DC counts from biopsies of male and female subjects, with and without upper respiratory allergy, were compared to determine if there was significant differences by gender.

RESULTS: When considering the biopsies from both nasal epithelium (epi) and nasal lamina propria (LP), females (9.418 LC/mmepi and 6.431 LC/mmLP) had a significantly higher DC count than males (5.464 LC/mmepi and 3.629 LC/mmLP). Further analysis determined that there was no significant difference in the concentrations of DCs in biopsies obtained from the oral mucosa, and when stratifying by presence or absence of upper respiratory allergies.

CONCLUSIONS: Variations in DC population concentration potentially contribute to the physiological differences in immune response between the two genders. Further investigation into immunological cell populations of various tissues could improve the understanding of gender differences in regards to the immune system.
693A Withdrawn

693 Cross-Reactive Carbohydrate Determinants (CCDs) Interference with Component Resolved Diagnosis on NOVEOS™*, ImmunoCAP® and IMMULITE® 2000.

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RATIONALE: Allergen specific IgE (sIgE) can bind CCD structures on plant and insect glycoproteins as well as peptide epitopes. These carbohydrate structures can display structural homology across many allergen groups leading to extensive cross-reactivity, obscure in vitro diagnostic results, and debatable clinical relevance. With the introduction of Component Resolved Diagnosis (CRD), non-glycosylated components can be utilized to prevent the detection of anti-CCD IgE and may improve clinical relevance. The aim of this study is to confirm anti-CCD IgE will not be detected on non-glycosylated components on NOVEOS, ImmunoCAP, and IMMULITE 2000.

METHODS: A panel of CCD-positive samples was selected based on their reactivity to several recombinant components. Samples were tested before and after inhibition with a commercially-available CCD inhibitor on NOVEOS, ImmunoCAP, and IMMULITE 2000.

RESULTS: ImmunoCAP IgE binding was reduced by samples preincubated with a CCD inhibitor while NOVEOS and IMMULITE 2000 resulted in minimal reduction.

CONCLUSIONS: The reduction of IgE binding to a non-glycosylated recombinant component from samples with a CCD inhibitor on ImmunoCAP suggests trace amount of CCD are still present in the test. This confirms other studies that have indicated the cellulose used as an allergen carrier on ImmunoCAP may elevate specific IgE result. NOVEOS, a microparticle-based chemistry, and IMMULITE 2000, bead-based technology, resulted in minimal IgE reduction with and without CCD inhibitor.

*These products are: ‘For Investigational Use Only,’ pending submission and clearance by the United States Food and Drug Administration. The performance characteristics of these products have not been established.

694 Colonization and persistence capacity of a multi-strain probiotic in food allergy.

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RATIONALE: The purpose of our study was: 1) Evaluate the baseline presence of Bifidobacterium longum BB536 (BL), Bifidobacterium breve M-16V (BB) and Bifidobacterium infantis M-63 (BI) in children with IgE mediated CMA and/or EA, children sensitized but not allergic, healthy controls; before, during and after administration of multi-strain probiotics containing 3.5 × 10^8 UFC of BL, BB and BI (Tribif®).

METHODS: Infants aged 10-14 months, allergic to egg/milk (Group I) received Tribif® for 30 days. Fecal samples at 0, 7, 15, 30, 60 and 90 days were evaluated by specific BL, BI and BB primers. Two control groups of egg/milk IgE-positive infants with negative food challenge (Group II) and IgE-negative healthy infants (Group III) were evaluated for BL, BI and BB in basal conditions.

RESULTS: A total of 33 patients were then enrolled: 12 patients for Group 1, 11 for Group 2 and 10 for Group 3. At baseline, BL and BB were present in the order of 10^4-10^5 cells/ml and Tribif® intake did not cause a significant increase during the time-course. At baseline, BI median concentration value was absent in the gut microbiota and its amount significantly increased from T1 to T3.

CONCLUSIONS: BL and BB are part of the normal bacterial microflora. A significant increase in BI concentration suggests that Tribif® does colonize the intestinal tract with good persistence after discontinuation.

All abstracts are strictly embargoed until the date of presentation at the 2019 Annual Meeting.
695 Human milk induces IgA class switch recombination in cord blood B-cells

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RATIONALE: Previously we have shown increased A Proliferation-Inducing Ligand (APRIL) and B-cell Activation Factor (BAFF) concentrations in colostrum are associated with protection against allergic disease. APRIL and BAFF, together with IL-10 and TGFb, are known to induce T-cell independent (TI) IgA class switch recombination (CSR) in B-cells. Our goal was to assess whether human milk containing these cytokines, would induce CSR in cord blood B-cells.

METHODS: B-cells were isolated from cord blood mononuclear cells (CBMCs) by IgD selection and were then cultured for 3-7 days with treatments: medium containing human milk or combination of APRIL and TGFb1. Cells were then analyzed by flow cytometry for detection of IgA1 and IgA2 positive B-cells.

RESULTS: B-cell CSR assay protocols were established. IgA B-cells were readily detectable following the assay protocol, using APRIL and TGFb1 stimulation as positive controls. Using the protocol we noted a robust IgA class switching following stimulation using sterile filtered human milk.

CONCLUSIONS: We have established a protocol that will allow more detailed assessment of several cytokines in human milk class switch recombination. Future experiments will characterize in detail which cytokines affect CSR and IgA production to elucidate the role of human milk in protection against onset of allergic disease.

696 Staphylococcus Aureus Induces IL-33, TSLP, and Muc5AC production by AERD Nasal Epithelium

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RATIONALE: Although Methicillin Resistant Staphylococcus aureus (MRSA) is associated with chronic rhinosinusitis (CRS), causative role and mechanism of MRSA leading to chronic inflammation seen in CRS has yet to be elucidated. Nasal epithelium provides the first line of defense in differentiating pathogenic from commensal bacteria. Increased permeability of nasal epithelium, decreased antimicrobial production and impaired mucociliary clearance are features of CRS. Regenerating islet-derived protein 3 gamma (Reg3g) is a C-type lectin with antimicrobial activity against MRSA. Previous studies showed that it’s produced by lung epithelium and improved clearance of MRSA in mice. Recent publications have linked MRSA colonization to nasal polyp production of IL-33 and Thymic stromal lymphopoietin (TSLP).

METHODS: In vitro coculture of nasal epithelium from different subjects were stimulated with MRSA. Trans epithelial electrical resistance (TEER) of air liquid interphase (ALI) was measured and RNA expression was analyzed at different time points with RT-qPCR.

RESULTS: Nasal epithelial TSLP expression increased after stimulation with MRSA. Furthermore, nasal epithelium from Aspirin-Exacerbated Respiratory disease (AERD) patient had increased IL-33, Muc5AC, Reg3g expression at baseline and enhanced induction of Muc5AC and TSLP with MRSA exposure. Furthermore, AERD epithelium showed decreased TEER when exposed to MRSA indicating impaired epithelial barrier integrity.

CONCLUSIONS: Nasal epithelium expresses antimicrobial C-type lectin, Reg3g and type 2 cytokines, IL-33 and TSLP upon encountering Staphylococcus aureus. We propose that persistent MRSA colonization leads to persistent type 2 cytokine driven inflammation leading to excess mucin secretion seen in CRS.

697 PM2.5 Exposure Induced Autophagy Activation via the ROS/AMPK/mTOR/ULK1 Signaling Axis in Macrophages

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RATIONALE: Potential effects of particulate matter with an aerodynamic diameter less than 2.5 μm (PM2.5) on innate immunity have raised concerns. As the first defense line, macrophages are able to induce inflammatory response. However, whether PM2.5 exposure affects macrophage polarizations and its underlying mechanisms remain unclear.

METHODS: THP-1 monocyctic leukemia cells were differentiated into macrophages using PMA. Intracellular ROS level was measured by flow cytometry. The levels of phosphorylation of AMPK, mTOR and ULK1 (Ser555 and Ser757) and expression of several critical regulators of autophagy were detected by western blot. The expression levels of cell surface markers (CCR7 and CD200R) and cytokines (TNF-α and CCL17) were detected by real-time PCR and ELISA, respectively. Additionally, specific inhibitors were used to address the molecular mechanisms.

RESULTS: PM2.5 exposure triggered autophagy in macrophages (up-regulation of Hsp90, ATG5, Beclin1 and ratio of LC3II/I), this was accompanied with increased ROS level and AMPK phosphorylation, inhibition of mTOR, up-regulation of p-ULK1 (Ser555) and reduction of p-ULK1 (Ser757). Furthermore, inhibition of ROS or AMPK activity abolished PM2.5-induced autophagy activation and changes of mTOR, ULK1, Hsp90, ATG5, Beclin1 and LC3II/I. PM2.5 stimulation up-regulated the expression of CCR7 and TNF-α, and down-regulated CD200R and CCL17. Pre-incubation of cells with NAC or compound C or chloroquine blocked PM2.5-induced changes of these markers and cytokines.

CONCLUSIONS: This study indicates that PM2.5 exposure enhanced inflammatory M1 polarization through ROS/AMPK/mTOR/ULK1 autopahgy axis, and suggests that targeting this pathway might have potential value in the management of inflammatory diseases.
A unique subset of PD-1+CXCR5 CD4+ T cells is involved in immunological mechanisms of IgG4-related disease

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RATIONALE: IgG4-related disease (IgG4-RD) is a chronic fibroinflammatory disease characterized by elevation of serum IgG4 level and infiltration of IgG4 plasma cells in various affected organs. However, the underlying immunological mechanisms involved in IgG4-RD remain unclear. In this study, we examined circulating PD-1+CXCR5 CD4+ T cells in IgG4-RD to address this issue.

RESULTS: The percentage and number of circulating PD-1+CXCR5 CD4+ T cells from patients with IgG4-RD (n = 53) patients with Sjögren’s syndrome (n = 16) and healthy volunteers (HV; n = 34) were analyzed. Circulating PD-1+CXCR5 CD4+ T cells were significantly elevated in IgG4-RD patients compared with those in HVs. Further analysis showed that there were marked positive correlations of the percentage of PD-1+CXCR5 CD4+ T cells with serum IgG4 level and number of involved organs. Moreover, the percentage and number of PD-1+CXCR5 CD4+ T cells were depleted in accordance with the reduction of serum IgG4 level after treatment with glucocorticoids. Interestingly, granzyme A (GZMA)+ cells were enriched in PD-1+CXCR5 CD4+ T cells and the percentage and number of GZMA+PD-1+CXCR5 CD4+ T cells were significantly elevated in IgG4-RD patients.

CONCLUSIONS: PD-1+CXCR5 CD4+ T cells are a dominant subset of circulating CD4+ T-cell populations in IgG4-RD patients, and the percentage of these cells is correlated with clinical manifestations of IgG4-RD. Further analysis of GZMA+PD-1+CXCR5 CD4+ T cells may lead to a deeper understanding of the pathogenesis of persistent inflammation and ectopic lymphoid follicle formation in IgG4-RD.

TGF-β present in breast milk is biologically active to induce IgA production in B-cells

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RATIONALE: The role of human breast milk in protection against allergic diseases is debated and the mechanisms are unknown. While breast milk is known to confer passive immunity to the infant in the first weeks of life, little is known regarding its effect on induction of IgA class switch recombination (CSR) through cytokines, including TGF-β and APRIL, found in large quantities in breast milk.

METHODS: IgG B-cells were selected from fresh cord blood and cultured overnight. The following day, cells were stimulated with TGF-β and APRIL or human milk serum with quantified high or low levels of TGF-β. Milk was also acid-treated to activate latent, inactive TGF-β. After incubating 7 days, each treatment group was assessed for IgA1 and IgA2 positive B-cells using flow cytometry.

RESULTS: We detected an increased quantity of IgA class switching in B-cells treated with TGF-β/APRIL or acid-activated milk serum. Milk with higher levels of TGF-β and APRIL induced higher levels of IgA class switched cells than milk with lower levels of both cytokines (21 fold change to baseline vs. 18 fold change). Non-acid-activated human milk induced little IgA class switching, indicating the importance of acid-activation for TGF-β bioavailability.

CONCLUSIONS: Increased expression of IgA following treatment with acid-activated human milk serum demonstrates the role of TGF-β in inducing IgA CSR. The relative contribution of APRIL remains to be determined. Thus, breast milk cytokines have the potential to contribute to the development of the infant immune system.
**701 Reduction in Spontaneous Reporting Rates of Hemolysis with IVIG After Implementation of an Immunoaffinity Chromatography Step for Isoagglutinin Reduction**

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**RATIONALE:** Isoagglutinins can mediate hemolytic reactions in non-O blood group patients receiving intravenous immunoglobulin G (IVIG). An immunoaffinity chromatography (IAC) step recently introduced in the production process of IVIG (Privigen\(^®\), CSL Behring, King of Prussia, USA) effectively reduces isoagglutinins. We assessed the impact of the IAC step (Ig IsoLo\(^®\)) on spontaneous hemolysis reporting rates for patients receiving Privigen\(^®\) at baseline (no isoagglutinin reducing measures) and after IAC implementation.

**METHODS:** Hemolysis reporting rates for baseline (2008–2013) and after IAC implementation (2016–2017) were extracted from the CSL Global Safety Database using the Standard MedDRA Query “Hemolytic Disorders Broad”.

**RESULTS:** In 2016–2017, the worldwide reporting rate of hemolysis decreased from 4.05 at baseline to 0.70 cases/1000 kg Privigen\(^®\) (83% reduction); cases of patients reported requiring blood/RBC transfusion decreased from 0.97 to 0.19 cases/1000 kg (80% reduction). In 2017 alone, when the proportion of IAC lots on the market was higher than in 2016, the hemolysis reporting rate was 0.32 cases/1000 kg (92% reduction) and only 1 patient required transfusion. Most patients experiencing hemolysis received IVIG for immunomodulatory therapy; hemolysis rate in these patients decreased from 3.09 to 0.52 cases/1000 kg. In patients on replacement therapy, hemolysis rate decreased from 0.28 to 0.12 cases/1000 kg. Reduction in hemolysis rate was greatest in patients with blood groups A and AB who are known to be at high risk.

**CONCLUSIONS:** Introduction of IAC isoagglutinin reduction step in the manufacturing process of an IVIG substantially reduced hemolysis reporting rates and the requirement for blood/RBC transfusion.

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**702 How Clinical Immunologists Can Impact Patient Care within a Cancer Center: A Tale of 3 Patients**

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**RATIONALE:** Immune-related adverse events (IRAEs) associated with checkpoint inhibitors can affect almost any organ system and certain patients likely have a predilection for immune dysregulation. Current guidelines for oncologists suggest treating IRAEs with systemic steroids. However, steroids are not likely to be the most efficacious treatment modality for certain IRAEs, and in some cases, patients may require more directed treatment regimens.

**METHODS:** The following patients were seen in our Smilow Cancer Center Immunology Clinic. An immune evaluation was done, including cytokine panels, immune deficiency flow cytometry, and inflammatory markers.

**Case 1:** A 61-year-old gentleman undergoing treatment for stage IV esophageal carcinoma received treatment with anti-PT-L1 immunotherapy. When he developed a rash, his oncologist stopped immunotherapy and began prednisone. He was diagnosed with psoriasis and initiated on a retinoid.

**Case 2:** A 44-year-old woman with stage I breast cancer treated with anti-PD-L1 immunotherapy developed severe parotitis, duodenitis, colitis, and b-cell lymphopenia. She had an incomplete response to systemic steroids, ultimately requiring infliximab and methotrexate.

**Case 3:** A 69-year-old female with existing RA was treated with anti-PD-1 immunotherapy for urethral melanoma and developed an RA exacerbation, which required high dose steroids and then rituximab long-term.

**RESULTS:** Given that Allergists and Immunologists are well-versed in immunology and experienced in treating disorders of immune regulation, such as CTLA-4 mutations, this specialty offers unique insight into both the pathophysiology and treatment of IRAEs due to immunotherapy.

**CONCLUSIONS:** A multidisciplinary team approach including Allergy and Immunology is beneficial when treating patients who develop IRAEs on cancer immunotherapy.

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**703 Perceptions of a Continuing Medical Education Activity to Increase Knowledge of Vaccination in Adults with Chronic Inflammatory Conditions Among Clinicians**

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**RATIONALE:** Patients with chronic inflammatory diseases are at increased risk for infections. Vaccination rates in this population are suboptimal. Vaccine knowledge among providers and patients is a significant barrier.

**METHODS:** A Continuing Medical Education (CME) activity was developed to increase pneumococcal and influenza rates in adults with chronic inflammatory conditions. Educational content incorporated updated CDC guidelines regarding pneumococcal vaccination. This activity was disseminated to AAAAI members in online and print formats, and to a single academic rheumatology, allergy, and immunology division in a live, interactive format. Descriptive statistics were used to evaluate confidence in vaccination practices and perception of the activity. Paired t-test was used to evaluate pre- and post-activity knowledge in a subset of participants.

**RESULTS:** Of 265 participants who completed the activity, 94% subsequently indicated confidence in applying current guidelines for pneumococcal and influenza vaccination and 85% perceived the quality of the content and format to be very good to excellent. Fifty-seven percent planned to change their practice. Of those who did not plan to change their practice, 61% felt that their current practice behaviors were reinforced. In 21 participants, knowledge was significantly increased after completing the activity (p=.0001), with a pre-test mean percent of 75% (SD 11.6%, range 70-80%) versus a post-test mean percent of 89% (SD 11.1%, range 85-95%).

**CONCLUSIONS:** This CME module was effective in increasing clinicians’ knowledge and confidence in vaccination for adults with chronic inflammatory conditions. Quality improvement endeavors can incorporate CME activities such as this one to increase vaccination rates.
704 Polymeric Plasma IgA Recovered from Cohn Fraction III Precipitate Binds Recombinant Human Secretory Component

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RATIONALE: Cohn fraction III precipitate (CFxIII-ppt) is a discarded byproduct of the recovery of IgG from pooled donor plasma using cold ethanol fractionation. Tons are discarded annually. We propose that recovered IgA has the potential to be a new orally administered immunoglobulin therapy.

METHODS: Water content of CFxIII-ppt was determined by weighing wet and then dried material. IgA was recovered from rehydrated CFxIII-ppt by jacalin affinity chromatography. Concentration of IgA was measured using a spectrophotometer. Proportions of monomer, dimer and polymer in IgA were determined by analyzing size exclusion chromatograms. ELISA demonstrated the association of J chain with IgA dimer and polymer. Immunoblotting showed dimer and polymer binding to recombinant human secretory component (rhSC). Antigenic specificity was determined by ELISA.

RESULTS: CFxIII-ppt is ~65% water. Up to ~15 mg of IgA is obtained per g of CFxIII-ppt. Recovered plasma IgA is 50.2 (+/-5.36 SD)% monomer, 49.8 (+/-5.3SD)% dimer and higher polymers (n = 7). The IgA dimer and higher polymer fractions contain J chain and readily combine with rhSC to form dimeric and polymeric semisynthetic secretory IgA. We previously reported that IgA recovered from CFxIII-ppt binds to Clostridium difficile toxins A and B as well as peanut extract. We now extend the known antigenic specificity of recovered IgA to include Campylobacter.

CONCLUSIONS: Plasma IgA from CFxIII-ppt is slightly less than 50% polymeric IgA (dimer plus larger polymers). Higher IgA polymer as well as dimer can be converted into secretory IgA. Pooled plasma contains IgA with reactivity to Campylobacter.

705 Stimulating Oxidative DNA Base Excision Repair in Mice Subjected to Klebsiella pneumoniae-induced Acute Respiratory Distress Syndrome (ARDS) Improves Genomic Integrity of Topoisomerases and Facilitates Innate Lung Inflammation

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RATIONALE: Cell activation stimulates Topoisomerase-dependent formation of DNA double strand breaks in the promoters of early-response genes. These breaks are sufficient to induce the expression of these of early-response genes. Here we hypothesized that improving the genomic integrity of Topoisomerase 2a (Top2a) in the lungs of mice that are being subjected to K. pneumoniae-induced ARDS augments innate immune response.

METHODS: To improve the genomic integrity of Top2a, recombinant rNEIL2, a DNA repair enzyme that initiates excision of oxidized DNA lesion via the DNA-base excision repair (DNA-BER) pathway, was transfected into the lungs of mice. In a control group, heat-inactivated rNEIL2 was transfected. These transfected mice were intranasally infected with 5 x 10^7 PFU of K. pneumoniae. Six hours post-infection, the lung genomic DNA was extracted and subjected to a high-sensitivity long-run real-time PCR technique for DNA-damage quantification (LORD-Q) of Top2a. Innate lung inflammation was quantified by performing BAL cell counts 48 hrs post infection.

RESULTS: Stimulating oxidative DNA-BER by transfecting the lungs with rNEIL2 prior to K. pneumoniae infection increased neutrophil recruitment by about 10-fold compared to mice transfected with heat-inactivated rNEIL2. K. pneumoniae infection induced 76.46 +/- 6.8 detected lesions in Top2a gene per 10Kb long genomic DNA in mice transfected with heat-inactivated rNEIL2. By contrast, in mice transfected with active rNEIL2, the infection induced only 54.74 +/- 8.1 detected lesions in Top2a gene per 10Kb, p < 0.04.

CONCLUSIONS: Stimulating oxidative DNA-BER in mice being subjected to K. pneumoniae-induced ARDS improves the genomic integrity of Topoisomerase 2a and augments innate immune response.
707 | Plantago Pollen Occurs Continuously Throughout the Spring and Summer Pollen Seasons in Central Ukraine

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RATIONALE: Plantain (Plantago) is an important pollen allergen in Europe. In Central Ukraine species of Plantago are found (P. major, P. lanceolata, and, to less extent, P. maxima, P. media) in a moderate climate zone located in the forest-steppe zone.

METHODS: Pollen collection from 2009 to 2018 used volumetric methods employing a Burkard trap placed at a height of 25 meters above the ground on the roof of Vinnitsa Medical University, Ukraine. Samples taken from March 1 until October 31 were analyzed by mean of three horizontal transects in years 2009 to 2011 and by means of twelve vertical transects at a bi-hourly mode in years 2012 to 2018 under light microscope with X400 magnification.

RESULTS: After season start, plantain pollen was found in aerobiological samples every day. Plantago pollen was recorded from the first days of May up to the middle of October. The longest pollen period for 116 days was seen in 2011 and the shortest, 69 days, in 2014. The highest concentration of 18 pollen grains per cubic meter was recorded on August 13, 2009. The average season was characterized by three periods of raised pollen concentration of plantain: in mid-May, in mid-June and in mid-August consistent with the flowering of different species of Plantago in Central Ukraine.

CONCLUSIONS: Pollen of Plantago species should be considered in hay fever diagnostics and prevention in Ukraine in patients with symptoms from May to October.

708 | Parental Observation of Environmental Exposures in the Home of Children With Asthma

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RATIONALE: Asthma is among the most common chronic diseases of childhood. Environmental exposures are common triggers for asthma. Rodents, cockroaches and mold have been reported in 55%, 40% and 48%, respectively, in homes of patients with asthma upon professional inspection. Carpeting, smoke exposure, and furry pets were also reported in 83%, 30%, and 57% of homes, respectively. We aimed to characterize environmental exposures recognized by parents/caretakers in the homes of children with asthma.

METHODS: Convenience sampling was utilized to enroll children who presented to the Allergy/Asthma/Immunology and Pulmonology Clinics at Children’s Mercy. Participants completed a questionnaire regarding their asthma and home environmental exposures and a descriptive analysis was performed.

RESULTS: Parents/caretakers (n=119) of children (mean/SD age 9.3 ± 4.1 years) with asthma completed the questionnaire. Seventy-five percent had persistent asthma and 70% were classified as poor/uncontrolled. Carpeting was present in more than 4 rooms in 43% of homes. Water leaks and/or mold, cockroaches and/or rodents in the home in the past 6 months were reported in 21% of respondents. Smoke exposure in the car/home during the last 6 months was reported in 16% of respondents and 59% reported cats and/or dogs in the home.

CONCLUSIONS: Carpeting and pets are commonly reported environmental exposures by parents of children with asthma. However, relatively few parents reported rodent/cockroach, water leak/mold, or smoke exposure. These potential triggers may be under-recognized in the homes of children with persistent and uncontrolled asthma. Interventions to improve layperson recognition may be useful in management.
710 Comparing the magnitude of meteorological variables and air pollutants as contributing factors to atopic dermatitis symptoms

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RATIONALE: Air pollution and meteorological variables play a role in the prevalence and progression of atopic dermatitis (AD). While it is clear that these factors contribute to the exacerbations of AD symptoms, less is known of the magnitude individual pollutants or meteorological variables contribute on AD symptoms.

METHODS: Using public available data (https://doi.org/10.5281/zenodo.56248), a multivariate linear regression was used to determine the relative weights of air pollutants and meteorological variables on AD symptom scores (SCORAD). Also, random forest was implemented to compare prediction models to classify the magnitude of air pollutants and meteorological variables.

RESULTS: When considering both meteorological and air pollutants together as predictors of SCORAD, DTR was highest (47.6%), and rainfall the lowest (2.3%). Among meteorological variables, the difference in magnitude ranged from 24 times lower (rainfall, temperature) to 2 times (RH); for pollutants, the highest was NO2 (11.3%), and the difference in magnitude ranged from 4 times to 2 times lower (NO2, O3, respectively). With different combinations of meteorological and pollutant variables, the prediction potential range from 50-60%.

CONCLUSIONS: Meteorological variables and air pollutants differ in their magnitude in which they are related to exacerbations of AD symptoms. Also, the results suggest that meteorological variables pose a greater impact on AD symptoms. Nevertheless, our models were not able to have strong prediction accuracy based on the available meteorological and air pollutant variables. Further analysis can determine the effects each pollutant and meteorological variable plays on AD symptoms.

711 Sensitization and Respiratory symptoms induced by Peach tree pollen in highly exposed Children and Adolescents.

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RATIONALE: Peach tree pollen (PTP) is relevant in sensitization in areas of great peach cultivars and induce several clinical entities involving airways. We studied PTP sensitization and symptoms in an exposed population of children and adolescents.

METHODS: We carried out a population study in Blanca (Murcia region, South-East Spain). We evaluated 6200 subjects who referred seasonal respiratory symptoms. They signed a written informed consent and answered an adapted questionnaire. We did prick tests (SPTs) to prevalent pollens, PTP and Pru p 3, as well as NPT with PTP to 11 randomly selected children and adolescents with positive SPT. We measured the response by symptoms score and acoustic rhinometry.

RESULTS: We included 659 subjects aged between 3 and 19 yo. No differences were found in gender. The 34% of them were sensitized to pollens: O.europaea 33%, P.pratense 26%; S.kali 19%, C.arizonica 17%, P.Judaica 13%, Pacerifolia 10% and A.vulgaris 9%. The 20% of them had positive SPT to PTP (median age 12 yo, 61% male, 89% atopic). The 11% were also sensitized to Pru p 3. These subjects referred Rhinitis (67%), Conjunctivitis (57%) and Asthma (18%). Six out of 11 NPT tested to PTP had a positive response.

CONCLUSIONS: In highly exposed children and adolescents, PTP is the third most prevalent in sensitization after olive and grass pollen and PTP induced symptoms after specific nasal challenge. The relevance of this pollen in non-work exposed subjects is shown in this work and we are actually characterizing the allergens involved.

712 The mite in the natural co-evolution of the trophic regions

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RATIONALE: In modern times it is known about climate change, an enormous responsibility is attributed to the human being, judged by the harmful effects to health, to the environment; Which is attributable to agents such as the mite; without taking into account that as living beings we are part of various vital plots associated with the process of natural co-evolution of the earth.

METHODS: Descriptive synthesis of multiple readings of the associated realities with the individuals that make up a systemic, dynamic and prospective cohort of a tropical city with a history of allergic diseases, defined in spatiotemporal and energy conditions determined by the vital conditions of the mite.

RESULTS: The biological, climatic and physicochemical latent variables showed a strong effect according to the spiral predictive simulation model (R2= 0.4) and a moderate effect of the energetic and socio-cultural variables (R2 <0.35).

CONCLUSIONS: Environmental dynamics biomass is transformed, the mite as a living being is integrated into the natural ecological cycles as opposed to the human lifestyles, somatizing as a risk factor.

713 Allergen Component Diagnosis of Patients with House Dust Mite Sensitization

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RATIONALE: The use of molecular allergy diagnostics may enhance specific allergen immunotherapy (AIT).

METHODS: 437 patients aged 34.6±5.4 years, 56.1% males 43.9% females, were assessed over five months in 2018. The allergochipALEX allowing major allergen component assessment was performed on patients sensitized to house dust mites, using Raptor Analysis MADs, (KU/L).

RESULTS: 106 (24.3%) were dust mite sensitized. Total serum IgE was elevated (294±4.3) in 89 (83.9%) individuals. Major components of D. pteronyssinus seen were: Der p 2 – in 88 (83.1%); Der p 1 - in 48 (45.3%); Der p 23 – in 48 (45.3%); Der p 5 – in 25 (23.6%); Der p 7 – in 18 (17.0%); and Der p 11 – in 9 (8.5%) ; major components of D. farinae: Der f 1 – in 67 (63.2%), Der f 2 – in 65 (61.3%); and tropomyosin Der p 10 in 9 (8.5%) of patients. Major components of Der p 2 and Der f 1 dominated, ranging from 0.12 kU/l to 38.2 kU/L, but 4 (3.8%) were sensitized only to Der p 5; 3 (2.8%) to Der p 23; 1 (0.9%) to Der p 11; and 9 (8.5%) co-sensitized to major components Der p 5, 7, 11 at higher levels (<p<0.05) of sIgE, than to Der p 2 and/or Der p 1.

CONCLUSIONS: Patients with sensitization to house dust mites may have combinations of sensitization to Der p 1 and Der p 2 and sIgE to Der p 5, 7, 11 and 23 suggesting optimization of AIT may require presence of multiple allergen components.
provocation relative to controls. Mechanistic studies failed to implicate rhinitis patients showed an augmented obstructive response to irritant
CONCLUSIONS: In this series of experiments, intermittent allergic showed no increases in mast cell tryptase, nor systematic alterations in neu-
not alter this response. Nasal lavage, performed on a subset of subjects, Double-blinded pre-treatment of subjects with a cholinergic blocker did
increases in nasal airway resistance in response to Cl2 provocation.

METHODS: A series of experiments was conducted utilizing 15 min. nasal-only exposures to dilute (1.0 ppm) chlorine gas (Cl2) as a provocation
Clean air served as a control exposure on separate days. A subset of sub-
Finally, in a stratified sample of 52 subjects, both allergic rhinitis and older age predicted significantly
increase in nasal airway resistance in response to Cl2 provocation. Double-blinded pre-treatment of subjects with a cholinergic blocker did not alter this response. Nasal lavage, performed on a subset of subjects, showed no increases in mast cell tryptase, nor systematic alterations in neu-

RESULTS: Subjective odor and irritation were rated, on average, as “slight” (< 1 on a 0-5 scale). Nevertheless, in a stratified sample of 52 subjects, both allergic rhinitis and older age predicted significantly increases in nasal airway resistance in response to Cl2 provocation. Double-blinded pre-treatment of subjects with a cholinergic blocker did not alter this response. Nasal lavage, performed on a subset of subjects, showed no increases in mast cell tryptase, nor systematic alterations in neu-

CONCLUSIONS: In this series of experiments, intermittent allergic rhinitis patients showed an augmented obstructive response to irritant
provocation relative to controls. Mechanistic studies failed to implicate mast cell degranulation, parasympathetic or neuropetide-mediated re-
flexes. Alternative mechanisms (e.g., epithelial cell activation) remain to be explored.

METHODS: Arthritis prone, DBA/1J male and female mice (8 week),
methods, were treated daily with ODE or saline for 5 weeks with collagen-induced arthritis (CIA) induced on days 1 and 21. Treatment groups included Sham (saline injection/saline inhalation), CIA (CIA/saline), ODE (saline/ODE); CIA+ODE (CIA/ODE). Bronchoalveolar lavage fluids, lung tissues, serum, and bones were collected.

RESULTS: ODE induced airway neutrophil influx, increases in inflamm-
atory mediators (TNF-α, IL-6, CXCL1, CXCL2), release of fibronectin (but not hyaluronan), and increased lung collagen staining as compared to sham. Co-exposure (CIA+ODE) resulted in reduced neutrophil and inflammatory mediator responses as compared to ODE alone, but lung tissue levels of hyaluronan, fibronectin and collagen staining were either augmented or remained increased in CIA+ODE. Arthritis inflammatory scores and serum anti-cyclic citrullinated peptide antibody were greatest in

CIĄ+ODE. Compared to male mice, female mice demonstrated reduced ODE-induced mediator release, hyaluronan and fibronectin as well as lower arthritis scores and serum autoantibody levels with co-exposure.

CONCLUSIONS: Autoimmune arthritis induction modulates the lung response to inhalant ODE exposure, impacting the inflammatory-intersti-
tial disease process. Congruent with epidemiologic findings, male mice were most susceptible to lung and articular disease resulting from ODE.

METHODS: As part of the New York City Neighborhood Asthma and Allergy Study, an asthma case-control study, 7-8 year-old children were recruited through a middle-income health insurance plan and followed to age 10-11. Serum samples were collected and their parents queried about ever being bitten by bed bugs at ages 7-8 and 10-11. Biotinylated cNP was bound to an ImmunoCAP and IgG antibodies measured in a subset of 20 children with and 30 children without a report of being bitten.

RESULTS: All 50 samples had some measurable IgG response. Children with a report of ever being bitten by age 10-11 had a higher geometric mean of IgG (2.3 mg/L [95% C.I. 1.5, 3.6]) than children without (1.1 mg/L [95% C.I. 0.81, 1.5]) (P=0.007). Of those reporting bed bug bites, 15 out of 20 had above median anti-cNP IgG values vs. 10 out of 30 among those without a report of ever being bitten (P=0.004).

CONCLUSIONS: Among NYC children, we detected serum IgG antibodies to a protein from C. lectularius. IgG concentrations were higher among children with a report of being bitten; however, we also observed some responses among those without a report of being bitten.
717 Psychological Profiles of Seasonal Allergy Patients in Vinnytsya, Ukraine

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RATIONALE: Seasonality of allergies to pollen and fungal spores may provoke obsession in sensitive individuals fearing the upcoming season. The leading psychologic profiles were assessed in patients having confirmed seasonal allergy.

METHODS: 44 patients, 24 females and 20 males having seasonal allergy were administered the MMPI (Minnesota Multiphasic Personality Inventory). Most were city inhabitants (55% of females and 75% of males) and most worked indoors (85% of males and 75% of females). Patients were seen at the National Pirogov Memorial Medical University in Vinnytsya, Ukraine.

RESULTS: Among men, 41.67% had a leading psycheotype on the 6th scale (rigidity, paranoia (Ra)) and over 25% had high scores on the 1st scale (hypochondriasis (Hs)). Among women, no leading psycheotype was seen, but 25% had simultaneous increase on three scales: the 2nd scale (depression (D)), the 3rd scale (hysteria (Hy)) and the 7th scale (psychasthenia (Pt)).

CONCLUSIONS: Men with pollen allergy have rigidity and paranoia characterized by accumulation of negative emotions, inability to solve problems with somatization in order to obtain secondary benefits. Women with pollen allergy show a complex psycheotype with increased depression, hysteria and psych asthenia. Psychotherapeutic support and psychologic pharmacotherapy should be considered in pollen allergic patients.

718 Aeroallergen and Foods Sensitization in Ecuadorian Adolescents From Two Different Regions

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RATIONALE: Environmental conditions are related to allergic sensitization (AS); few studies have described these associations with AS. Ecuador has different regions (Andes, Coast and Amazon) that allows to study these associations. The aim of this study is to report the AS to inhalants and foods among adolescents that live in Andes and Subtropic.

METHODS: A total of 1338 adolescents participated, 870 from Andes and 462 from Subtropico. To assess IgE mediated sensitization skin prick tests were used, with a total of 21 inhalants and 20 foods (ALK-Abelló). Sensitization was defined if wheal exceeded 3 mm to negative control. Prevalence rates of AS were reported in percentages; Pearson Chi-Square test was used to compare the prevalence rates of AS between the regions.

RESULTS: Most prevalent aeroallergen were house dust mites (D. pteronyssinus 36.4%, D. farinae 35.3% and B. tropicales 26.1%), cockroach (22.5%) and grasses (17.4%). There was no difference in prevalence of AS to house dust mites between the two regions. Cockroach AS was higher in Subtropical region (28.4%) than in Andes (19.4%) (p < 0.001). Higher sensitization to grass pollen was found in Andes respect to Subtropic (20.6 vs 11.5, p < 0.001). The most frequent food allergens were shrimp, whitefish and peanut (4.5%, 3.6%, 3.4%, respectively). We only found a higher sensitization to shrimp in the Subtropical versus Andean area (3.7 vs 6.6, p < 0.05).

CONCLUSIONS: AS is prevalent in Andean and subtropical adolescents in Ecuador, with differences in both inhalants and food sensitization between two regions. The allergological study should be focused by regions.

719 Bioinformatics and Proteomics Evaluations of Potential IgE Cross- Reactive Proteins in Novel Edible Insects and Shrimp for Food Safety

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RATIONALE: Historically, insects have been consumed in many countries, although rarely in Europe and U.S. The European Food Safety Authority recently recognized mealworm as a potential cross-reactive novel food with risk of allergic cross-reactivity for those with shrimp allergy. Regulators in the United States are asking developers to evaluate products containing cultured insects (crickets) for risks for crustacean allergic subjects, which we evaluated.

METHODS: Transcriptomes of cricket, mealworm, silkworm, and locust and allergenic crustaceans were compiled using de novo and reference based assemblers. Transcripts were compared to allergens in AllergenOnline.org via Blastx, focusing on sequences of tropomyosin and arginine kinase. Abundance of mRNA of these proteins were estimated using RNA-seq quantification with RSEM software. Protein levels were measured using untargeted proteomics by LC-MS/ MS to estimate the abundance of tropomyosin and arginine kinase. Potential IgE epitopes were predicted using five immunoinformatics programs. The predicted epitopes were compared to published epitopes from allergenic arthropod sequences. Specific IgE binding assays were performed to test IgE cross-reactivity using available shrimp and insect allergic sera.

RESULTS: High sequence identities were found with high abundance transcripts of tropomyosin and arginine kinase compared to sequences of shrimp allergens. Proteomics confirmed the presence of isoforms. Direct binding and inhibition assays using protein extracts noted positive IgE binding for some allergic subjects.

CONCLUSIONS: Some crustacean-allergic consumers are likely to experience cross-reactions if they consume foods containing proteins from crickets, mealworm, silkworm, or locust. Allergists should be aware and alert crustacean allergic patients.

720 The N-terminal Leader Sequence of Walnut Jug r 2 is a cross-reactive allergen

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RATIONALE: Peanut allergic individuals may also react to walnuts. Peptides from the N-terminal leader sequences (LS) of Jug r 2 (J2LS) are predicted to be cross-reactive, and have been shown to compete for peanut-specific IgE binding to Ara h 2. Our goal was to characterize the role of the J2LS in cross-reactivity among nuts.

METHODS: A 13 mer consensus sequence peptide (CSP) was designed based on an alignment of 3 similar (according to Structural Database for Allergic Proteins) polyglutamne rich, repeat sequences from the J2LS and a major IgE binding epitope of Ara h 2. An anti-consensus sequence peptide antibody (CSA) was generated and used to detect proteins in different nut extracts by western blot. CSA-binding bands were excised from SDS-PAGE and identified by mass spectroscopy. Competitive inhibition ELISA was used to measure the inhibition of CSP antibody and serum IgE binding to nut extracts with the consensus sequence peptide and variants thereof.

RESULTS: The J2LS is present in walnut extracts. The anti-CSP antibody recognizes multiple bands in various nuts, all of which are identified as known allergens. The CSP and variants are shown to inhibit the CSA and serum IgE from binding to extracts of peanut, walnut, cashew, pistachio and almond. The binding pattern of the CSA seems to mimic the IgE-binding pattern of almond allergic patients’ sera to almond extract.

CONCLUSIONS: The J2LS and most likely other vicilin LSs are present in mature peanut and tree nut seeds and could contribute to cross reactions in those allergic to peanuts or tree nuts.
**Sensitization Profiles to Hazelnut Allergens across the United States of America**

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**Rationale:** Measurement of IgE antibody to hazelnut components can aid in the prediction of allergic responses to the food. The objective of this study was to investigate the relationship between patient demographics (age, location) and patterns of allergic sensitization to hazelnut components across the USA and to investigate the degree of correlation between hazelnut sensitization with sensitization to other tree nuts, peanuts and their components.

**Methods:** Sera from 10,503 individuals with hazelnut extract-specific IgE (>0.35 kU/L) were analyzed for IgE antibodies to Cor a 1, 8, 9 and 14 by ImmunoCAP. A subset of these patients were analyzed for IgE antibodies to peanut, walnut and cashew nut IgE along with associated components.

**Results:** Among hazelnut sensitized individuals, children (<3 yrs) were predominantly sensitized to Cor a 9 and Cor a 14. Conversely, Cor a 1-specific IgE sensitization was much higher in adults than children, especially in the Northeastern USA. Cor a 8 sensitization was relatively constant (near 10%) across all ages. Cosensitization of hazelnut with other tree nuts as well as peanuts was shown to be related to correlation of IgE concentrations of individual component families.

**Conclusions:** We conclude that sensitization to individual hazelnut components is highly dependent on age and/or geographic location. Component correlations suggest that cosensitization to hazelnut and walnut may be caused either by their PR-10 allergens, nsLTPs or seed storage proteins whereas hazelnut/p walnut cosensitization is more caused by cross-reactivity of PR-10 (Cor a 1 and Ara h 8) and nsLTPs (Cor a 8 and Ara h 9).

**Informatics Analysis of Cross-Reactivity of Food Allergens in South Asian Cuisine**

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**Rationale:** Food allergy in South Asians is rising worldwide but there is limited understanding of the allergenicity of ethnic foods. Knowledge of the allergens and their cross-reactivity could significantly improve the management of food allergy in consumers of South Asian cuisine.

**Methods:** Based on a Pubmed literature review of 1343 publications documenting allergenicity of South Asian food allergens, we compiled a cumulative matrix of the number of independent reports of allergenicity and cross-reactivity. We compared the frequency of cross-reactivity with the taxonomic separation between food species. For cross-reactive species, we examined the list of known allergenic proteins to highlight the probable molecular basis of cross-reactivity.

**Results:** Based on our informatics analysis, we report the following categories of ethnic foods in South Asian diets: a) unlikely to be allergenic (e.g., horse gram, bitter gourd); b) allergenic in isolation (e.g., eggplant, saota); c) allergenic with reports of cross-reactivity (e.g., chickpea with pea, lentil, pigeon pea, peanut, soybean, kidney bean, black gram, sesame). We created a phylogenetic tree of South Asian foods to serve as an evolutionary guide to cross-reactivity. We provide a putative list of allergenic molecules that are likely to be the basis of the observed cross-reactivity (e.g., vicilin, cupin family).

**Conclusions:** Based on published literature, we have summarized allergen cross-reactivity in South Asian cuisine. While our results need further biological and clinical validation, our novel findings have the potential to guide care (e.g., diagnosis, avoidance, desensitization) in all food-allergic individuals who ingest South Asian foods, either occasionally or habitually.

**Molecular and Immunobiochemical characterization of cysteine protease from Phaseolus vulgaris.**

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**Rationale:** Studies have shown that Phaseolus vulgaris is a major sensitizer in Indian population. In the present study, cysteine protease from P. vulgaris was cloned, expressed and purified for immunobiochemical studies.

**Methods:** In silico approach was employed to study allergenicity of P. vulgaris sequences from NCBI and cysteine protease was selected for studies. Synthetic gene was subcloned into pET28a+ vector and affinity purified. Purified protein was tested for IgE binding using patients’ sera. Homology modelling was used to generate three dimensional model for cysteine protease and B & T-cell epitopes was identified using in silico tools.

**Results:** Allergenicity assessment showed that cysteine protease shared 56-70% identity with Act d 1, Act c 1, Car p 1, Ana c 2 and Der f 1 allergens. Furthermore, multiple sequence alignment revealed homology of conserved motifs. Cysteine protease was cloned, expressed and purified which resolved at 42 kDa. Nine out of twelve patients’ sera showed IgE binding with purified protein. Rictinus communis protease was used as template for homology model having 63% homology. Model showed overall quality factor of 96% in ERRAT and PROCHECK for the model showed that 92% of the residues were in most favourable regions of Ramachandran plot. However, the model requires loop refinement for discontinuous epitopes. Ten linear B-cell epitopes were predicted using in silico tools.

**Conclusions:** Cysteine protease was identified as allergen from P. vulgaris and showed significant identity with known allergens. Three-dimensional homology model was generated for cysteine protease and ten B-cell epitopes were identified by in silico tools.
724 Shared Cooking Equipment in Restaurants: A Quantitative Risk Assessment for Peanut-Allergic Consumers

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RATIONALE: Previous research confirmed the potential risk of accidental exposure to peanut for peanut-allergic consumers if dining at restaurants that share utensils when preparing various Asian dishes. The current study further expands knowledge surrounding possible transfer of peanut residue through shared cooking equipment.

METHODS: Shared equipment kitchen-based experiments were performed to investigate possible transfer of peanut-containing sauces into peanut-free dishes. The amount of residue (mg) sticking to professional cooking equipment (wok, sauce pan, mixing bowl) was measured after preparation of single-serve meals, before and after cleaning. Peanut-containing versions of popular sauces were used to represent three major themes in Asian cooking: sugar-based Pad Thai and General Tso’s sauces, and an oil-based Indian coconut curry.

RESULTS: Shared cooking equipment had mean potential transfer amounts of 830 – 15800 mg sauce (48 – 1559 mg peanut protein), dependent on equipment and recipe. In the majority of cases (32 of 35), no measurable residue was found after common cleaning practice (brief scrub with brush and warm water, no dishwasher sanitation assistance). However, in a few cases, up to 0.2 g sauce residue (up to 20 mg peanut protein) remained after cleaning.

CONCLUSIONS: Warm water and brush cleaning reduces the amount of peanut residue. Nevertheless there is a remaining risk of accidental exposure to peanut. Prior dose-response research indicates that 25% of the peanut-allergic population is predicted to have an allergic reaction when exposed to 20 mg peanut protein. This study confirms potential risk to a peanut-allergic consumer when Asian restaurants cook with shared pans or mixing bowls.

725 Grasshopper Sensitization In Patients Allergic To Crustaceans, House Dust Mite and Cockroach. Should Products Containing Grasshopper Come With A Warning?

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RATIONALE: We have previously described Anaphylaxis after first ingestion of grasshopper (GH) in patients who had a prior history of systemic reactions after eating crustaceans. These patients also had high levels of house dust mite (HDM) and cockroach (CR) allergy. The common cross reacting allergen was identified as Tropomyosin. In this abstract we report GH sensitivity in patients allergic to crustaceans, HDM and CR.

METHODS: Freeze-dried commercial GH (locusta migratoria) were made into a 1:10 w/v 50% glycerine in saline solution by the usual method. After obtaining informed written consent, patients and controls were skin tested (ST) by the Prick/puncture (PP) method to 1:10 w/v GH, and to 10 k AU HDM, 1:10 w/v lobster, 1:20 w/v crab and 1:10 shrimp extracts.

RESULTS: Control patients who had negative ST to HDM, crustaceans, shrimp and crab, had negative ST to GH. Crustacean allergic patients showed 93.2% reactivity to GH. CR allergic patients 64.7% positive ST to GH and HDM positive patients 22.8% positive ST to GH.

CONCLUSIONS: These results show a high % of ST reactivity to GH in patients who had no occupational nor recreational exposure to grasshoppers, but were sensitized to crustaceans, cockroach and HDM. These patients are potentially at risk for anaphylaxis if they eat GH. Recent reports of anaphylaxis to ingested grasshopper from China and Singapore, and the recent recommendation of the WHO advising entomophagy as a solution to world hunger, indicate the possibility of an increasing incidence of GH anaphylaxis. Should insect containing products carry a warning for allergic patients?

726 Hemocyanin Is A Shrimp Allergen In The U.S.: Clinical And Immunological Profiles Of Food Challenge-Proven Shrimp Allergic Patients

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RATIONALE: Tropomyosin is considered the major shrimp allergen. Hemocyanin is recognized as a shrimp allergen in Spain and Italy, but has been identified as a cross-reactive allergen between arthropods and shrimp in the U.S. We aim to identify allergens associated with shrimp allergy.

METHODS: Patients with history of reaction upon shrimp ingestion with +specific IgE (sIgE)/skin prick test (SPT) or avoiding shrimp due to +sIgE/SPT were recruited. All patients underwent shrimp oral food challenge (OFC) except those with recent history of anaphylaxis upon shrimp ingestion. Immunoblotting was done to assess IgE binding (band intensity/area) to shrimp proteins. T-test analysis was performed.

RESULTS: Twelve shrimp allergic (SA; 7 +OFC and 5 had history of anaphylaxis) and 18 shrimp sensitized (SS; -OFC) were enrolled. SA patients had IgE binding to more shrimp proteins with greater intensity than SS patients (tropomyosin 37 kDa, p = 0.03; hemocyanin 75 kDa, p = 0.01; hemocyanin 72 kDa, p = 0.01; arginine kinase [AK] 50 kDa, p = 0.04; myosin light chain [MLC] 18 kDa, p = 0.01). The most common IgE binding in shrimp allergic patients was to tropomyosin (91.7%), hemocyanin (75 and 72 kDa, both 58.3%), AK (50%), then MLC (25%). In sensitized patients, the most common IgE binding was to tropomyosin (55.6%), hemocyanin 72 kDa (22.2%), then hemocyanin 75 kDa (5.6%).

CONCLUSIONS: Combination of multiple IgE binding to shrimp proteins by immunoblotting can potentially predict who is at risk for clinical reactivity to shrimp, potentially minimizing the need for an OFC. Our study shows hemocyanin may be an important allergen in shrimp allergic patients in the U.S.
Simultaneous Quantification of Major Food Allergens Using Fluorescent Multiplex Array

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RATIONALE: Quantification of food allergens is increasingly important for dose assessments of food preparations used in oral immunotherapy (OIT), food allergy prevention, and monitoring safety in the food industry. Our aim was to develop and validate a multiplex immunoassay capable of simultaneously measuring eleven major food allergens from peanut, cow’s milk, shellfish, egg, cashew, soy and hazelnut.

METHODS: The multiplex array was developed on the Luminex xMAP system. Microspheres coupled to specific monoclonal antibodies were used for allergen capture. Biotinylated specific monoclonal or polyclonal antibodies were used for detection. Reference standards were formulated from natural or recombinant allergens, with purity established by mass spectrometry. A full method validation was performed to determine parameters of linearity, range, limits of quantification and detection, accuracy and precision of the multiplex food immunoassay.

RESULTS: Full method validations were completed for the eleven major food allergens. The standard curves for all analytes allow for quantification over a broad dynamic range. The limits of detection (LLOD) were as low as 0.01 ng/mL. Intra- and inter-assay accuracy and precision for three samples assayed in triplicate on four occasions passed acceptance criteria within the range of 70-130% recovery and a coefficient of variation of <15%.

CONCLUSIONS: A quantitative, accurate and precise multiplex immunoassay was validated for the simultaneous detection of eleven major food allergens. The multiplex array provides a sensitive and efficient tool for measuring specific food allergens, as opposed to generic food source proteins, with potential applications for risk assessment in the food industry and standardization of OIT products.

The NMR structure and IgE Epitopes of Ara h 1 Leader Sequence

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RATIONALE: The vicilins from peanut, walnut, cashew and pistachio are considered major allergens and are translated with leader sequences (LS) that are cleaved before yielding the mature protein. While previous work has shown that some contain immunodominant IgE epitopes, their structure has not been solved.

METHODS: Linear IgE epitopes were identified using microarrays generated by printing 15-mer peptides overlapping by 10 aa on slides and incubating with peanut allergic sera. IgE binding by allergic sera was detected with a fluorescently-labeled antibody. Western blots and mass spectrometry were used to show the presence of the LS in peanut and walnut seeds. The NMR structure of the Ara h 1 LS was determined and the IgE binding sites modeled on this structure.

RESULTS: The epitopes with the highest degree of IgE binding were clustered within regions that were near cysteine residues. Of the patients tested, >90% showed IgE binding to those epitopes even if they recognized no other epitopes in the Ara h 1 LS. The NMR structure showed 4 of the cysteine residues are disulfide bonded and hold together two parallel alpha helices. IgE binding is shown to be located at the junction of the C-terminal region of the alpha helices and the beginning of each flexible loop.

CONCLUSIONS: The results indicate that cysteine residues known to confer high structural stability to allergens may also coincide with areas of increased IgE binding frequency and intensity in Ara h 1 LS. The LS contains multiple immunodominant epitopes and may contribute to cross-reactivity and nut allergy.
**ABSTRACTS**

**ABSTRACT 730**

**IgE and IgG4 Epitope Profiles for the Major Peanut Allergens from Peanut Allergic Patients Undergoing Oral Immunotherapy**

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**RATIONALE:** Peanut oral immunotherapy (OIT) is a promising treatment to desensitize peanut allergic patients. Our aim was to identify and assess changes in IgE and IgG4 epitopes of the major peanut allergens, Ara h 1, 2, 3, and 6, recognized by peanut allergic patients undergoing peanut OIT in the US.

**METHODS:** Microarray slides containing synthetic overlapping 15-mer peptides offset by 5 aa of the major peanut allergens, Ara h 1, 2, 3, and 6, were incubated with sera from 27 peanut allergic patients from the US enrolled in Phase 2 and Phase 3 peanut OIT trials. The pre-trial and post-trial sera were collected between 5 months to a year apart, and were tested for IgE and IgG4 binding to the linear peptides using immunofluorescence.

**RESULTS:** IgE and IgG4 epitope maps for the four major peanut allergens were developed. While IgE binding patterns to the immunodominant epitopes (recognized by >70% of the sera) for each allergen did not seem to change much, there was significant changes in the intensity of the antibody binding for a majority of patient sera. Also, the peptide-specific IgE/IgG4 immunofluorescence ratios from pre-trial sera were higher than the post-trial sera.

**CONCLUSIONS:** These results demonstrated that peanut OIT induces a shift in the IgE/IgG4 peptide-binding ratios in peanut allergic sera, but does not seem to alter the actual peptide binding patterns significantly after 1 year of OIT. This type of knowledge can be useful in the identification of peptide biomarkers that may indicate desensitization or tolerance of allergic individuals to peanut.

**ABSTRACT 731**

**The Efficacy of Walnut IgE Component Testing in Determining Walnut Sensitivity**

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**RATIONALE:** Prior studies indicate that walnut component testing (WCT) may serve as a better indicator for clinical reactivity than skin prick testing (SPT) and IgE measurements. This study was undertaken to specifically assess the utility of WCT in determining clinical reactivity in nut allergy.

**METHODS:** A retrospective chart review was performed on four patients who underwent WCT to jugl r 1 and 3. None of the patients ate products containing walnuts (PCW) at the time of WCT due to prior positive allergy testing with PCW. Three of the patients reported tolerating PCW prior to allergy testing and one developed throat itching upon ingestion. The charts were reviewed for demographic data, birch specific IgE (bIgE), wIgE levels, walnut rJug r 1 and 3 levels, and a trial of PCW.

**RESULTS:** Average total IgE=660 (SD: 517.25; N=4), bIgE=9.58 (SD=7.41; N=4), wIgE=0.49 (SD=0.13; N=4). Both walnut rJug r 1 and 3 were reported as <0.10 in each of the patients. All four patients tolerated walnuts during in-office or home challenge.

**CONCLUSIONS:** This was a pilot study undertaken to investigate the utility of WCT. This study suggests that WCT can determine clinical reactivity in birch pollen allergic patients with positive wIgE.

**ABSTRACT 732**

**FENUGREEK: A HIDDEN ALLERGEN TO CONSIDER IN PEANUT ALLERGIC PATIENTS.**

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**RATIONALE:** Fenugreek (Trigonella foenum-graecum) is a legume plant traditionally used as spice in Indian-style foods. Although it has been used since ancient times, its allergenicity has only been reported in the last two decades, often as hidden allergen, in peanut allergic patients.

**METHODS:** A 10-year-old girl, with known peanut allergy was referred to our unit with a history of severe anaphylaxis after eating curried chicken. Skin prick testing (SPT) and slgE measurements (ImmunoCAP Thermostherm®) were performed with the implicated curry and its components and peanut. IgE-binding-protein molecular mass study (SDS-PAGE - Immunoblotting) was also performed with the curry powder and its ingredients, fenugreek (grains and powder) and a whole extract of roasted peanut. Immunoblotting inhibition studies were also carried out.

**RESULTS:** SPT were positive to peanut (13 mm), curry powder (18.5 mm), fenugreek (23 mm). The diameter of the wheal on SPT with the remaining spices contained in curry was less than the histamine control. Specific IgE: peanut >100 KU/L, curry 35.20 KU/L, fenugreek 45 KU/L, Ara h 2 >100 KU/L. SDS-PAGE-Immunoblotting: The peanut protein band pattern was in accordance with previous studies. Curry and fenugreek extract showed similar pattern: IgE-binding bands 50, 28 and 22 kDa (same molecular mass bands are observed in peanut pattern). Cross-reactivity study with curry and fenugreek extract as solid phase: peanut extract inhibited completely IgE binding to fenugreek and curry extract.

**CONCLUSIONS:** Cross reactivity between peanut and fenugreek is demonstrated. Physicians might be aware about possible curry allergy in peanut-allergic patients.

**ABSTRACT 733**

**Beef Sensitization in Pediatric Patients in the Midwest**

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**RATIONALE:** Food allergy is on the rise. It is estimated that 8% of children and 6% of adults have food allergies. It is about 3-15% of pediatric patients have meat allergy. Beef allergy is the most reported one among meat allergy. It can reach up to 6.5% in atopic dermatitis pediatric patients. The aim is to assess the sensitization rate to beef in pediatric patient in the Midwest.

**METHODS:** Laboratory results of 483,490 specific IgE evaluations were reviewed to identify patients with positive IgE to beef. IgE determinations were performed from the year 2000 to 2015 on pediatric patients, ages 0.5 to 18 years, using the ThermoFisher ImmunoCap instrument. A test was considered positive when specific IgE values were greater than 0.35 KU/L.

**RESULTS:** 509 individual patients were identified. Of those, 128 (25%) patients had positive IgE to beef; 86 (67%) were male while 42 (32%) were female.

**CONCLUSIONS:** The prevalence of beef sensitization in pediatric patients in the Midwest of the US is similar to previously reported in the literature. Allergist need to be aware of beef allergy since beef is not one of the eight major food allergens in pediatric patients.
Skin Dendritic Cells Progressively Subvert The Activation Of Pathogenic Type-2 Immunity Upon Epicutaneous Allergen Immunotherapy

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RATIONALE: Epicutaneous specific-immunotherapy (EPT) is a promising treatment for food allergies leading to a higher tolerance threshold. The desensitization process has been shown to be dependent on EPT-induced regulatory T cells and correlated with profound immune deviation. To date, little is known about the contribution of skin dendritic cells to the efficacy of EPT.

METHODS: To address this question, we used a preclinical mouse model of allergy to ovalbumin (OVA) in which sensitized mice were EPT-treated once a week with OVA-containing patches for 48h over an 8 weeks period. Dynamics and phenotype of skin dendritic cell (sDC) subsets were assessed by flow cytometry and transcriptomics analysis. DC function was further characterized by in vitro T-cell assays and conditional DC-depleted mouse models.

RESULTS: Our results show that, while sDC subsets (Langerhans and dermal conventional cDC1 and cDC2) retain their capacity to capture OVA in the skin throughout EPT treatment, the numbers of OVA+ DCs emigrating towards the draining lymph nodes progressively decreased after 3 to 8 weeks of treatment. In addition, their maturation status was also downregulated, as notably shown by weaker CD86 surface expression. Consequently, EPT DCs progressively lost their capacity to efficiently prime/reactivate antigen-specific CD4+ Th2 cells, in contrast to Treg stimulation. We are currently investigating the mechanisms by which each skin DC subset subverts the activation of pathogenic type-2 immunity to prevent the development of allergic symptoms.

CONCLUSIONS: Taken together, our results open new avenues to better understand the complex mechanisms that lead to the efficacy of EPT.

Efficacy and Safety of Epicutaneous Immunotherapy for Peanut Allergy in Subjects With and Without Atopic Dermatitis

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RATIONALE: In the pooled Phase 3, randomized, double-blind, placebo-controlled trials (P3PCT), PEPITES and REALISE, peanut-allergic children aged 4-11 years were treated with daily epicutaneous immunotherapy (EPT) with a 250-µg peanut patch (VP250) or placebo (PBO). PEPITES assessed EPT safety and efficacy, while REALISE assessed EPT safety without requiring food challenges. It is important to establish whether underlying skin disease affects the safety or efficacy profiles of EPT.

METHODS: Post-hoc analysis of the P3PCT explored differences in safety and efficacy among subjects with and without a diagnosis of ongoing atopic dermatitis (AD) at baseline.

RESULTS: Treatment-emergent adverse events (TEAEs) were common in P3PCT (92% in VP250; 87% in PBO), consisting primarily of local skin reactions that were clinically managed with mildly potent topical corticosteroids and antihistamines. In the VP250 and PBO arms, respectively, among the AD subjects, 92% and 85% of subjects experienced a TEAE; 92% and 88% in non-AD subjects. In subjects with ongoing AD, there was no increased frequency of a TEAE of eczema distant from the patch site with VP250 (15%) vs PBO (15%); among those without AD, 2% and 1% experienced, respectively. Within PEPITES, differences in Month 12 responder rates between VP250 and PBO were significant in both AD (p<0.001) and non-AD (p<0.01) subgroups. There was no detectable difference in placebo-corrected treatment responders between the subgroups (interaction p-value = 0.80).

CONCLUSIONS: Efficacy assessments were consistently in favor of VP250, irrespective of AD status at study entry. Safety assessments were similar in AD and non-AD subjects.

The combined effect of Lactobacillus rhamnosus and egg oral immunotherapy in a mouse model of egg allergy: Preliminary study

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RATIONALE: This study was aimed to analyze the effect of probiotics administrated simultaneously during oral immunotherapy (OIT) in a mouse model of egg allergy.

METHODS: C3H/HeJ mice were sensitized by intragastric administration of ovomucoid (OM). As OIT, increasing doses of OM were administrated orally to sensitized mice. Lactobacillus casei variety rhamnosus (Lcr35) was also administrated. The mice were divided into 4 groups; controls (no OIT), OIT, Lcr35, and OIT plus Lcr35 (OIT+Lcr35). The effect of OIT and Lcr35 treatment was estimated using symptom score, rectal temperature, OM-specific IgE, IgA, IgG1, IgG2a by ELISA and histology stain of small intestine.

RESULTS: The severity of anaphylaxis decreased in all treatment groups. Simultaneous administration of Lcr35 during OIT further reduced the severity of anaphylaxis as compared with controls and OIT. The protective effects still remained 2 weeks after off-treatment in all treatment groups. A significant decrease of OM-specific IgA, IgG1 and IgG2a levels in both OIT and OIT+Lcr35 group. However a significant decrease in OM-specific IgE level was observed only in OIT+Lcr35 treated mice, and sustained 2 weeks after off-treatment. Mucin amount in small intestine was reduced by OIT, OIT+Lcr35 and Lcr35 treatment with the lowest level in OIT+Lcr35 group.

CONCLUSIONS: We found that Lcr35 treatment during OIT had some synergic effect for protection from anaphylaxis in a mouse model of egg allergy. These findings are need to be confirmed by mouse studies including more detailed immunological profiles and human studies.
Jörg Tost, Yimin Shen, Elodie Roche, Camille Plaquet, Veronique Dheilly, Lucie Mondoulet, Christian Daviaud, Christophe M. Dupont, MD, Hugh A. Sampson, MD, FAAAAI, and Vincent Dioszeghy, PhD.

**Rationale:** Immunotherapy is a promising treatment for food allergy with oral (OIT) and epicutaneous (EPIT) immunotherapy protocols being investigated in late-phase clinical trials. There is increasing evidence that molecular mechanisms differ between the two types of immunotherapy. In this study, we investigated the kinetics of miRNA expression patterns underlying the therapeutic effect of EPIT and OIT.

**Methods:** BALB/c mice were orally sensitized to peanut and treated with EPIT, OIT or not treated (sham). Mice (n = 168) were sacrificed during treatment at 1, 2, 4, 6 and 8 weeks; and 8 weeks after the end of treatment. MiRNAs were analysed in sorted splenic CD4+ cells using high-throughput sequencing on a HiSeq4000 and validated in an independent experiment (n = 84) by LNA–enhanced qPCRs.

**Results:** Global miRNA profiles reproducibly distinguished EPIT-treated mice from controls and/or OIT-treated mice early after initiation of treatment. Up to 200 MiRNAs were found differentially expressed (padj < 0.05) between protocols with a large overlap of MiRNAs between adjacent time points. MiRNAs common to both immunotherapy protocols included miRNAs controlling T cell differentiation and function (e.g., miR-24-3p and miR-193b-3p), but most miRNA changes were specific to each protocol. Notably, expression changes of miRNAs previously associated with allergy and asthma including the paradigmatic anti-inflammatory mir-146a/b-5p were only detected in EPIT treated animals.

**Conclusions:** Immunotherapy leads to early and reproducible changes in miRNA expression specific for OIT or EPIT respectively, shortly after the initiation of treatment. Our study provides further evidence for diverging molecular alterations underlying different immunotherapy protocols pointing to different molecular mechanisms of action.

**Withdrawn**
**740 Dosing and Safety of Peanut Food Equivalents After Immunotherapy Trials**

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**RATIONALE:** Regular peptide consumption after immunotherapy may provide continued protection against accidental exposures, however limited data exists regarding its long-term safety.

**METHODS:** Past participants in peanut immunotherapy trials were enrolled in a longitudinal observational study. Those desensitized to ≥300mg of peanut were instructed to incorporate dietary peanut. We reviewed peanut food equivalent dosing and associated reactions in 55 subjects who completed oral (OIT) or sublingual immunotherapy (SLIT) studies between 2010-2017.

**RESULTS:** The majority of subjects were male (55%), Caucasian (94%), and participated in an OIT trial (73%). Peanut consumption was continued in 49/55 (89%) subjects. Adverse reactions, including EoE in one subject, and taste aversion were causes for discontinuation. Median peanut consumed was 600 mg (mean 808 mg, 100-4800 mg). Thirty-one subjects (74%) consumed peanut daily. Lower peanut consumption correlated with older age (r = -0.17). Ten (23.8%) subjects reported reactions with urticaria, gastrointestinal symptoms, and oropharyngeal pruritus, the most common. The majority of reactions were treated with antihistamines; however 1 reaction required epinephrine and 2 required EMS. There was no correlation between peanut dose and reactions. Participants in SLIT trials consumed less peanut (median 500 mg, mean 543 mg) compared to OIT participants (median 600 mg, mean 955 mg); however more reactions with dosing were reported with OIT (7/10).

**CONCLUSIONS:** The majority of subjects continued dietary peanut up to 8 years after study completion. Food equivalents may be a safe option for maintaining desensitization. Further study is needed to understand the impact of age and types of immunotherapy on peanut consumption and reactions.

**741 Irradiated Almond Flour Meets Established Criteria for use in Oral Immunotherapy**

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**RATIONALE:** Almond, a popular tree nut, can cause IgE-mediated allergic reactions. Almond flour from various vendors are often contaminated with high levels of microbes. Irradiation is a method that can decrease bioburden, however, irradiated almond flour used in oral immunotherapy (OIT) trials has not been characterized. We aimed to quantify relative amounts of the major almond allergen (Pru du 6) and bioburden levels present in irradiated almond flour used in OIT trials and assess whether these parameters are stable.

**METHODS:** SDS-PAGE gels and densitometric analysis of Pru du 6 were used to assess allergen content in almond flour exposed to gamma irradiation (Minimum/Maximum Dose of 5.0kGy – 30.0kGy). Bioburden testing was conducted on two different lots of irradiated almond flour for the presence of Escherichia coli, salmonella, yeast, mold, and total aerobic bacteria.

**RESULTS:** Relative amounts of the major almond allergen (Pru du 6) was similar between the two different lots of irradiated almond flour and remained stable over a twelve month period (with a variance of ≤10%). E. coli and salmonella were absent from both lots of irradiated flour. Yeast, mold, and total aerobic bacteria were within established US Pharmacopeia guidelines on both lots tested and remained within the criteria over a period of twelve months.

**CONCLUSIONS:** Irradiated almond flour used as a drug product contains the major almond allergen and has low bioburden levels. Both these parameters remain stable over a 12-month period and met criteria established by FDA for an orally delivered drug product.

**742 Identification of Peanut-Allergic Participants for Oral Immunotherapy With AR101 Using Clinical Reaction History and Immunologic Markers Without Oral Food Challenge – A Comparison Between RAMSES and PALISADE Trials**

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**RATIONALE:** RAMSES, a phase 3, multicenter, randomized, double-blind, placebo-controlled, real-world safety study of AR101 (an investigational oral biologic drug used in oral desensitization immunotherapy), used readily available clinical data to identify eligible participants. We sought to compare baseline characteristics of participants in RAMSES to those from PALISADE, a phase 3 trial of AR101, which in addition to clinical data, utilized a screening double-blind, placebo-controlled food challenge (DBPCFC) to determine eligibility.

**METHODS:** RAMSES enrolled participants ages 4-17-years-old in North America with a physician-confirmed diagnosis of peanut allergy, skin prick test (SPT) mean peanut wheal diameter ≥8mm, and peanut sIgE ≥14kUA/L. PALISADE enrolled participants based on clinical history, SPT mean peanut wheal diameter ≥8mm and/or peanut sIgE ≥0.35kUA/L, and reaction at screening DBPCFC. Summary statistics for baseline characteristics are compared between RAMSES and PALISADE participants 4-17-years-old.

**RESULTS:** Subjects in both studies (RAMSES N=505; PALISADE, N=496) were predominantly male (63.4%; 57.3%) and Caucasian (78.2%; 78.4%) with a median age of 9-years (both trials). Atopic comorbid disease frequencies were comparable between trials: allergic rhinitis (74.5%; 71.8%), atopic dermatitis (59.2%; 62.1%), other food allergies (52.7%; 65.5%), and asthma (49.5%; 52.8%). Peanut sIgE (median [IQR]: 93.5kUA/L [42.8, 201.0]; 71.3kUA/L [19.7, 202.0]) and SPT wheal diameter (median 13.5mm [10.5, 19.0]; 11.0mm [9.0, 15.0]) were similar.

**CONCLUSIONS:** Baseline characteristics appeared similar in RAMSES and PALISADE participants, despite the former study not requiring a DBPCFC. This suggests that it is feasible to identify potentially eligible peanut-allergic individuals with the use of readily available clinical data, which aligns with routine clinical practice.
743 Peptide-based immunotherapy enhances vitamin A metabolism and induces RORγ+ regulatory T cells

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RATIONALE: Oral immunotherapy (OIT) with peptides has proved more effective than that with intact allergens in providing desensitization against food allergy. The mechanism by which food peptides confer higher protection was investigated.

METHODS: BALB/c mice sensitized to egg white (EW) with the aid of cholera toxin (CT) were subjected to OIT with intact and pepsin-hydrolysed EW (EP). Changes in the caecal microbiota and its metabolism, generation of barrier-protective responses in the small and large intestine and expansion of regulatory T cells were studied.

RESULTS: Treatment with EP was superior to that with EW in terms of reduction of anaphylaxis and levels of specific antibodies. OIT with EP, but not with EW, modulated the microbiota by restoring the levels of some members of the order Clostridiales (clusters IV and XIVa) that were affected by CT-induced sensitization. Mice treated with EP exhibited upregulated intestinal expression of Il22 and Muc2, which encode for factors that contribute to reinforce the epithelial barrier function, as well as Aldh1a1, Aldh1a2 and Tgfβ1, that take part in the conversion of vitamin A into retinoic acid. Tolerance induced by EP paralleled the enhanced expression of Foxp3, Rorc and Il17 in non-lymphoid and lymphoid tissues and the development of Foxp3+ cells that simultaneously expressed RORγt.

CONCLUSIONS: The benefits of peptide OIT were associated to vitamin A metabolism and development of immune cells that depend on RORγt for their transcriptional regulation.

744 Alternative dosing of omalizumab as an adjunct therapy during multiallergen oral immunotherapy in food allergic patients

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RATIONALE: Oral immunotherapy (OIT) is a promising treatment option for desensitizing patients to their food allergens. Little is known about whether desensitization rates differ among children, adolescents, and adults.

METHODS: In a double-blind, placebo-controlled, randomized study, 120 peanut allergic participants aged 7-55 years old were randomized to receive peanut or placebo OIT over 104 weeks. Twenty-five participants were randomized to receive placebo, while 95 underwent build-up to a maintenance dose of 4 g peanut protein daily. Treatment assignments currently remain blinded, and treatment allocation is not yet known. Double-blind, placebo-controlled food challenges (DBPCFCs) to peanut were conducted at week 104 to assess desensitization. Chi-squared tests were performed to assess percentage of success in 3 age groups in the blinded dataset: age < 12 years (children), 12-17 years (adolescents), and 18-55 years (adults).

RESULTS: Alternative dosing of omalizumab as an adjunct therapy during multiallergen oral immunotherapy (mOIT) trials is typically dosed based on the FDA approved asthma dosing guidelines targeting a monthly dose of at least 0.016 mg/kg/(IU/mL). However, dose-finding studies have yet to be performed to provide guidance on the minimum dose necessary for food allergy.

METHODS: In the intent-to-treat population, consisting of 69 children, 29 adolescents, and 22 adults, 77%, 62%, and 45%, respectively, successfully passed the week 104 food challenge to a cumulative tolerated dose of 4 g of peanut protein (p = 0.0184). Among those who remained in the study and underwent DBPCFCs at week 104 (per-protocol), 82%, 75%, and 67%, respectively, were successful (n = 65, 24, 15, respectively)(p = 0.42).

CONCLUSIONS: Our preliminary data suggest that LD and SD omalizumab dosing have a similar rate of AEs and TTM in this pilot mOIT study. Further phase 2 randomized controlled trials are needed to better define optimal dosing strategies for omalizumab in food allergy.

745 Desensitization rates to peanut protein during OIT among children, adolescents, and adults

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RATIONALE: Food allergies affect children and adults worldwide. Oral immunotherapy (OIT) is a promising treatment option for desensitizing patients to their food allergens. Little is known about whether desensitization rates differ among children, adolescents, and adults.

METHODS: Participants aged 7-18 years (n = 41) with multiple food allergies were enrolled and received three monthly doses of 150 mg of omalizumab prior to initiating mOIT for 16 weeks. Each participant’s standardized omalizumab dose was calculated by dividing their 150 mg dose by their weight and total IgE. Participants were grouped according to this standardized dose, with those receiving less than 0.016 mg/kg/(IU/mL) categorized as low-dose (LD) and the remainder were categorized as standard-dose (SD). Rates of adverse events (AEs) and time to OIT maintenance dose (TTM) between the two groups were analyzed.

RESULTS: Thirty-four participants were categorized as receiving LD (<0.016 mg/kg) omalizumab; seven participants received SD (≥0.016 mg/kg) of omalizumab. The median per-person AE rates for LD and SD were 0.123 and 0.0083, respectively (p = 0.07). At 16 weeks, 56% and 71% of participants in the LD and SD groups, respectively, had reached maintenance (p = 0.68).

CONCLUSIONS: Our preliminary data suggest that LD and SD omalizumab dosing have a similar rate of AEs and TTM in this pilot mOIT study. Further phase 2 randomized controlled trials are needed to better define optimal dosing strategies for omalizumab in food allergy.
All abstracts are strictly embargoed until the date of presentation at the 2019 Annual Meeting.

746 Dendritic Cell Frequencies are Early Markers of Desensitization in Peanut Oral Immunotherapy

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RATIONALE: Dendritic cells are important mediators in the early presentation of antigen and regulation of the differentiation of T cells. Peanut oral immunotherapy (POIT) results in desensitization in most peanut allergic individuals (responders), but not in others due to allergic reactions (non-responders). Delineation of early immunologic changes contributing to desensitization would help clarify the POIT mechanism of action. Here we analyze dendritic cell (DC) populations in pediatric POIT subjects.

METHODS: In a phase 1 single-center study, 15 subjects between 5-12 years with peanut allergy on POIT underwent immune evaluation at 0, 6, 12, and 24 weeks after initiation of therapy and responders were compared to non-responders. The distribution frequency of plasmacytoid DCs (pDCs), myeloid DCs (mDCs) and tolerogenic DCs (DC10s) from peripheral blood samples were measured in vitro. One-way ANOVA was used for analysis.

RESULTS: Non-responders to POIT demonstrated a higher frequency of inflammatory pDC, IL-6 producing populations (Lin-HLADR+CD123+IL6+) (p=0.047) and a lower frequency of tolerogenic DC10 populations (Lin-HLADR+CD1c+CD14+) (p=0.004), compared to responders. POIT responders demonstrated a decline in OX40L expressing mDCs (Lin-HLADR+CD1c+OX40L+) (p=0.0357). Overall non-responders demonstrated a larger decline in DC10s compared to responders (p=0.0041).

CONCLUSIONS: POIT responders have reduced OX40L expressing mDCs and increased DC10s, suggesting a shift away from Th2 polarization. In contrast, non-responders demonstrated an increase in proinflammatory pDCs producing IL-6, which may contribute to the inhibition of Treg mediated suppression. In conclusion, these findings suggest that dendritic cells could potentially serve as an early marker of desensitization in subjects undergoing POIT.

747 Back to Life, Back to Reality – What Happens after Peanut Immunotherapy? A Long-Term Follow up Study on Perceptions of Safety and Lifestyle

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RATIONALE: Regular peanut consumption after immunotherapy may provide protection against accidental exposures, but limited data exists regarding long-term effects on patient perceptions of safety and lifestyle.

METHODS: Past participants in peanut oral (OIT) or sublingual (SLIT) immunotherapy studies at UNC between 2010-2017 were enrolled in a longitudinal observational study. Those demonstrating tolerance to ≥300mg of peanut were instructed to incorporate dietary peanut. A Qualtrics survey was administered via telephone to assess patient/parental perceptions of safety and lifestyle.

RESULTS: 55 patients (median 2.9 yrs (1.2mo-7.5yrs) post-study completion) completed the survey. 89% reported continued peanut ingestion. 98% of parents “definitely” or “probably” felt their child was safer, 92.8% and 94.5% “definitely” or “probably” felt their child’s quality of life and parental quality of life was improved, respectively. 87.3% consumed products labeled “may contain peanut”, 92.7% felt more comfortable eating at restaurants, and 87.5% of parents were more comfortable with their children in unsupervised social settings. 50% of patients who discontinued peanut reported definite or probable improvement in all survey parameters. Notably, 65.5% reported allergies to other food(s). 85% carried epinephrine autoinjectors “often”, and only 60% saw an allergist annually.

CONCLUSIONS: Regular ingestion of peanut food after completion of food immunotherapy is associated with improved perceptions of safety and life satisfaction in patients and parents persisting years after study completion. Benefit was seen even in patients discontinuing peanut ingestion or also having allergies to other food(s). Unintended consequences may include increased risk-taking behavior, such as not carrying an Epipen or following up regularly with an allergist.

748 Component IgE and IgG4 levels in patients with natural tolerance or oral immunotherapy treatment

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RATIONALE: Biomarkers of sustained unresponsiveness following oral immunotherapy (OIT) are actively being investigated. Unlike children desensitized through OIT, food-allergic children who develop natural tolerance (NT) do not usually require daily allergen ingestion to maintain tolerance. We sought to evaluate biologic differences between these populations, focusing on egg and milk.

METHODS: We assessed whole and component IgE and IgG4 titers of milk (Bos d4,5,8) and egg (Gal d1,2,3) to individuals 36 weeks post-OIT regimen (n=13 milk, 26 egg), and with NT (n=20 milk, 30 egg). NT was defined as prior doctor diagnosed food allergy with history of reaction, followed by self-reported outgrowth.

RESULTS: Patterns between egg and milk differed. The egg-NT cohort had significantly (FDR-adjusted P<0.01) more patients below the limit of detection for egg-specific or component IgE than children desensitized by OIT. While 45% of egg-NT children had detectable levels of IgE to at least one component, 56% of post-egg OIT children had detectable levels to all three components. For milk, only Bos-d8-specific IgE was significantly (FDR-adjusted P<0.01) lower in NT children than in those treated by OIT. No significant differences were detected in IgG4 levels between NT and post-OIT patients for either allergen.

CONCLUSIONS: While changes in IgG4 are similar between groups, OIT does not appear to reduce component-IgE to comparable NT levels within the studied time frame. Further, these differences in IgE trends may be allergen specific. Understanding mechanistic differences between NT and OIT will provide insight for potential therapeutic targets and aid in directing post-OIT care.
Epicutaneous Immunotherapy (EPIT) for Peanut Allergy in Young Children

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RATIONALE: Daily EPIT with Viaskin peanut patch (VP) has been shown to be superior to placebo (PBO) in desensitizing peanut-allergic children aged 4-24 years. VP has not been investigated previously in children aged <4 years.

METHODS: EPITope is an ongoing double-blind, placebo-controlled, randomized Phase 3 trial to assess VP safety and efficacy in peanut-allergic children aged 1-3 years. Here we present the study design and an overview of overall baseline demographics for the first part of the trial (dose selection). Among the inclusion criteria are serum peanut-specific IgE >0.7 kU/L; peanut skin prick test (SPT) largest wheal diameter >6 mm; and reaction on double-blind, placebo-controlled food challenge to an eliciting dose of ≥300 mg peanut protein.

RESULTS: Peanut-allergic children (n=51; 67% male) 1-3 years of age have been enrolled and randomized to treatment with either PBO, 100 mcg VP, or 250 mcg VP. Mean serum peanut-specific IgE at entry was 86.3±158.8 kU/L, and mean peanut SPT largest wheal diameter was 13.6±4.5 mm. Eighty-two percent of subjects were diagnosed previously (as reported by investigator) with food allergy other than peanut (20% milk); 94% atopic dermatitis, 37% allergic rhinitis, and 20% asthma/bronchial hyperactivity/wheezing. Mean age of subjects at first diagnosis was 1.05 years. Recent Data and Safety Monitoring Board evaluation considered both doses to be well tolerated with a good safety profile.

CONCLUSIONS: Age at diagnosis highlights the need for peanut allergy treatment in younger children. Consistent with studies in older children, peanut-allergic subjects in this EPIT clinical trial are highly atopic.

Long Term Follow-up of Oral and Sublingual Immunotherapy for Peanut Allergy

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RATIONALE: Immunotherapy for food allergy is being investigated as a potential treatment. There is limited data on long-term outcomes of food immunotherapy.

METHODS: We contacted 21 subjects who participated in a randomized trial comparing oral versus sublingual peanut immunotherapy (NCT01084174). Follow-up data was collected by telephone questionnaire and/or clinical follow-up 3-8 years after study completion to assess long-term peanut consumption and reaction rates.

RESULTS: Of the 21 subjects, 16 were given recommendations for home peanut consumption. Follow-up data was available on 15/16. At last contact, 57% (12/21) were ingesting peanut. 8/12 were regularly eating >1 gram of peanut protein (median 1.9 grams, range: 1 to 4.4) and 4 were eating <1 gram (1 trace amounts only, range: trace-0.75). Over the last 12 months of follow-up, the longest time without eating peanut ranged from 2-21 days (median 7 days). Symptom frequency with peanut ingestion ranged from never (1/12), rarely (9/12), regularly (1/12), or with most exposures (1/12). Most common symptoms included oral pruritus, lower respiratory issues, and gastrointestinal complaints. Reactions were treated with antihistamines (1/12 subjects), albuterol (5/12), H2 blocker (1/12), or epinephrine (2/12). One individual needed epinephrine for 2 reactions. Exercise and missed doses were the most cited factors associated with reactions. Taste was the most common reason why subjects limited peanut intake, followed by reactions and anxiety. 14/15 continue to carry epinephrine, 8 of whom also have a non-peanut food allergy.

CONCLUSIONS: Long-term outcomes of peanut immunotherapy are mixed, with many patients returning to peanut avoidance and/or reporting symptoms with peanut ingestion.

Association Between History of Epinephrine Use and Dose-Related Adverse Event Rates During Oral Immunotherapy

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RATIONALE: Oral immunotherapy (OIT) for individuals with food allergy is often perceived to be unsafe, especially in patients who have received epinephrine in the past. In a multi-allergen OIT clinical trial, we have analyzed whether baseline use of epinephrine is associated with an increased rate of dose-related adverse events during OIT.

METHODS: In an ongoing clinical trial, 53 participants aged 4 to 20 years old have completed a phase 2 clinical trial involving OIT with multiple foods. These participants consumed doses over 18 weeks and reported adverse events through an electronic diary. Dose-related adverse event (DRAE) rates for each participant were calculated by dividing the number of DRAEs by the number of doses consumed, and participants were grouped according to history of epinephrine use prior to study enrollment. Mean rates between groups were compared through a t-test.

RESULTS: A total of 1112 DRAEs were reported by the participants. Among the DRAEs, 81.1% were gastrointestinal symptoms, 9.44% were respiratory symptoms, and 5.22% were cutaneous symptoms. The mean DRAE rates were 12.3% for those with (n=22) and 21.5% for those without (n=31) a history of epinephrine use due to accidental exposure prior to start of OIT (p=0.08).

CONCLUSIONS: For this sample size, a history of epinephrine use for a food allergen prior to initiating OIT was not associated with higher dose-related adverse event rates. Conducting this analysis with a larger sample size would be of interest for future studies.
**752 Modified Peanut Oral Immunotherapy Is Safe and Effective After Failed Food Challenges**

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**RATIONALE:** Oral immunotherapy (OIT) for foods is safe and effective. Standard OIT regimens for peanut start with protein doses in the microgram range, but many patients fail peanut food challenges after consuming large amounts of peanut protein and are good candidates for modified protocols.

**METHODS:** We performed a retrospective chart review to identify patients seen between July 2016 and August 2018 who failed peanut challenges and chose to start a modified OIT protocol at ≥25% of the failed dose the day after the challenge.

**RESULTS:** Forty patients were identified ranging in age from 7 months to 18 years with a median age of 23 months. Initial OIT doses ranged from 2mg to 1167mg with a mean dose of 204mg protein dose. Fourteen patients have completed peanut OIT and are on a maintenance daily dose of at least 2 teaspoons peanut butter (2334mg peanut protein). Twenty-six patients are in the dose escalation phase. Initial total peanut and Ara h 2 IgE values ranged from 0.1 to 34.3kU/L and 0.12 to 16.2kU/L, respectively. Seven patients (17.5%) were treated with epinephrine during challenges, but no patients have required epinephrine during the OIT process.

**CONCLUSIONS:** Initiating a modified OIT regimen at ~25% of the failed dose the day after a peanut challenge should be considered in patients without a previous history of anaphylaxis, even those with significant levels of IgE to Ara h 2. This may be of particular benefit to young children with a history of mild reactions to peanut.

**753 Oral Immunotherapy to Peanut in Children with Mild and Moderate Peanut Allergy Results in Long Term Tolerance**

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**RATIONALE:** Little is known about outcome of individually customized OIT in children with mild to moderate peanut allergy.

**METHODS:** Medical records of children who received OIT from one allergist in an academic practice (ML) were reviewed for history and outcome of OIT.

**RESULTS:** 129 Children received OIT from 2012-18, with 101 receiving peanut OIT alone and 28 peanut with other foods. Peanut butter was used; starting dose was individually customized by last dose tolerated historically or through oral food challenge (OFC), and maintenance dose ranged from 1 to 2 teaspoons peanut butter (or 8 to 16 peanuts). Of the 101 children, 53 are on daily maintenance, 17 are still updosing, 12 discontinued or were lost to follow up, 19 completed OIT and are consuming serving-size amounts of peanut 2-3 times weekly or ad lib. They are not avoiding peanut in their diet otherwise. Of the 19 completers, reactions to pre-OIT peanut OFC were mild in 13, moderate in 4. Duration of OIT was (mean±SD)1.05±0.4 years. At start of OIT, age was 5.3±2.6 years, peanut serum IgE1.15±0.9 KU/L and peanut prick skin test wheal14.25±8.9 mm, which decreased to 0.8±0.6 KU/L and 5.07±3.2 mm, respectively, at end of OIT.

**CONCLUSIONS:** In an average of one year, OIT using peanut butter or plain peanuts in an individually customized dosing in children with mild to moderate peanut allergy resulted in long term tolerance with decreased sensitization.
755 **Duodenal Eosinophil Counts Decrease in Patients with Celiac Disease After Starting a Gluten Free Diet**

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**RATIONALE:** Eosinophilia has been reported in the intestinal mucosa of patients with celiac disease (CD). The number of eosinophils in the lamina propria (LP) of the duodenum has been correlated with histologic architectural distortion. It is unknown whether instituting the gluten-free diet (GFD) affects eosinophil counts in the mucosal lesion of CD.

**METHODS:** We identified 25 adults with CD who had initial and follow-up duodenal biopsies. A gastrointestinal pathologist examined each biopsy separately and recorded the following variables: Marsh score, intraepithelial (IE) lymphocytosis (> 30 per 100 epithelial cells), LP granulocytotic inflammation (increased eosinophils compared to normal mucosa or any extravascular neutrophils), and maximum eosinophil count per high-powered field (HPF).

**RESULTS:** The initial diagnostic biopsies had significantly increased rates of IE lymphocytosis (88% vs 20%, p=0.0003) and LP eosinophilia (72% vs 20%, p=0.0003) as compared to the follow-up biopsies, while rates of extravascular neutrophils were not significantly different between diagnostic and follow-up biopsies. The mean maximum eosinophil count in a single HPF was increased in the diagnostic biopsy as compared to the follow-up biopsy (45.5 vs 18.7, p<0.0001). At follow-up biopsy, the mean maximum eosinophil count per HPF was increased in biopsies with persistent villous atrophy as compared to those without (27.8 vs 15.8, p=0.015).

**CONCLUSIONS:** In patients with CD, LP duodenal eosinophils are higher at diagnosis than on follow-up biopsies; this decrease over time may be related to the GFD. The implications for risk of allergic disease development in this population warrant further investigation.

756 **Development of a Novel Emergency Action Plan for Food Protein-Induced Enterocolitis Syndrome**

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**RATIONALE:** Food protein-induced enterocolitis syndrome (FPIES) is an underrecognized non-IgE-mediated food hypersensitivity. Management of acute reactions can be a medical emergency, however treatment is vastly different compared to IgE-mediated anaphylaxis. Emergency action plans (EAPs) outline recommended lay and medical care during acute reactions. Lack of treatment guidance in an FPIES EAP may hinder patients from receiving proper care.

**METHODS:** A literature review of FPIES management was performed. Public access webpages for U.S. and international allergy professional organizations plus food allergy and FPIES advocacy groups were evaluated for content including available EAPs and FPIES management letters. An internet search was performed using the keyword “FPIES action plan” to catch any missed resources.

**RESULTS:** One of 3 advocacy groups provided an EAP mostly comprised of free text fields without medical management. No U.S. allergy organizations provided FPIES letters or plans on their websites. One of 3 international allergy organizations provided a true symptom-based EAP, however no treatment recommendations were included. No EAPs or emergency department letters mentioned use of ondansetron. Given the lack of a consensus EAP incorporating medical management, we created a FPIES EAP (to mimic the IgE-mediated food allergy EAP widely accepted in Illinois) with recommendations for hydration, ondansetron and steroids.

**CONCLUSIONS:** We were unable to find EAPs including treatment recommendations for FPIES reactions. Our novel templated emergency management plan may be a useful tool for management of acute FPIES reactions for home, school and emergency department settings. Future studies will ascertain family and provider utilization and feedback.
**758 A Prospective Cohort Study on Association between 25-Hydroxyvitamin D Level, Food Allergies and Environmental Allergies in Children**

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**RATIONALE:** Low levels of 25-hydroxyvitamin D \(25(OH)\text{vitamin D}\) is seen in children with food allergy. However, the association between \(25(OH)\text{vitamin D}\) and environmental allergies are not known. Our study aimed to explore the relationship between \(25(OH)\text{vitamin D}\) and diagnosis of food and environmental allergies.

**METHODS:** We prospectively enrolled 105 children who presented to our allergy clinic for evaluation of food and environmental allergies. A detailed allergen exposure history was assessed by questionnaire. Serum \(25(OH)\text{vitamin D}\) with total and allergen-specific IgE levels (food allergy profile, childhood allergy profile with reflexes, June grass, lambquarters, corn ragweed, Timothy grass, maple, cottonwood, elm and oak) were obtained.

**RESULTS:** The prevalence of low \(25(OH)\text{vitamin D}\) levels (<30ng/ml) in patients less than 18 years is 1-10% (CDC-NCHS data). In our study, we found that in patients with food allergies, the prevalence of vitamin D insufficiency (20-30ng/ml) and deficiency (<20ng/ml) is 37.5% and 32.5% respectively. The prevalence of vitamin D insufficiency and deficiency in patients with environmental allergies is 35.9% and 34.6% respectively. The median \(25(OH)\text{vitamin D}\) level in children with mice allergy is significantly lower compared to children without mice allergy (19.9ng/ml[IQR 15.4-24.9ng/ml] vs 25.6ng/ml[IQR 18.7-33.1ng/ml], p = 0.0456). The median \(25(OH)\text{vitamin D}\) level did not differ in patients with other environmental allergies (23.85ng/ml vs 25.6ng/ml, p = 0.5041) and food allergies (25.4ng/ml vs 24.2ng/ml, p = 0.9778).

**CONCLUSIONS:** We did not find an association between \(25(OH)\text{vitamin D}\) and food allergies. Low levels of serum \(25(OH)\text{vitamin D}\) is seen in children with allergies to mice.

**759 Deficits and Opportunities in Allergists' Approaches to Food Allergy Teasing/Bullying**

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**RATIONALE:** Children with food allergies are twice as likely to be bullied compared to children without food allergies. The goal of this study was to understand what percentage of allergists view teasing/bullying as a problem in their food-allergic pediatric patients and how often allergists inquire about teasing/bullying.

**METHODS:** An online survey was administered to a random 20% representative sample of AAAAI members.

**RESULTS:** Response rate was 10.4% (98/941). Of respondents, 63.2% thought food-allergic children experienced more teasing/bullying than non-food-allergic children. Nearly half (49.0%) of respondents inquire about teasing/bullying at least some of the time. Less than half (42.7%) of respondents felt very comfortable asking about teasing/bullying and only 21.9% felt very comfortable helping patients and families address this issue. The most common direction provided was notifying the school (83.7%). Other commonly suggested actions included confronting the bully/bully’s family (28.6%) [of note, this approach is not typically recommended by experts] and referral to a mental health provider/social worker (22.4%). The most common barriers identified to asking patients/families about teasing/bullying were lack of time (42.1%), resources (25.3%) and knowledge (12.6%). Resources on bullying (28.4%) and more knowledge on the topic (24.2%) were areas identified to be most helpful to facilitate allergist inquiry on this topic.

**CONCLUSIONS:** A significant number of allergists are unaware that bullying/teasing is an issue for food-allergic patients. Allergists may benefit from education and resources to recognize and address this problem.
Quantifying Exposure to Food Allergens From Household Dust

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RATIONALE: Exposure to food allergens is a pre-requisite to the development of food allergy. It is not fully understood what level of exposure to allergens or what route of exposure is most important for allergic sensitization. Previous studies have suggested that food allergens present within household dust may contribute to allergic sensitization via the skin of individuals at risk of developing food allergies.

METHODS: We sought to determine the precise levels of common food allergens within household dust. Samples of settled dust were collected from various houses within Europe. The levels of 7 common food allergens were simultaneously quantified using a multiplex immunoassay. Allergens assessed were from peanut (Ara h 3 and Ara h 6), milk (Bos d 5), egg (Gal d 2), hazelnut (Cor a 9), cashew (Ana o 3) and shrimp (Tropomyosin). Each of the allergens assessed were readily found within household dust.

RESULTS: The major allergens from egg (Gal d 2) and milk (Bos d 5) were found to be the most abundant food allergens in dust. As much as 275 μg of allergen per gram of dust was found. The least abundant food allergen was the major hazelnut allergen Cor a 9.

CONCLUSIONS: Our data pointed out the severity of FPIES and importance of recognition of this disorder in developing countries. Cow’s milk was the most common food trigger and was associated with more severe presentation and protracted course than other foods.

Food Protein Induced Enterocolitis Syndrome (FPIES): Data from a Tertiary Care Center in Developing Country

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RATIONALE: Food Protein Induced Enterocolitis Syndrome (FPIES) is a non-IgE-mediated food allergy. In developing countries, FPIES may be under-recognized and misdiagnosed as gastrointestinal infection. We sought to characterize the clinical features of FPIES in a tertiary care center in Thailand.

METHODS: We collected data of the patients who were diagnosed as FPIES and prospectively followed at King Chulalongkorn Memorial Hospital between 2008-2018. Diagnosis of FPIES was confirmed based on clinical criteria and/or oral food challenge. Data regarding patient characteristics were collected.

RESULTS: Twenty-six infants with FPIES were identified, 38 % were male. Median age of first episode was 4 months and median age of diagnosis was 7 months. The most common causative foods were cow’s milk (62%) and egg (15%), followed by soy (8%), fish (8%), banana (8%) and rice (4%). FPIES with multiple foods were identified in 4% of patients. Severe malnutrition occurred in 15 % of patients at presentation of which 50 % required intensive care unit admission due to complication of malnutrition and infection. All cases of severe malnutrition were due to chronic FPIES caused by cow’s milk. Tolerance developed in 46% of patients. The median age when tolerance was established was 4 years for cow’s milk, 2.5 years for egg and 2 years for banana.

CONCLUSIONS: Our data pointed out the severity of FPIES and importance of recognition of this disorder in developing countries. Cow’s milk was the most common food trigger and was associated with more severe presentation and protracted course than other foods.

The Intriguing Allergy To LTP: Guilty Foods After A Survey.

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RATIONALE: Non-specific lipid transfer protein (nsLTP) is a panallergen and largely the main cause of primary plant-food allergy in Spain. Due to the high immunological cross-reactivity among different nsLTPs and variable clinical transcendence, it is difficult to indicate foods that patients might eat in the future. The aim was to determine the prevalence of food eliciting allergy among nsLTP allergic patients.

METHODS: A structured questionnaire including questions on symptoms to 83 plant-foods was applied to well-known nsLTP allergic patients. LTP allergy was diagnosed by history, sensitization to Pru p 3 and/or challenge test when needed. Patients sensitized to PR-10, profilin, Ara h 1-2-3 were excluded.

RESULTS: Thirty-one nsLTP allergic patients (9 male and 22 female; mean age 30; 7-60 years) were included. Sixty eight percent of the patients were allergic to pollen. Fifty eight percent of the patients reported systemic symptoms after eating plant-food, more frequently reported by non-pollen allergens (70.0% vs 52.4%; p<0.05). A cofactor was involved in only five cases(6%). The main guilty foods eliciting allergic reactions were peach (100%), apricot (69.2%), walnut (63.3%), hazelnut (62.5%), peeled peach (59.3%), peanut (58.1%), peeled apricot (50%), chestnut (48%), pistachio (44.8%), etc. Curiously, some plant-foods containing allergenic nsLTPs elicited symptoms in less than 10% (tentil, asparagus, pomegranate, strawberry, pumpkin, wheat, or less than 20% (barley, corn, lettuce, mustard, pear, green bean, or tomato).

CONCLUSIONS: Rosaceae fruits (Prunoideae) and nuts were the most frequent plant-food eliciting symptoms in nsLTP allergic patients. Nonetheless, other plant-food containing allergenic nsLTP elicited symptoms in less than 10% or 20% of the patients.

Food Protein Induced Enterocolitis Syndrome (FPIES): Data from a Tertiary Care Center in Developing Country

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Monday
764 Acid Suppression in Infancy is not Prospectively Associated with Childhood IgE-Mediated Food Allergy

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RATIONALE: Recent retrospective research associated early life acid suppressive medication with food allergies. We sought to prospectively evaluate the association between acid suppressive medication in infancy and development of IgE-mediated food allergy in early childhood.

METHODS: The Gastrointestinal Microbiome and Allergic Proctocolitis (GMAP) Study is an ongoing prospective observational cohort study of 1003 healthy newborn infants designed to evaluate the development of food allergies in their first 3 years of life. IgE-mediated food allergy was determined by independent agreement of two allergist reviewers based on clinical reactivity and documented IgE sensitivity.

RESULTS: 797 infants were analyzed (46% female, 89% term, 31% delivered via caesarian-section, 8% neonatal antibiotics) with a current median age of 36 [19, 54] months. 153 (19%) were exposed to acid suppressive medication, 45 (5%) were exposed to a proton pump inhibitor delivery via caesarian-section, 8% neonatal antibiotics) with a current median age of 36 [19, 54] months. 153 (19%) were exposed to acid suppressive medication, 45 (5%) were exposed to a proton pump inhibitor, 115 (13%) were exposed to a histamine-2 receptor antagonist, in their first six months of life. To date, 51 (6%) of children have developed a confirmed or probable IgE-mediated food allergy, most commonly to egg, peanut, tree nuts, and milk. Use of acid suppressive medication in the first six months of life was not associated with development of IgE-mediated food allergy in early childhood (OR 0.77 [0.31, 1.71], p = 0.59).

CONCLUSIONS: Contrary to a recent retrospective report, early exposure to acid suppressive medication is not prospectively associated with development of IgE-mediated food allergy by age 3 in this cohort.

765 Postnatal probiotics and allergic disease in very preterm infants: sub-study to the ProPrems randomized trial

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RATIONALE: Probiotic supplementation pre and/or post natal has been suggested to prevent allergic disease, in particular eczema; however no studies have investigated probiotics for prevention of allergic diseases in very preterm infants. We therefore aim to evaluate the effect of a postnatal probiotic combination on development of allergic diseases and atopic sensitization, in very preterm infants in early childhood.

METHODS: This sub-study was an a priori secondary outcome of the Australasian ProPrems multi-centre, double-blind, placebo-controlled randomized trial. ProPrems randomized 1099 very preterm infants to receive a probiotic combination or placebo from soon after birth until discharge from hospital or term corrected age (CA), whichever was earlier. Victorian infants were eligible for this sub-study. Allergic disease incidence in the first two years of life was assessed by questionnaire, clinical examination and skin prick tests to common allergens. Logistic regression models were used to determine the association between probiotics administration and allergic disease outcomes, adjusting for baseline imbalances.

RESULTS: 281 of 453 eligible infants were included. Data were analysed (127 probiotic group, 154 placebo group). The median corrected age (CA) was 16 months CA in both groups at allergy assessment. The incidence of allergic diseases (eczema, atopic eczema, food allergy and wheeze) and atopic sensitization in the first two years of life was similar in the probiotic and placebo groups.

CONCLUSIONS: This study found no effect of postnatal administration of a probiotic combination on the incidence of allergic diseases or atopic sensitization in the first two years of life.

766 Tick Salivary Extract Induces Alpha-Gal Allergy in Alpha-Gal Deficient Mice

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RATIONALE: Development of slgE to galactose-alpha-1,3-galactose (alpha-gal) and red meat allergy has been associated with tick bites; however, controlled experiments directly linking tick bites with alpha-gal allergy are lacking. In this study, we immunized mice deficient in alpha-gal (AGKO) with tick salivary gland extract (TSGE) to determine whether alpha-gal slgE response and red meat allergy would develop.

METHODS: Ten week old AGKO mice on C57B16J background were given either Amblyomma americanum TSGE intradermally (50 μg) or saline on days 0, 7, 21, 28, 42. IgE and IgG were assessed on day 56 by ELISA. Mice were challenged orally with 400 mg pork meat on day 64 and core body temperature was measured.

RESULTS: Compared to controls, mice treated with TSGE had elevated total IgE and IgG at day 56 (0.60±0.12 ng/mL vs 113.2±24.77 ng/mL, p<0.0001; 98.07±10.32 μg/mL vs 253.4±38.93 μg/mL, p<0.0001, respectively). Alpha-gal slgE was increased in response to TSGE treatment (undetected vs 40.3 pg/mL). Core body temperature decreased following pork challenge with maximal decrease at 30 minutes in the TSGE-treated mice (34.39±0.56°C) but not in control mice. Interestingly, female mice had higher total IgE responses to TSGE treatment (179.1±39.86 ng/mL but male mice had larger declines in mean body temperature (-3.18°±0.82°C).

CONCLUSIONS: AGKO mice treated with TSGE recapitulate the delayed allergy to red meat seen in humans and establish the central role of tick bites. In addition, our model serves as a platform for mechanistically studying this new food allergy – already revealing potentially important sex-related differences.
Diarrhea in an infant: food protein induced enterocolitis or very early onset inflammatory bowel disease

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Rationale: Food protein induced enterocolitis (FPIES) is a non-IgE mediated food allergy diagnosed in infants and toddlers presenting with severe vomiting and diarrhea leading to shock in 15% of cases. Consulting allergists should keep very-early onset inflammatory bowel disease (VEO-IBD), defined as IBD diagnosed in children 6 years of age or younger in the differential. IBD in this young age group tends to be more severe and is associated with immune dysregulation.

Methods: We present a case of VEO-IBD followed by database review of all patients with VEO-IBD at a large referral center.

Results: Our patient is a two-month-old, full term, breastfed female, with a two-week history of lethargy and poor feeding followed by projectile vomiting and profuse watery diarrhea. She was ill-appearing, hypotensive, and admitted to intensive care unit. She was treated with fluid resuscitation and antibiotics. Extensive evaluation was negative for infectious, anatomic and oncologic processes. Trial of elemental formula due to FPIES concerns led to resolution of vomiting but frequent, watery stools persisted. EGD and flexible sigmoidoscopy revealed apoptosis, active and chronic inflammation consistent with VEO-IBD. Immune evaluation was normal.

Four hundred fifty patients in our institution were diagnosed with VEO-IBD. Of the entire cohort, 30% had prior a diagnosis of FPIES whereas those diagnosed under two, 69% had prior diagnosis of FPIES.

Conclusions: This case and our experience have demonstrated that VEO-IBD is often initially diagnosed as FPIES. The presentation of persistent diarrhea, blood in the stool, and vomiting in infants or toddlers should prompt the evaluation for VEO-IBD.

Epidemiological Determinants of Food Protein Induced Enterocolitis Syndrome

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Rationale: Food protein–induced enterocolitis syndrome (FPIES) is a non-IgE mediated food allergy characterized by delayed onset severe vomiting and lethargy. Despite the increasing clinical awareness of FPIES, the condition continues to be under diagnosed and there is limited epidemiological data available. This study aimed to improve our knowledge of FPIES by further characterizing the patient population.

Methods: Data was obtained through a retrospective chart review of patients with the diagnosis of FPIES at two main local hospital systems in Rochester, NY. Charts were reviewed for patient demographics, feeding history, symptoms, allergy testing, atopic history, and family history.

Results: In total, 44 charts were reviewed. The majority of patients had symptoms to oat (52%), rice (29%), cow’s milk (21%), and soy (11%). All patients developed symptoms within 1.5 – 3 hours. The average length to diagnosis was 8.43 months from symptom onset and 70% patients had 3 or less episodes prior to diagnosis. Co-morbid atopic conditions and/or a family history of atopy were present in 75% of patients.

Conclusions: By further characterizing FPIES, we can better understand the disease process and improve our care of patients with the condition. This study demonstrates the significant lag in diagnosis from symptom onset. Physicians should be aware of FPIES and raise the suspicion of the disorder in the appropriate clinical scenario, especially in patients with other allergic conditions, as our study showed the majority of patients had other allergic disorders. We hope to expand our data by including other hospitals in the near future.

Serological Profile of Children Undergone Cow’s Milk Oral Immunotherapy

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Rationale: Cow’s milk allergy (CMA) is characterized by an inappropriate immune response to cow’s milk protein (CMP), and is a leading cause of anaphylaxis in children. Oral immunotherapy (OIT) has been shown to induce tolerance in children with CMA and alters the CMP-specific serum immunoglobulin (Ig) E and IgG4 levels. However, the dynamics of CMP-specific serum IgE and IgG4 over the course of milk OIT have not been determined.

Methods: Forty-two children with confirmed CMA by history, skin prick test, and oral food challenge were studied during a controlled trial of OIT to CMA at the Montreal Children’s Hospital. Serum was collected at specific time points during the escalation phase which ended at 200 ml of CM and then followed for 12 months while consuming dairy. We used ELISA to measure the serum IgE and IgG4 specific for CMPs: α-lactalbumin (ALA), β-lactoglobulin (BLG), and casein.

Results: CMP-specific serum IgE peaked before the 25ml dose then decreased throughout the remaining escalation phase and maintenance phase while CMP-specific serum IgG4 gradually increased. CMP-specific IgE was predominantly ALA and casein-specific, whereas CMP-specific IgG4 was predominantly BLG and casein-specific.

Conclusions: Successful cow’s milk OIT induces significant changes in the levels of CMP-specific serum IgE and IgG4. Both serum IgE and IgG4 has high specificity for casein. In addition, serum IgE has higher specificity for ALA over BLG, while serum IgG4 has higher specificity for BLG over ALA. The results suggest a differential effect in antibody formation which may preclude complete tolerance against ALA following OIT.
770 Immune Mechanism of Desensitization through Rapid Multi-food Oral Immunotherapy

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RATIONALE: Using stored peripheral blood mononuclear cells (PBMCs) from a published randomized, controlled, phase 2 trial employing anti-IgE adjunct treatment for multi-food oral immunotherapy (OIT), we aimed to identify potential immune mechanisms associated with successful desensitization of participants in this rapid multi-food OIT study.

METHODS: High dimensional mass cytometry was performed on PBMCs from n=41 participants desensitized through rapid multi-food OIT. Briefly, PBMCs frozen pre- and post-OIT (week 36) were thawed, stimulated with PMA/fononycin to determine cytokine production by immune cell subsets, followed by staining with a comprehensive panel of metal-conjugated antibodies. To study the immune changes in peanut-specific CD4+ T cells, PBMCs from a subset of study participants treated with peanut (n=20) were independently stimulated with 200 μg/ml peanut solution. Unstimulated PBMCs were examined in parallel. Stained cells were acquired on a Helios mass cytometer. Data were analyzed using FlowSOM-based unsupervised clustering, and the findings were validated by manual gating.

RESULTS: We observed a significant increase in the median expression level of IL-10 post-OIT, primarily in γδ T cell and regulatory T cell clusters. Peanut-specific CD4+ T cells showed a marked decrease in IL-4 expression post-OIT. Interestingly, total effector memory CD4+ T cells showed a decrease in the expression of GPR15, a gut homing marker associated with Th2 pathogenesis, and CCR4, a surrogate marker for Th2 polarization, post-OIT. (FDR-adjusted P < 0.01 for each finding)

CONCLUSIONS: Rapid multi-OIT confers successful desensitization possibly through IL-10-mediated energy driving an immune shift away from a Th2 phenotype.

771 IL-18 overexpression promotes eosinophils-mediated peanut-induced intestinal allergy

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(1) IL-18 overexpression promotes eosinophils-mediated peanut-induced intestinal allergy

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RATIONALE: Baseline eosinophils reside in the gastrointestinal tract; however, excessive eosinophils accumulate in the blood and tissues in several allergic disorders. Recently, we reported that (IL-18) mature and promote naive eosinophils into the pathogenic eosinophils. Therefore, we tested the hypothesis whether in vivo induced IL-18 promotes eosinophils associated intestinal allergy in mice.

METHODS: We generated enterocyte IL-18 overexpressed mice using rat intestinal fatty acid-binding promoter (Fabpi) and examine tissue IL-18 overexpression and eosinophilia by performing real-time PCR, ELISA, and anti-MBP immunostaining analyses.

RESULTS: We show that Fabpi-IL-18 transgenic mice overexpressed IL-18 mRNA and protein along with marked increases of eosinophils in the blood, and jejunum. Further, we show that IL-18 induced intestinal eosinophilia is independent to IL-5, L-13, and eotaxin-1. As a comparable tissue eosinophilia was observed in IL-13-deficient-Fabpi-IL-18 mice and partial tissue eosinophilia is observed in eotaxin-deficient-Fabpi-IL-18 and IL-5-deficient-Fabpi-IL-18 transgenic mice compared to the Fabpi-IL-18 mice. Most importantly, we show that IL-18 overexpression in the intestine promotes eosinophil-associated peanut-induced allergic responses in mice.

CONCLUSIONS: Taken together, we provide direct in vivo evidence that the enterocytes induced expression of IL-18 promotes eotaxin-1, IL-5, and IL-13 independent intestinal eosinophilia that signifies the role of IL-18 in promoting EGID pathogenesis.

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Untargeted Metabolomic Profiling Identifies Disease-Specific Pathways in Food Allergy and Asthma

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RATIONALE: Food allergy (FA) affects an increasing proportion of children in the US and other developed countries for reasons that remain largely unknown. A deeper understanding of pathogenic mechanisms active in FA may lead to much needed diagnostic and prognostic biomarkers of disease and improved treatment options.

METHODS: Children with asthma alone, children with FA alone, children with both FA and asthma as well as healthy pediatric controls were recruited in the Allergy clinic at Boston Children’s Hospital. Mass spectrometry-based untargeted metabolomic profiling was performed on serum samples (n=35 for FA or asthma alone and FA/asthma; n=20 for controls) looking at global metabolism.

RESULTS: Untargeted metabolomic analysis revealed differential profiles of altered metabolites in patients’ groups. In comparison to both controls and children with asthma, FA was uniquely associated with a marked decrease in sphingolipids - in particular sphingomyelins and ceramides - as well as lysocephospholipids. Among atopic children, differences in aromatic amino acid metabolism and metabolism of secondary bile acids were observed between food allergic and asthmatic children. Among children with FA, the metabolomic profile of those with asthma was indistinguishable from that of children without asthma.

CONCLUSIONS: Both unique and shared metabolomic alterations were detected in children with FA, asthma, or both, likely reflecting overlapping but distinct mechanisms and environmental influences operative in these disorders. Lower levels of sphingolipids and ceramides observed in food allergic children may affect the interplay between microbiota and immune cell subsets in the gut, including in K T cells.

Egg Oral Immunotherapy (OIT) Induces More Rapid Desensitization and Sustained Unresponsiveness (SU) in Egg-Allergic, Baked-egg Tolerant Children than the Addition of Daily Baked-egg Products

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RATIONALE: Egg-allergic, baked-egg tolerant children incorporating baked-egg products (BEPs) into their diets may accelerate development of tolerance to all forms of egg compared to strict egg-elimination diets. We investigated whether egg-OIT and BEPs had comparable efficacy in establishing desensitization and SU to unbaked-egg.

METHODS: 52 baked-egg tolerant subjects (3.5-16.8 y/o) identified by baked- and unbaked-egg DBPCFCs were randomized to receive BEPs (~2g baked-egg protein daily; N=28) or egg-OIT (2.5g egg-white protein daily; N=24 [Egg OIT-Randomized]) for up to 2-years; 40 additional subjects intolerant to baked-egg were assigned to egg-OIT [Egg OIT-Assigned]. Desensitization- and SU-DBPCFCs (cumulative dose=7444mg egg-white protein) were performed after 2-years of treatment.

RESULTS: Egg-OIT-treated baked-egg tolerant children were significantly more likely to develop desensitization (87.0% vs 22.2%, p<0.001) and SU (43.5% vs 11.1%; p=0.009) at 2 years than BEPs-treated subjects, whereas egg-OIT in baked-egg tolerant versus baked-egg intolerant children revealed differences in SU (43.5% vs 17.9%; p=0.031) but not desensitization (87.0% vs 69.2%, p=0.15). In Year-1, the median percent of doses/subject with any adverse reaction was 2.8% for Baked-egg, 3.9% for Egg-OIT-Randomized and 12.6% for Egg-OIT-Assigned subjects; most dosing symptoms were mild. Dosing compliance was ~90% of expected doses in BEPs-treated versus >95% for both egg-OIT groups. Eight (28.5%) BEPs-treated subjects withdrew compared to 3 (12.5%) Egg-OIT-Randomized and 7 (17.5%) Egg-OIT-Assigned subjects. Egg OIT-Randomized subjects experienced significantly greater increases in egg-white and egg-component IgG4 and IgG4:IgE ratios at Year-1 than the BEPs-treated group.

CONCLUSIONS: Egg-OIT appears superior to BEPs in inducing both desensitization and SU in egg-allergic, baked-egg tolerant children.
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**776 Longer-Term Safety and Efficacy Measures of AR101 Oral Immunotherapy for Peanut Allergy: Results from a Phase 3 Follow-On Study**

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**RATIONALE:** Of subjects who completed the phase 3 study of the experimental treatment AR101 for peanut allergy (PALISADE), 76% of AR101-treated subjects vs 5.4% of placebo-treated tolerated ≥600mg of peanut protein at exit double-blind, placebo-controlled food challenge (DBPCFC). Adverse events (AEs) were mostly mild-to-moderate in severity. The ability to tolerate doses >1000 mg and safety beyond the initial maintenance period has not been established and initial findings from the ongoing study are reported.

**METHODS:** PALISADE completers were eligible to enter the follow-on study and continue AR101 daily maintenance for 6 months before the next DBPCFC, which included an additional 2000 mg challenge dose. AEs and discontinuations were recorded and compared to the prior 6-month maintenance period.

**RESULTS:** 117 of 316 (37%) AR101-treated PALISADE subjects enrolled in the daily maintenance regimen; the remainder were assigned to other dosing regimens (not included in this analysis). 100 (85%) subjects have completed both maintenance periods (PALISADE 88% vs follow-on 81.2%). Three subjects (2.6%) discontinued due to AEs, 2 were treatment-related (1 EoE, 1 mild systemic reaction). The median tolerated dose was 1000mg with 49% of subjects to date being able to tolerate the highest challenge dose of 2000mg. Of the subjects who tolerated <1000 mg at PALISADE exit, 64% (27/42) could tolerate a higher challenge dose after extended maintenance.

**CONCLUSIONS:** 300 mg daily of AR101 was well tolerated in the ongoing follow-on study; the majority of subjects could tolerate higher challenge amounts (1000 mg and 2000 mg) of peanut protein after additional maintenance.

**777 Description of Subjects Reporting Reactions to Mammalian Meat Who Test Negative for IgE to Galactose-α-1,3-galactose (α-Gal)**

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**RATIONALE:** The oligosaccharide α-Gal has recently emerged as a regionally important cause of anaphylaxis to mammalian meat; however, other allergens can also contribute to meat allergy. We sought to describe subjects who were evaluated for suspicion of mammalian meat allergy but who tested negative for IgE to α-Gal.

**METHODS:** As part of an IRB-approved observational study, 254 patients with histories of suspected allergic reactions (urticaria and anaphylaxis) to mammalian meat were enrolled from central Virginia. Serum was obtained and subjects completed detailed case histories. Assays were conducted for total IgE, as well as specific IgE (sIgE) to α-Gal, cat, beef, pork, gelatin, cat serum albumin, bovine serum albumin and pork serum albumin standard ImmunoCAP assays.

**RESULTS:** Using a cut-off of 0.35 IU/mL, sIgE to α-Gal was detected in 238 of the 254 subjects. Of the 16 remaining subjects, 10 (63%) described onset of symptoms occurring ≥ 2 hrs after mammalian meat ingestion. Specific IgE testing supported a diagnosis of pork-cat syndrome in 3 subjects (sIgE detected to cat, pork and cat serum albumin ≥0.1 IU/mL), 5 were found to have low-titer α-Gal sIgE (ie. 0.1-0.34 IU/mL) and 3 had detectable sIgE to beef (≥ 0.1 IU/mL) suggestive of primary beef allergy.

**CONCLUSIONS:** In central Virginia sIgE to α-Gal is a common cause of anaphylaxis to mammalian meat, however other causes such as pork-cat syndrome, primary beef allergy, and gelatin allergy should also be considered.

**778 Clinical Relevance Of Mollusc Sensitisation In Crustacean-allergic Patients**

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**RATIONALE:** Shellfish is a common cause of food allergy with an estimated prevalence at 0.5-2.5%. Tropomyosin, the major allergen in shrimp, is currently considered as a cross-reactive panallergen amongst invertebrate species. Crustacean-allergic patients are often co-sensitised to molluscs.

**METHODS:** A retrospective analysis was performed for all open oral food challenges (OCFs) to molluscs conducted at a tertiary UK Allergy Centre from 2011 through 2017. OCFs were offered to patients with primary allergy to crustaceans in the absence of probable reactions to molluscs or a concrete history of recent exposure. Crustacean allergy was diagnosed based on strong history of reactivity with confirmatory positive skin prick tests (SPTs) and/or serum specific IgE (sIgE).

**RESULTS:** Twenty crustacean-allergic patients who had negative OCFs to molluscs were identified (pass rate 100%). OCFs were performed to bivalves (40%), cephalopods (15%) or both classes (45%). Concurrent atopy was prominent. SPTs and/or sIgE were positive to bivalves (mussel 45%, oyster 40%, scallop 45%) and cephalopods (squid 45%, octopus 20%).

**CONCLUSIONS:** Co-sensitisation to molluscs is common in patients with primary allergy to crustaceans. In the absence of a concrete history of exposure or recent reactions, OCFs to molluscs should be considered to avoid unnecessary dietary restriction. Clinical reactivity between crustaceans and molluscs may be less than expected based on immunologic cross-reactivity.
**779** Oral Immunotherapy for Multiple Foods

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**RATIONALE:** Oral immunotherapy (OIT) is an emerging approach to desensitize food allergy, increase patient safety and improve quality of life. This abstract summarizes our clinical experience with simultaneous, multiple-food OIT in children.

**METHODS:** Patients were selected for OIT based on having food allergies unlikely to resolve spontaneously, motivation for consistent participation in OIT, and no symptoms of eosinophilic esophagitis. Food allergy diagnosis was based on a convincing history of immediate-type hypersensitivity with positive skin test and/or serum specific IgE, or reaction to oral food challenge (OFC). Starting dose for OIT was determined from reaction threshold at OFC or from clinical history. All included food allergens were given together, daily at home, and updosing was done in the clinic every 2 to 4 weeks. Once the maintenance dose was reached it was continued daily long term, with repeat allergy testing every 6 months.

**RESULTS:** 48 children (29 male, 19 female) ages 2-18 years were desensitized to 2-11 foods (most commonly 2 to 4 foods). The foods included peanut, tree nuts, seeds, legumes and egg. Mild to moderate allergic reactions occurred during OIT in 42% of patients, mostly oral allergy symptoms, perioral hives or abdominal pain. No allergic reactions occurred during OIT in 42% of patients, mostly oral allergy symptoms, perioral hives or abdominal pain. No allergic reactions were reported after the first 3 months of maintenance dosing. There were 5 ED visits for allergic reactions during OIT, compared with 20 post-diagnosis ED visits before starting OIT. Four patients stopped OIT due to symptoms, anxiety, or time constraints.

**CONCLUSIONS:** Simultaneous, multiple-food OIT is a practical and effective approach for children with multiple food allergies.

**780** Deciphering the Walnut-Pecan Allergy Paradigm Using Component Resolved Diagnostics

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**RATIONALE:** Current diagnostic methods for diagnosing walnut and pecan allergy are limited. The utility of walnut components to improve food allergy, increase patient safety and improve quality of life. This abstract summarizes our clinical experience with simultaneous, multiple-food OIT in children.

**METHODS:** Patients were selected for OIT based on having food allergies unlikely to resolve spontaneously, motivation for consistent participation in OIT, and no symptoms of eosinophilic esophagitis. Food allergy diagnosis was based on a convincing history of immediate-type hypersensitivity with positive skin test and/or serum specific IgE, or reaction to oral food challenge (OFC). Starting dose for OIT was determined from reaction threshold at OFC or from clinical history. All included food allergens were given together, daily at home, and updosing was done in the clinic every 2 to 4 weeks. Once the maintenance dose was reached it was continued daily long term, with repeat allergy testing every 6 months.

**RESULTS:** 48 children (29 male, 19 female) ages 2-18 years were desensitized to 2-11 foods (most commonly 2 to 4 foods). The foods included peanut, tree nuts, seeds, legumes and egg. Mild to moderate allergic reactions occurred during OIT in 42% of patients, mostly oral allergy symptoms, perioral hives or abdominal pain. No allergic reactions were reported after the first 3 months of maintenance dosing. There were 5 ED visits for allergic reactions during OIT, compared with 20 post-diagnosis ED visits before starting OIT. Four patients stopped OIT due to symptoms, anxiety, or time constraints.

**CONCLUSIONS:** Simultaneous, multiple-food OIT is a practical and effective approach for children with multiple food allergies.

**781** Increasing Incidence and Prevalence of Food Allergy Diagnoses among U.S. Active Duty Service Members, 2000-2017

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**RATIONALE:** Food allergies have risen in the past several decades, though epidemiologic data are limited. The military reflects a young adult population with access to healthcare that may help to better describe the epidemiology of food allergies.

**METHODS:** Data were obtained from the Defense Medical Surveillance System, a U.S. military personnel database containing medical encounter data from all fixed medical facilities in the Military Health System (MHS). Cases of food allergy among active component service members were identified by having record of an outpatient encounter in an MHS allergy specialty clinic with an ICD-coded diagnosis of food allergy, food anaphylaxis, or other adverse reaction to food between 2000 and 2017. Incidence and prevalence rates were calculated and stratified by military and demographic characteristics.

**RESULTS:** During the 18-year surveillance period, incidence of food allergy increased from 8.2 to 108.4 cases per 100,000 person-years and prevalence increased from 20.1 to 436.0 cases per 100,000 persons. In 2017, incidence and prevalence was highest among females, non-Hispanic Blacks, service members older than 35 years, and those in the Air Force, compared to their respective counterparts. Incidence was higher among service members stationed in the Midwest, although prevalence was higher among those stationed in the South and Midwest.

**CONCLUSIONS:** In the military, an IgE-mediated food allergy can be disqualifying for entry and specific career specialties. However, given the increasing numbers of service members affected by this condition, the military may wish to consider new policies to allow applicants and members with avoidable food allergies to serve successfully.
**782 Component-resolved Diagnosis of IgE-mediated Fish Allergy with Grass Carp Allergens**

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**RATIONALE:** Grass carp is a commonly consumed fish species in Hong Kong and Southern China. We investigated the utility of grass carp allergens for diagnosing IgE-mediated fish allergy in Chinese children.

**METHODS:** IgE reactivity against parvalbumin, enolase and aldolase of grass carp were measured by enzyme-linked immunosorbent assay in 76 pediatric subjects with clinical history of IgE-mediated fish allergy. IgE titers against these grass carp allergens were compared with IgE reactivity to cod extract and recombinant cod parvalbumin r Gad c 1 as measured by ImmunoCAP, which is the conventional surrogate for fish allergy diagnosis.

**RESULTS:** Grass carp parvalbumin was found to be the dominant allergen in our study population where IgE reactivity to this allergen was observed in over 80% of our subjects. In contrast, sensitization to enolase and aldolase were only observed in less than 20% of subjects and the IgE reactivity was generally low. IgE reactivity to grass carp parvalbumin was significantly higher than recombinant cod extract or cod parvalbumin r Gad c 1. The former allergen demonstrated superior diagnostic sensitivity for fish allergy at the cut-off of 0.35 kUA/L.

**CONCLUSIONS:** Grass carp parvalbumin is a better tool for fish allergy diagnosis in our population when compared to conventional cod extract or cod parvalbumin. The clinical relevance of grass carp enolase or aldolase remains dubious.[This study is funded by Innovation and Technology Fund (ITS/082/17) of Hong Kong SAR Government]

**783 Case-control Study on Epidemiologic Factors Influencing The Occurrence of Immediate Wheat Allergy Among Thai Children**

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**RATIONALE:** Increasing number of wheat allergic children has been observed in Thailand. The outbreak of immediate type wheat allergy caused by a hydrolyzed wheat protein (HWP) facial soap has been described in Japan. This study aims to assess factors associated with the development of wheat allergy in children include the use of HWP containing baby products.

**METHODS:** Children under 5 years of age with a history of IgE-mediated wheat allergy and age-matched healthy control were enrolled. The questionnaire was used to investigate the association between wheat allergy, demographic and environmental factors.

**RESULTS:** Thirty-eight wheat allergic patients and 38 healthy children were enrolled. The mean age was 2.86 years with mean age of onset 7.8 months. Most of them (94.3%) developed their symptoms at the first time of wheat ingestion. The absolute breastfeeding duration, family income, cesarean section rate were significantly higher among cases (P=0.047, 0.0012, 0.015, respectively). There was no significant difference between the onset of wheat introduction, the average amount of maternal wheat consumption during pregnancy or breastfeeding and family history of atopy. History of exposure to HWP product was higher in wheat allergic patients compared to controls (52.6% VS 42.1%). Previously used HWP/ oat products were found in 27 (71.1%) of wheat allergy group and 16 (42.1%) of control group. (P=0.03, aOR 3.01; 95%CI 1.12-8.14) The median level of sIgE to wheat was 2.8 kUA/l (IQR 1.15-35.6).

**CONCLUSIONS:** HWP/oat products were associated with an increased risk of wheat allergy. It might explain by early cutaneous sensitization from these products.

**784 Ara h6 – another piece in the peanut puzzle**

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**RATIONALE:** Diagnosis of peanut allergy is based on case history, serology measurements and confirmation by oral food challenge. The majority of patients with peanut allergy have elevated IgE towards Ara h2, thus being the superior serological marker for clinical peanut allergy. Few have, however, absent or very low titers of IgE towards Ara h2 nor any other known peanut specific protein (Ara h1, Ara h3, Ara h8, or Ara h9) which could explain their clinical reactivity. We are aiming to describe IgE to a new available peanut component (Ara h6) in relation to clinical reactivity.

**METHODS:** Samples from 134 challenge-positive and 25 negative peanut patients aged 1-26 years, previously analyzed with ImmunoCap (Thermofisher) for specific IgE to peanut and to known peanut components were reanalyzed for Ara h6. IgE levels were correlated and diagnostic values generated using RUC curve analyses.

**RESULTS:** We found high concordance between Ara h6 and Ara h2 (r=0.93). Diagnostic values for Ara h6 were better than for Ara h2: AUC was 0.95 vs. 0.90 and sens/spec. 88.0/83.3 vs 87.3/66.7. Ara h6 were able to explain clinical reactivity in 9/17 patients without detectable levels of IgE to Ara h2. Further, patients tolerant to peanut but with IgE to Ara h2 had no explain clinical reactivity in 9/17 patients without detectable levels of IgE to Ara h2. Further, patients tolerant to peanut but with IgE to Ara h2 had no detectable IgE to Ara h6. Combining the diagnostic capacity of Ara h2 and Ara h6 increased the overall sensitivity to 96.2%.

**CONCLUSIONS:** Measurement of Ara h6 adds additional information to the serological profile of peanut allergic patients, and increases the diagnostic accuracy in patients suspected of peanut allergy.
Prevalence of sesame allergy in U.S. children with IgE-mediated food allergy

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RATIONALE: Current U.S. federal law does not require food manufacturers to declare sesame in their products, although sesame is considered a major allergen in other parts of the world. The exact prevalence of sesame allergy in the U.S. is unknown. The diagnosis is challenging as there are no identified sesame-specific IgE or skin prick test thresholds that predict clinical reactivity.

METHODS: 72 consecutive patients (median age 9.5; IQR: 9) with IgE-mediated food allergy were assessed for clinical reactivity to sesame and peanut/tree nuts. Sesame allergy was defined as an immediate hypersensitivity to sesame at home or via clinic food challenge, and tolerance as the ability to ingest concentrated sesame (tahini) with no symptoms. Sesame-specific and total IgE were measured by ImmunoCAP.

RESULTS: Twelve (16.6%) of 72 patients with food allergy were allergic to sesame and 60 were tolerant. Sesame sIgE levels were higher in the allergic group (median 26.40 kUA/L versus 1.96 kUA/L, respectively; p<.000339). Of those allergic to sesame, 9/12 (75%) were also allergic to peanut or any tree nut, compared to 26 (43.3%) in the tolerant group. Adjustment for total serum IgE did not improve the ability of sesame sIgE to predict allergy.

CONCLUSIONS: Sesame allergy is common among children with IgE-mediated food allergy in this cohort, and often co-occurs with peanut/tree nut allergy. Further investigation will examine age of sesame introduction into the diet, ability of sesame allergic patients to tolerate seeds/oil, and the effect of eczema and elevated total IgE on modifying the utility of sesame IgE in predicting allergy.

Long term follow up of egg tolerance in egg allergic patients challenged to baked egg

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RATIONALE: Baked egg (BE) is tolerated by approximately 70% of egg-allergic children. In this study, we follow-up patients who tolerated baked egg oral food challenges (BE-OFC) and characterize their tolerance to non-baked, regular lightly cooked egg, e.g., scrambled egg or French toast.

METHODS: We performed retrospective chart reviews of egg allergic patients who visited Mount Sinai pediatric allergy clinic from January 2008 to December 2017 and passed BE-OFCs to muffin baked with egg. We characterized their progression to non-baked egg.

RESULTS: Among 50 patients, median age of 4.9 years (IQR: 3.1-9), 62% male at the time of the BE-OFC. Forty-two patients (84%) continued to ingest BE products by the first follow up appointment (median: 9 months; IQR: 6-16) and subsequently 1 year after passing BE-OFC. Eight patients (17%) discontinued BE within 1 year, due to symptoms with ingestion at home (62.5%) or fear of home introduction (37.5%). Symptoms reported by patients with home introduction were mostly mild, such as oral itching (50%), hives (25%) or abdominal pain (37.5%), however there was one report of anaphylaxis. Sixty-three percent of patients reporting symptoms with home introduction discontinued BE. Thirty-five patients (83%) eating non-baked egg.

CONCLUSIONS: The majority of subjects passing BE-OFC added BE to regular diet at home. Our data confirms previous findings that tolerance to non-baked egg is achieved in the majority of patients ingesting BE. Tolerance is also sustained long-term in patients who ingested baked egg products.

Withdrawn

Development of a cashew nut allergy mouse model to evaluate the efficacy of epicutaneous desensitization treatment

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RATIONALE: The prevalence of cashew allergy has increased in recent years. To develop an epicutaneous immunotherapy (EPIT) treatment to cashew allergy, the availability of an anaphylaxis animal model for preclinical studies is a prerequisite.

METHODS: Mice (N = 8) were sensitized to cashew using an oral or cutaneous sensitization protocol. Following sensitization, mice were challenged orally with cashew extracts. Anaphylactic reactions were assessed by measuring body temperature, clinical symptoms and mucosal mast cell proteases (mMCP-1/7) levels in serum. Similar results were obtained in the mice challenged 8 weeks after the end of sensitization.

CONCLUSIONS: A robust mouse model of cashew anaphylaxis was developed to evaluate the efficacy of EPIT for desensitization to cashew allergy.
789 Walnut Syrup is not Allergenic in Individuals with a Documented Walnut Allergy

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RATIONALE: Walnut syrup is produced from the sap of walnut trees and is an emerging gourmet food product. While the production of walnut syrup does not include processing of the walnut kernel, the allergenicity of walnut syrup in individuals with a known tree nut allergy to walnuts is unknown. We hypothesize that walnut syrup is not allergenic to individuals with a documented tree nut allergy to walnuts.

METHODS: To determine if the walnut allergenic protein is found in walnut syrup, we first measured protein levels using ELISA in walnut syrup samples. We next recruited nine individuals with history and skin-test confirmed allergy to walnut to participate in a food challenge of walnut syrup. The food challenge was performed by board-certified allergists and performed in the clinical research center at Cincinnati Children’s Hospital Medical Center. The endpoints measured were objective or subjective evidence of an allergic reaction.

RESULTS: Three samples of walnut syrup were obtained from three farms and submitted to The Institute of Agriculture and Natural Resources Food Allergy Research and Resources Program to assay for the walnut allergy protein. For all three samples, protein levels were below the limit of quantitation by ELISA. Nine individuals, average age 18.9 years, range 8-31 with documented walnut allergy had negative skin prick testing with walnut syrup, and completed a food challenge with no allergic reaction observed.

CONCLUSIONS: Walnut syrup does not contain the allergenic protein causing allergies in individuals with a walnut allergy, and ingestion of the syrup does not lead to an allergic reaction.

790 Fast and efficient cloning of human IgE, IgG1 and IgG4 antibodies specific for beta-lactoglobulin from cow milk by Polymerase Incomplete Primer Extension (PIPE)

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RATIONALE: While 2-3% of infants, only 0.49 - 0.6% of adults, are affected by IgE-mediated immediate type allergy to cow milk, because milk allergy can be “outgrown”. The role of IgG1 or IgG4 in this mechanism remains to be explored in molecular and cellular studies. Therefore, we aimed here to generate antibodies of diverse subclasses sharing the same variable region of the major milk allergen beta-lactoglobulin (BLG) (Jylhä et al. 2016). We used the new Polymerase Incomplete Primer Extension (PIPE) cloning method (Ilieva et al., 2017).

METHODS: Vectors of the IgE, IgG1 and IgG4 antibodies were transformed into E. coli, validated by colony-PCR and positive clones expressed in the Exp293F cells. The antibodies were purified by affinity chromatography and correct assembly controlled by non-reducing SDS-PAGE. The totally generated yields of recombinant proteins were measured with a BCA protein assay and specific binding to BLG was checked by dot blot, ELISA and ISAC112 allergen microarray.

RESULTS: One transfection (30nl) yielded 2.2 mg of anti-BLG IgE, 0.8 mg of IgG1 and 1.9 mg of IgG4 antibodies. Immunoassays confirmed the correct assembly of all antibodies and their specific binding to BLG.

CONCLUSIONS: In summary, we could show that PIPE cloning is an efficient and fast method to generate functional antibodies of various subtypes in high quantity. These antibodies will be applied as tools to shed more light onto the mechanism of cow milk allergy.

791 Determining Best Tests of Baked Egg Tolerance in Egg Allergic Subjects

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RATIONALE: The utility of skin prick testing (SPT) and specific IgE (sIgE) to identify children for baked egg oral food challenge (OFC) is variable. We sought to characterize predictors, including basophil activation testing (BAT), of baked egg OFC outcome.

METHODS: A retrospective review of 129 open baked egg OFC performed between 2007-2014 at the Ann & Robert H. Lurie Children’s Hospital of Chicago was conducted. Available SPT to egg white and sIgE to egg and ovomucoid were collected. A subset of study and control subjects had BAT performed to ovalbumin, ovomucoid and whole egg. Parametric and non-parametric statistical testing was used as appropriate. Receiver operating characteristic curves (ROC) and logistic regression models predicting OFC outcome were generated.

RESULTS: Thirty-four patients (median age 4.7 years) failed baked egg OFC (26.4%). A history of atopic dermatitis was more prevalent among patients that failed baked egg OFC (p = 0.052). Egg white sIgE at OFC was significantly higher amongst patients that failed baked egg OFC (8.7 kU/L versus 3.6 kU/L, p = 0.002) and the area under the ROC curve (AUC) for egg white sIgE at OFC was 0.72. BAT to ovalbumin best discriminated baked egg tolerant from control subjects (AUC = 0.812, p = 0.014), while BAT to ovomucoid best distinguished baked egg tolerant subjects from those who cannot tolerate baked egg (AUC = 0.87, p = 0.018).

CONCLUSIONS: Egg white SPT, sIgE and ovomucoid sIgE were inadequate to distinguish tolerance of baked egg among egg allergic subjects. While not yet commercially available, ovomucoid BAT performed superiorly to distinguish egg allergic patients that tolerate baked egg.
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RATIONALE: Current guidelines recommend early peanut introduction to all infants, with physician supervised introduction for those with skin prick test (SPT) 3-8mm. Many of these infants will have supervised introduction deferred to a subsequent visit and some never return for follow-up. It is currently unknown if and how peanut SPT results change over time in infants.

METHODS: We performed a 5-year retrospective review of all infants who had peanut SPTs placed at two separate time points during the first 24 months of life. Infants at risk of peanut allergy were defined as having a history of atopic dermatitis and/or any other food allergy. Infants were excluded if they had ingested peanut prior to either SPT. The Wilcoxon signed-rank test was used to compare the differences between the distributions of wheel size at both tests, paired for each patient.

RESULTS: Among the 51 infants at risk for peanut allergy, there was a significant difference between the first and second SPT with an average increase of 1.6mm (mean duration between SPTs=5.8 months, p=0.006). This difference increased to an average of 2mm (p=0.001) when excluding 7 infants who had an initial SPT of ≥8mm. Sub-group analysis showed no significant changes in SPT associated with differences in gender, ethnicity, eczema severity, or time between SPTs.

CONCLUSIONS: Peanut SPT size can increase over time in infants at risk for peanut allergy who are avoiding peanut. This supports the need for timely introduction of peanut into the diet of infants with SPTs <8mm.

793 Intranasal nanoemulsion adjuvant vaccine prevents allergic reactions from milk allergy without eliminating serum IgE

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RATIONALE: Most immunotherapies for food allergy require prolonged treatment protocols and do not often lead to long-term allergy protection, which is typically lost within weeks of stopping therapy. Our group has developed an intranasal (IN) nanoemulsion adjuvant that redirects allergen-specific Th2 responses towards Th1 and Th17 and protects from allergen challenge after only four administrations. Here, we investigate the ability of this technology to modulate allergy in a long-term murine model of cow’s milk allergy.

METHODS: Mice were sensitized intraperitoneally with 2 doses of bovine casein protein, administered with aluminum hydroxide. Six weeks after sensitization, mice received four, monthly IN immunizations with nanoemulsion formulated with casein. The mice were subsequently challenged with allergen at 4, 10 and 16 weeks after the final vaccine dose. Control animals were identically sensitized but received IN allergen without eliminating serum IgE.

RESULTS: As compared to control, IN vaccine blocked physiological responses to allergen challenge, and protection persisted for at least 16 weeks. The vaccine modulated casein-specific Th2 immunity and induced Th1 and Th17 cytokines as well as IL-10. There was also a reduction of mast cell numbers in the small intestine. However, while immunized animals showed significantly decreased Th2 cytokine responses, casein-specific IgE remained elevated in the serum.

CONCLUSIONS: IN nanoemulsion vaccine induces long-term protection from anaphylaxis and significantly modulates Th2 immunity despite the persistence of IgE. The sustained unresponsiveness suggests that the nanoemulsion vaccine is changing the allergic phenotype in a manner different from traditional desensitization.

794 First ever real-world safety analysis of preschool peanut oral immunotherapy

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RATIONALE: In 2017, published clinical trial data in 40 subjects demonstrated for the first time that preschool peanut oral immunotherapy (P-OIT) was safe, with predominantly mild symptoms reported and only one case of anaphylaxis requiring epinephrine. We sought to examine whether these findings would hold true in the real world, outside a research setting.

METHODS: As part of a Canada-wide quality improvement project, academic and community allergists administered P-OIT to children who had 1) a positive SPT (≥3mm) or sIgE (≥0.35kU/L) and a history of reaction, or 2) no ingestion history and a positive sIgE (≥0.35kU/L). Patients had bi-weekly clinic visits for updosing, and consumed the dose daily at home between visits, up to a maintenance dose of 300 milligrams over a target of 16 weeks. Symptoms were classified using the World Allergy Organization Subcutaneous Immunotherapy Reaction Grading System (1 mildest, 5 most severe).

RESULTS: Of 220 patients who started P-OIT in 2017-18, 195 completed buildup, and 25 dropped out (11.4%). Twenty-one (84%) dropped experienced reactions. Of all participants, experienced reactions during buildup(average 2.3 reactions per patient).53% grade 1, 43% grade 2, 1.2% grade 3, and 2.4% grade 4. Nine patients (4.1%) received epinephrine(4 in-clinic, 5 at-home), representing 1.76% of reactions (9/512).

CONCLUSIONS: We are the first to describe preschool P-OIT in a real-world multi-center setting. We confirm with a much larger sample that the treatment is safe, as symptoms experienced were generally mild and few reactions received epinephrine. These data support availability of preschool peanut OIT outside research.
Physician and Parent Comfort, Awareness, Barriers, and Implementation of the Guidelines for the Prevention of Peanut Allergy

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RATIONALE: Utilization of the NIAID-sponsored Expert Panel Guidelines for preventing peanut allergy is under-studied, so we explored stakeholder views.

METHODS: Surveys were administered to a convenience sample of physicians (50 [90% pediatricians]) and parents (100) of infants under age 1 year in multiple practice settings in NYC. Surveys described the guidelines.

RESULTS: Most physicians (84%) were guideline-aware, most commonly via colleagues and the AAP newsletter. Physicians’ mean comfort was 4.1 (5-point Likert scale, very comfortable to very uncomfortable). Among Guideline-aware physicians, 60% followed them as written; the remainder modified the approach regarding testing, referrals, introduction time, or patient selection. The greatest physician-perceived implementation barriers were parental acceptance (60%), fear of giving peanut early (46%), and access to allergists (24%). Physicians identified patient handouts (78%) and more infant-safe forms of peanut (52%) as needed resources. For parents, 58% were Guideline-aware, and 90% indicated comfort with early introduction. Among parents with infants over 6 months, peanut-feeding rate was 37% total; among guideline-aware parents in this group, feeding rate was 100%. Pediatricians, internet and friends were the most common sources of information for parents. The greatest parent-identified barriers were fear of reaction (36%), choking (11%), and lack of infant-safe forms (6%). Parents identified a need for more physician advice (44%), brochures (24%) and allergist access (18%).

CONCLUSIONS: Guideline awareness and comfort was high among physicians in this cohort, but many modified the approach. Physicians perceived parental acceptance as a major barrier, yet almost all parents reported comfort. Physician advice and written materials were highlighted as needed resources.

Estimating the Probability of Tolerating Each Challenge Dose of Peanut Protein at Exit Double-Blind, Placebo-Controlled Food Challenge: Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial (PALISADE) of AR101

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RATIONALE: In a phase 3 study of the experimental treatment AR101 for peanut allergy, 67.2% of AR101-treated subjects vs 4% of placebo tolerated >1000mg of peanut protein at exit double-blind, placebo-controlled food challenge (DBPCFC). We determined the single highest tolerated dose (SHTD) of peanut protein at exit double-blind, placebo-controlled food challenge (DBPCFC). We determined the single highest tolerated dose (SHTD) at exit and estimated the probability of tolerating each challenge dose ≤1000mg for the AR101- and placebo-treated groups.

METHODS: SHTDs (mild/no allergy symptoms) at screening and exit DBPCFC were recorded for intention-to-treat (ITT; n = 372 AR101; n = 124 placebo) and for subjects who completed the study (complete, n = 296 AR101; n = 116 placebo) (4-17-years-old). Subjects without an exit DBPCFC were assigned the screening SHTD. A discrete hazards model (treatment-group effect; region; screening SHTD) estimated probability of tolerating each exit dose; hazard ratio was determined (Wald statistic).

RESULTS: The greatest SHTD at screening was 30mg in both groups (37.6% AR101; 42.7% placebo). At exit DBPCFC, SHTDs for AR101 and placebo ITT, respectively, were 50.3% and 2.4% at 1000mg; 16.9% and 1.6% at 600mg; 9.4% and 4.0% at 300mg; 92% of subjects receiving placebo had SHTD of 1-100mg. The adjusted hazard ratio (AR101:placebo) for the probability of tolerating each challenge dose at the exit DBPCFC was 0.15 (95% CI: 0.11-0.19) for the ITT group and 0.05 (95% CI: 0.03-0.06) for those who completed the study.

CONCLUSIONS: AR101 treatment showed a statistically significant treatment effect, consistent with meaningful clinical benefit over placebo. AR101-treated subjects had an 85% increased probability versus placebo to tolerate any dose in the exit challenge ≤1000 mg (ITT), increasing to 95% if subjects completed the study.
Could Early Peanut Introduction In Atopic Infants Increase The Risk of Peanut Induced FPIES?

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RATIONALE: The NIAID recommends early introduction to peanut in atopic infants. However, implementation of this recommendation has resulted in some allergic reactions, early and late. Food protein induced enterocolitis syndrome (FPIES) is uncommon (<1%), especially to peanut. We hypothesize that early peanut introduction in these infants may contribute to peanut induced FPIES.

METHODS: From 2017, infants (4-12 months) with atopic dermatitis were challenged with peanut. Infants were given standard peanut up dosing to a total of 7.75 g over 90 mins. Parents were then advised to continue with 2 teaspoons of peanut flour or butter in diet twice weekly henceforth. Infants who initially tolerated PN in office were followed at home for any delayed allergic response, suspicious of FPIES. Some infants were invited back to office for FPIES confirmation by standard protocol.

RESULTS: Between January 2017 and July 2018, 4 out of 32 (12.5%) high risk infants challenged with peanut had delayed vomiting 2 to 3 hours post peanut ingestion, after initial tolerance. All four patients were initially tolerant to peanut in office. One patient was confirmed to have FPIES from subsequent repeat challenge as per the protocol above. Peanut has been withheld from all four patients’ diets henceforth.

CONCLUSIONS: FPIES to peanut is uncommon, accounting for 1.9% of all FPIES cases. We report a significantly higher incidence of peanut induced FPIES reactions (12.5%) in atopic infants with early peanut introduction. Physicians should be conscious of FPIES reactions that may occur at home as a consequence of early peanut introduction.

Analysis of Alternative Thermal Processing Methods on Peanut Allergenicity Using Nuclear Magnetic Resonance (NMR) Spectroscopy

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RATIONALE: Peanut allergy is considered the most severe of all food allergies as it is the leading cause of fatal anaphylaxis. Evidence suggests that the allergenicity of peanuts is significantly increased in its roasted form when compared with raw. Our project aims to develop alternative processing methods to decrease the allergenicity of peanut.

METHODS: Advanced Glycation End products (AGEs) are considered to be the main cause of increased allergenicity. We first used High-Resolution Magic Angle Spinning (HR-MAS) and solution 1H NMR to take snapshots of the carbohydrate signatures of the peanuts under different conditions. Peanuts were ground into a paste, dissolved in n-hexane for defatting and subsequently analyzed by NMR. Protein extracts from raw, roasted (150°C, 30 minutes) and boiled (100°C, 2 hours in water) peanuts were used to quantify IgE binding via competitive ELISA using serum samples from peanut-sensitive patients.

RESULTS: Defatting of the peanut prior to HR-MAS and solution NMR analyses revealed significant differences between the small molecule profiles of both raw and roasted peanut. Sucrose was dominant in raw peanut while abundant levels of glucose were observed in the roasted form. Competitive IgE binding assay of the extracts revealed no difference in IgE binding between raw, roasted and boiled peanuts.

CONCLUSIONS: The results suggest that NMR spectroscopy is a useful tool for determining small molecule profile differences between different states of the peanut. However, in contrast to recent findings, our results indicate no relevant difference in IgE binding between conditions of non-thermally (raw) and thermally (roasted and boiled) processed peanuts.

Natural Course of Immediate-Type Peanut Allergy in Children

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RATIONALE: Spontaneous resolution of peanut allergy is less likely to occur compared with milk or egg allergies. We aimed to evaluate the natural course of peanut allergy in Korean children and analyze the prognostic factors.

METHODS: We retrospectively collected data from 215 children with peanut allergy. Diagnosis of peanut allergy was defined as a positive oral food challenge (OFC) or convincing history of allergic symptoms within two hours of single ingestion of peanut. Remission of peanut allergy was determined by either negative OFC or parental report of no reaction after peanut ingestion at home. The Kaplan-Meier curve was used to predict resolution of peanut allergy. Demographic information, peanut-specific IgE at diagnosis, eosinophil count in the peripheral blood, family history were analyzed to identify prognostic factors of remission using Cox proportional hazard model.

RESULTS: Boys were 134 (62.33%) and the median (interquartile range, IQR) age at diagnosis of peanut allergy was 32 (20-52) months. Median (IQR) duration of follow-up was 72 (45-102) months. In Kaplan-Meier survival analysis, 10.3% and 31.9% of peanut allergy were resolved at 6 and 12 years of age, respectively. Children with peanut specific IgE > 3 at diagnosis (HR, 13.63; 95% CI 1.01-184.96) was associated with the remission of peanut allergy in multivariable analysis.

CONCLUSIONS: In Korean children with peanut allergy, one-third of patients resolved at 12 years. Tolerance development in peanut allergy is associated with peanut-specific IgE at diagnosis.
Five Year Follow-Up Of Early Intervention Peanut OIT Showed Characteristics of Sustained and Prolonged Clinical Benefit

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RATIONALE: Long-term outcome data following oral immunotherapy (OIT) are sparse. We previously showed high rates of sustained unresponsiveness with early-intervention peanut OIT in preschool children, and report here the first follow-up data from a longitudinal post-treatment study.

METHODS: Caregivers of all 32 participants completing the parent trial were invited to complete a follow-up phone survey assessing the following domains associated with peanut consumption: Quantity, frequency, tolerability, safety, and lifestyle impact.

RESULTS: Survey response rate was 75% (n = 24). Mean follow-up interval was 62 months. Twenty-three subjects (96%) continue peanut consumption, including 92% who ignore precautionary labels. Twenty-two (92%) reported no allergic symptoms following ingestion; 2 (8%) reported transient mild symptoms. One subject (4%) with multiple food allergies (92%) reported no allergic symptoms following ingestion; 2 (8%) reported transient mild symptoms. One subject (4%) with multiple food allergies stopped consuming peanut two years after study completion due to transient mild symptoms. Spearman correlations were used and p < 0.05 was deemed significant.

CONCLUSIONS: Five years after early-intervention OIT, most caregivers reported improved lifestyles and safe and well-tolerated consumption of peanut. Some participants developed features suggesting sustained and prolonged clinical benefit from peanut OIT. Further follow-up is needed.

Predictors of allergic symptoms and anaphylaxis during peanut oral immunotherapy

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RATIONALE: Peanut oral immunotherapy (POIT) can be an effective therapy for peanut allergy (PA), but adverse reactions are common. Risk factors for allergic reactions, including anaphylaxis during treatment, remain uncertain.

METHODS: This study is a retrospective chart review of 595 PA patients (3-48 years old, mean 9 years) who received POIT over 8 years. Frequency of allergic symptoms related to a patient’s peanut-specific IgE, Ara h1 and Ara h2, and skin test size were analyzed. Asthma, atopic dermatitis, and aeroallergen sensitivity were evaluated as potential risk factors for allergic symptoms. Spearman correlations were used and p < 0.05 was deemed significant.

RESULTS: 519 patients (87%) reached a maintenance dose of 2.5 peanuts per day. During build-up, 54 patients (9%) experienced anaphylaxis, 506 patients (85%) experienced gastrointestinal (GI) symptoms, 276 (46%) experienced cutaneous symptoms, and 118 (20%) experienced respiratory symptoms. Elevated peanut-specific IgE correlated with respiratory symptoms. Ara h1 (p = 0.022) and GI (p < 0.001) symptoms. Ara h1 (p = 0.041) and Ara h2 (p = 0.010) correlated with GI symptoms. Atopic dermatitis correlated with developing cutaneous symptoms during build-up phase (p < 0.001). During maintenance, 98 patients (17%) experienced anaphylaxis. There was not a correlation between baseline peanut IgE or peanut components and the occurrence of adverse reactions during the maintenance phase of treatment.

CONCLUSIONS: POIT is a safe therapy for patients with PA, the majority of symptoms were mild. Baseline peanut IgE, Ara h1, and Ara h2 appear to be predictive of experiencing allergic symptoms during build-up phase, but not during maintenance phase. The presence of atopic dermatitis may be predictive of cutaneous symptoms during POIT.

Triggers and Management of FPIES in a Pediatric US population.

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RATIONALE: Food Protein Induced Enterocolitis Syndrome (FPIES) is a non-IgE mediated reaction to food, affecting infants and young children; it can be severe and may result in shock. The aim of our study was to identify the triggers, characteristics and treatment approach of FPIES in a pediatric US population.

METHODS: A retrospective electronic records review of children presenting with FPIES over a 3-year period.

RESULTS: We identified 74 cases of FPIES between 2015-2018. Median age of first episode was 5 months and median age of diagnosis was 13 months. The majority were white (90%). Female to male ratio was 1:1. 45% (34/74) of patients had atopic dermatitis, 19% (14/74) allergic rhinitis, 7% (5/74) an IgE-mediated food allergy and 7% (5/74) asthma. In 31% (23/74) of the patients only one trigger food was identified, while 18% (13/74) had two food triggers. In 51% (38/74), three or more trigger foods were identified and included rice (53%), milk (49%), vegetables (43%), fruits (40%), oats (35%), soy (31%), meat (13%) and fish (1%). Most patients had a negative SPT (74%, 55/74) or specific IgE (66%, 49/74) to their FPIES trigger food(s). Dietetic consultation was provided in 76% (56/74). ER visits occurred in 54% (40/74) and 24% (18/74) required hospitalization. Sepsis workup was performed in 22% (16/74) of our population and abnormal labs were found in 5% (4/74).

CONCLUSIONS: In our cohort there was an 8-month delay in the diagnosis of FPIES suggesting that this condition is still under-recognized. Dietetic evaluation has increased compared with previous reports.
Accidental Exposures to Peanut and Other Food Allergens: Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial (PALISADE)

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RATIONALE: Current management of peanut allergy is strict allergen avoidance coupled with prompt recognition and symptomatic treatment if exposure occurs. In subjects undergoing peanut desensitization using AR101, an investigational oral biologic with a characterized peanut protein profile, accidental exposures to peanut and other allergens were reported.

METHODS: A phase 3 study of experimental peanut desensitization with AR101 recorded discrete accidental food allergen exposures (unintended ingestion of the allergenic food), related adverse events (AEs), and associated rescue medication (subjects aged 4-17-years-old). Eligible subjects reacted to ≤100mg peanut protein as determined by a screening double-blind, placebo-controlled food challenge.

RESULTS: 66% of subjects reported food allergies other than peanut at enrollment. 19.6% (n=77/372) of actively-treated subjects reported 106 accidental exposures while on study: 33 subjects’ (8.9%) were attributed to peanut, 50 subjects’ (13.4%) to other foods. 33.1% (n=40/124) placebo-treated subjects reported 56 accidental exposures: 15 subjects’ (12.1%) were attributed to peanut and 28 subjects’ (22.6%) to other foods. Peanut exposures leading to AEs (active n=29, 7.8%; placebo n=14, 11.3%) requiring treatment (active n=24, 6.5%; placebo n=13, 10.5%) were observed in both treatment groups, but were reported less frequently in the AR101 group. Within the actively treated group, peanut exposures leading to AEs or requiring treatment were lower in the maintenance (1.6%) versus AR101 group. Peanut exposures leading to AEs or requiring treatment were lower in the maintenance (1.6%) versus placebo group.

CONCLUSIONS: Accidental exposures attributed to peanut were reported less frequently, had fewer associated AEs, and required less rescue medication in the actively treated group compared to the placebo group. Underreporting of exposure possibly occurred if no/mild symptoms were experienced.

Is Emergency Room Care After Home Use Of An Epinephrine Auto Injector Always Needed?

Deanna K. Hamilton, RN

RATIONALE: Emergency room evaluation and observation of patients who have used an epinephrine auto-injector to treat an allergic food reaction at home is the standard of care. Requiring patients to go to the ER after epinephrine injection often deters families from administering epinephrine. Withholding or delaying treatment with epinephrine increases the risk of death from anaphylaxis. We hypothesized that this standard could be modified to prompt the early and more frequent use of epinephrine during an allergic reaction without decreasing patient safety.

METHODS: A chart review of 47 pediatric subjects who received epinephrine treatment during a food challenge was conducted. All food challenges were initial screening challenges for research study participation. This group was selected for review because of the high likelihood of allergic reaction. The goal was to see which subjects needed additional medical intervention after the initial dose of epinephrine and therefore would have benefited from ER care.

RESULTS: Of the 47 charts reviewed 13 (27.6%) of subjects required additional treatment after Epinephrine use to resolve symptoms. Nine (19.1%) needed a second dose of Epinephrine and 4 (8.5%) needed an additional dose of oral antihistamines.

CONCLUSIONS: These findings suggest over 1 out of 4 patients will need additional medical intervention after the initial Epinephrine dose. Therefore the recommendation of seeking ER care after emergency auto injector use is still valid given the high likelihood that additional treatment will be needed. Additionally improved patient education on the importance of early epinephrine use and ER care may be needed.

Third-Party Evaluation Of The Nima Peanut Sensor: A Consumer Device for the Detection of Peanut in Food

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RATIONALE: For individuals with peanut allergy, avoiding illness can at times be difficult due to undetermined amounts of allergens in foods. A portable consumer device for testing peanut levels in foods could aid. Described are independent validation studies to evaluate the performance of such a newly developed portable peanut sensor for foods.

METHODS: In one study, 29 differently available quality control and reference materials obtained from various accredited providers were tested in replicates of 6 using the device. An additional evaluation was performed using 10 food matrices spiked to concentrations of peanut ranging from 5 ppm to 100 ppm, with the 0 ppm matrices used as negative controls.

RESULTS: The first study yielded an average Accuracy of 98.7% (± 1.8% CL) at the device LOD of 10 ppm, and above. The average True Positive Rate (TPR) was 98.9% (± 2.2% CL). For the second study, Accuracy was 99.2% (± 1.1% CL) and the TPR was 100% for approved samples. The device correctly identified samples spiked to 10 ppm and above that had also been identified with ELISA testing as containing peanut above the LOQ of the assay.

CONCLUSIONS: Independent validation of the peanut sensor device indicated that at 10 ppm peanut detection, the device has the potential to aid sensitive individuals in their daily food choices.
RATIONALE: Some studies suggest that the BAT more accurately predicts clinical peanut allergy than skin testing or serum IgE levels, potentially reducing the need for OFCs. However, basophils are not stable ex vivo and activation testing must take place within 3-4 hours of sample collection to achieve reliable results, thus excluding this test from most clinical settings. We tested a novel BAT prototype methodology developed by Beckman-Coulter, which can be done in the clinic and shipped to a central lab, to evaluate whether BAT results were stable over several days.

METHODS: Thirty subjects with a history of peanut allergy, elevated concentrations of peanut antigen (0.0001-10 mg/ml) and activation was measured by flow cytometry at 0, 1, 3 and 5 days post-stimulation. The dose-response curves were summarized using area under the curve (AUC). Mixed-effect models and intra-class correlation coefficients (ICC) were used to compare results across days.

RESULTS: Twenty-six (87%) subjects had basophil activation (>15% CD63+) to at least one concentration of peanut extract. AUC had high agreement between day 0 and the subsequent days (ICC=0.97%) and was not significantly different from day 0 on days 1 (p=0.717) and 3 (p=0.365). Day 5 activation remained positive but slightly lower than day 0 (p=0.004).

CONCLUSIONS: With the tested methodology, cytometric analyses can be performed up to 5 days after sample collection with excellent precision, which could make BAT available for use in the standard clinical setting.

808 Frequency of allergic symptoms during build-up and maintenance phases of peanut oral immunotherapy

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RATIONALE: Peanut oral immunotherapy (POIT) is an effective treatment for desensitizing peanut allergic patients, but the frequency of adverse reactions has limited its widespread use in clinical practice. This study reviews the frequency of allergic symptoms POIT patients experienced at a food allergy treatment center.

METHODS: This is a retrospective chart review of 595 patients (3-48 years old, mean age 9 years) with peanut allergy who received POIT over 8 years. Outcomes included percentage of patients who experienced allergic symptoms during build-up and maintenance phases (tolerating ≥2.5 peanuts per day) of POIT.

RESULTS: 519 patients (87%) reached maintenance dose. During build-up phase, 506 patients (85%) experienced at least 1 episode of gastrointestinal (GI)-related symptoms. The majority were mild, including abdominal pain (68%) and oral itch (50%). During build-up, 276 patients (46%) experienced cutaneous symptoms, 118 patients (20%) experienced respiratory symptoms, and 54 patients (9%) had at least one episode of anaphylaxis. Once patients reached maintenance, they experienced fewer GI (24%), cutaneous (14%), and respiratory symptoms (6%). During maintenance phase, 98 patients (17%) experienced at least one episode of anaphylaxis. Of those who experienced anaphylaxis, exercise-induced anaphylaxis occurred in approximately 20% of patients in build-up and maintenance. No patient hospitalizations or fatalities were observed as a result of treatment. Eight patients (1.3%) developed eosinophilic esophagitis (EOE) during POIT.

CONCLUSIONS: POIT can be a safe, effective treatment for most patients with PN allergy. Mild GI or cutaneous symptoms were common, and anaphylaxis was observed in both build-up and maintenance. EOE occurred rarely in this patient population.

809 Infant Peanut Allergy Testing in the Post-LEAP World

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RATIONALE: NIAID addendum guidelines for early peanut introduction with screening for specific at-risk populations were introduced in 2017. We hypothesize that in practice, these guidelines are not being followed consistently by pediatricians and allergists.

METHODS: Retrospective chart review of infants <11 months tested for peanut allergy in outpatient Allergy clinic between January 2017 and February 2018.

RESULTS: One-hundred infants had peanut testing (81 as screening and 19 post introduction for reaction concern). Of 81 patients screened, 67 were referred by pediatricians (40% met NIAID screening guidelines). Of patients meeting NIAID guideline criteria for screening (33), 12 had negative SPT (75% introduced peanut successfully; 1 reacted at home), 8 had SPT wheel of 3-7mm (75% were recommended avoidance), and 5 had SPT wheel >7mm (100% were recommended avoidance). Referrals not meeting criteria included family history of food allergy (52%), mild-moderate eczema (100%). Of those not meeting guidelines but screened (48), 24% were asked to avoid peanut based on testing, and 10% (5) reacted on subsequent introduction. Of the 19 patients referred for reaction concern after introduction at home, 5 would have met criteria for screening.

CONCLUSIONS: Majority of infants being screened in the Allergy clinic do not meet NIAID guidelines. Reasons for referrals not meeting guidelines include mild-moderate eczema and family history of food allergy. Infants who meet criterion for screening prior to introduction are also being missed. Guideline to offer challenges to patients SPT 3-7mm is often not followed.
810 Preferences in Terminology Used to Describe Oral Immunotherapy Varies Based on Physician Utilization

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RATIONALE: Real-world data from a diverse sample of allergists/immunologists were collected to better understand preferred terminology utilized in oral immunotherapy (OIT), especially when communicating with patients.

METHODS: An online, self-administered survey was fielded to U.S. allergists/immunologists (12/28/2017-1/27/2018). Eligibility criteria included: completed training ≥3 years ago; spent ≥20% of time in direct patient care; and managed ≥50 patients with food allergy. Responses were stratified by whether physicians treated patients with OIT in the past year (OIT and non-OIT users).

RESULTS: 101 allergists/immunologists participated (OIT users n=48; non-OIT users n=53). OIT users were more likely to be from a hospital/academic-based clinic compared to non-OIT users (34% vs 9%); while non-OIT users were more likely to be in a private practice or other outpatient clinic compared to OIT users (91% vs 56%). “Reactive dose” during oral food challenge (OFC) was defined as the dose when symptoms occur (69.4%; 61.2%, respectively), but also as the lowest dose (8.2%; 20.4%) or cumulative dose (14.3%; 6.1%) when symptoms occur. “Tolerated dose” was defined as highest dose tolerated without symptoms (20.4%; 42.3%), the dose when no symptoms occur (36.7%; 23.1%), or as cumulative tolerated dose without symptoms (16.3%; 5.8%). Overall, 81% agreed that “tolerated dose” was most clinically meaningful. The majority (83.3%; 92.4%) felt stronger consensus among clinicians regarding OIT terminology would be extremely/very useful.

CONCLUSIONS: While variability in definitions for OIT terminology was evident, both OIT and non-OIT users agreed that “tolerated dose” was the most clinically meaningful for patients to know, and that consensus in OIT terminology is needed.

811 Comparisons of in-house wheat skin prick test extracts for the diagnosis of wheat dependent exercise induced anaphylaxis (WDEIA)

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RATIONALE: Skin prick test (SPT) and specific IgE (sIgE) to wheat help diagnose wheat dependent, exercise-induced anaphylaxis (WDEIA) in addition to food and exercise challenges. However, commercial wheat extract and sIgE to wheat provide unsatisfactory results. We determined the performance of in-house wheat extracts for SPT and compared them with commercial extract as well as sIgE to wheat and α5-gliadin, for the diagnosis of WDEIA.

METHODS: Nine patients with WDEIA and 9 controls with history of wheat allergy and negative wheat challenges, were recruited. SPT using 4 in-house extracts (wheat Coca’s, wheat sodium base (SB), gliadin and glutenin solutions), and commercial extract, were performed. sIgE to wheat and α5-gliadin were measured.

RESULTS: Patients with WDEIA were significantly older (15.3 vs 5.3 years, p=0.01) and had later onset of symptoms compared to controls (5.5 vs 0.6 years, p=0.001). The mean wheal diameter of SPT of all, except commercial extract, were significantly larger in WDEIA compared to controls (p<0.05). sIgE to α5-gliadin, but not to wheat, was significantly higher in WDEIA compared to controls (p=0.0001). Using their best cut-offs by the ROC curve, the sensitivities of in-house wheat-Coca’s, SB, gliadin, glutenin, and commercial extracts, sIgE for wheat and α5-gliadin were 77.8%, 66.7%, 88.9%, 77.8%, 44.4%, 77.8% and 88.9%, respectively. The specificities were 66.7%, 77.8%, 88.9%, 88.9, 88.9%, 66.7% and 100%, respectively. sIgE to α5-gliadin provided the best positive and negative likelihood ratio (+LR = α, -LR = 0.11) followed by SPT to gliadin (+LR = 8, -LR = 0.12).

CONCLUSIONS: sIgE to α5-gliadin and SPT with gliadin extract were useful tools in diagnosing WDEIA.

812 Safety of Food Challenges in Infants Under 1.5 years: A Retrospective Analysis

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RATIONALE: Limited data suggests that severe reactions during infant oral food challenge (OFC) are rare. Here we report OFC outcomes among young infants at a single center.

METHODS: We retrospectively reviewed outcomes of OFC in a single center over 10 months. Analysis included all children aged less than 1.5 years who underwent OFC based on clinician assessment of history and testing. Failure was defined as any objective symptom requiring either cessation of feeding and/or treatment.

RESULTS: Of 60 infant food challenges (median age 11 months, IQR 9-12), there were 20 failures (33%), including 9 peanut, 5 baked egg, 2 cow milk, 2 tree nut, 1 unbaked egg, and 1 wheat. Symptoms among those failing were most often cutaneous (80%, N=16) and gastrointestinal (35%, N=7). Two (10%) developed cough; none had respiratory distress. Of failures, 30% (N=6) were given epinephrine; 4 for urticaria with emesis, and 2 for diffuse urticaria. Median skin prick test (SPT) wheal diameter for failures was 7 mm (IQR 3-8); for passes, 3 mm (IQR 2-4). Of 23 challenges for peanut, 39% (N= 9) were failures; median SPT wheal for peanut failures was 6.5mm (IQR 4-8); for passes, 2 mm (IQR 0-3.5). No infant with peanut SPT ≤2 mm failed.

CONCLUSIONS: Infant OFC may be safely conducted in the office. Need for intervention with epinephrine in 10% of OFC (30% of failures) suggests a benefit of screening and in-office challenges. Introduction of peanut at home for infants with SPT diameter less than 2mm appears to be safe.
RESULTS: Food allergy prevalence in the US and Australia is 6.7% and 11%, respectively. There was a statistically significant higher proportions of 1-year-old children diagnosed with egg and peanut allergies in Australia. The proportion of peanut allergies in the US was lower (0.9, CI 0.8-1.0) compared to Australia (7.6, 6.9-8.4), and egg allergies in the US was also lower (1.5, 1.48-1.6) compared to Australia (13.57, 12.6-14.5). The proportions of milk and shellfish allergies show no statistical significance.

CONCLUSIONS: Though both regions share similar food allergies, Australia had a higher prevalence than the US when comparing egg and peanut allergies. Evaluating the rates in geographically different regions may give insight on the contributing factors of food allergies, concerning ethnicity and environment.

Racial Differences in Food Allergy Outcomes among Children in the United States

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RATIONALE: Racial/ethnic disparities in IgE-mediated food allergy (FA) have not been extensively studied. This study describes differences in FA-related outcomes among major racial/ethnic groups in the United States.

METHODS: A population-based web/phone survey was administered between 2015-2016, resulting in parent-proxy-report data for 38,408 children. Children with suspected non-IgE mediated allergies (e.g. oral allergy syndrome and/or intolerances) were excluded via stringent symptom-report criteria. Complex survey-weighted proportions and multiple logistic regression models compared FA prevalence, and other characteristics by race.

RESULTS: Findings indicate that 6.5% [95% CI: 5.1-8.3] of Asian children, 7.0% [6.4-7.6] of White children, 8.4% [7.2-9.7] of Hispanic/Latino children, 8.8% [7.5-10.5] of Black children, and 8.1% [6.6-10.0] of multiple/other race children have current FA. The proportion of food-allergic children reporting lifetime FAED visits for FA treatment ranged from 37.4% of White children to 47.3% and 49.2% of Black and Hispanic allergic children, respectively. Similar differences emerged when examining rates of FA-related ED visits in the last year. However, rates of physician-diagnosed FA and current epinephrine auto-injector prescriptions did not differ significantly by race among individuals meeting stringent criteria for IgE-mediated FA after adjustment for demographics, FA characteristics and atopic comorbidities. In similarly adjusted models, odds of experiencing severe reaction symptoms did not differ by race, although food-allergic Black and Asian children had significantly elevated odds of multiple FAEDs compared to Whites (OR 1.9-2.0; p<.05).

CONCLUSIONS: These national data indicate that FA prevalence and ED visit rates appear elevated among Black and Hispanic US children compared to their White and Asian peers.
Prevalence and Evaluation of Shellfish Allergy in a Large Urban Hospital System

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RATIONALE: Shellfish allergy is one of the most common food allergies self-reported in adults. It is estimated to be 60% of seafood allergy in the United States. However, prevalence of physician diagnosed shellfish allergy is unknown. The aim was to characterize the prevalence of shellfish allergy in our population.

METHODS: We used clinical looking glass database to retrospectively identify patients who were seen in the primary care setting (Internal Medicine (IM), Family Medicine (FM) clinics) and allergy clinics at Montefiore Medical Center from 2014-2016 with a diagnosis for shellfish allergy. Crab, lobster and shrimp IgE levels were collected, when performed.

RESULTS: Of 199,203 patients seen in Internal medicine (IM) and family medicine (FM) clinics, 2,255 (1.13%) had documented shellfish allergy. Of these, 324 (14%) were seen in allergy clinic. An additional 4,133 patients were not seen in IM or FM clinics but had documented shellfish allergy. Total population of individuals with documented shellfish allergy was 6,388. Of these, 6,388 individuals, the number of individuals that were seen in allergy clinic was 529 (8.3%). Only 88 (1.4%) had IgE levels for crustacean shellfish checked. Of these, 45 (51.1%) IgE level was <0.35 kU/L.

CONCLUSIONS: Based on our data, even though large portion of the population carries a documentation of shellfish allergy, only a small portion had serum specific IgE to crustacean shellfish checked. Half had negative results. This suggests that we may be over estimating true shellfish allergy. Further prospective studies need to be done to identify those who have true IgE mediated shellfish allergy.

Early Egg Introduction to Infant Diet and Egg Allergy Prevention: Meta-Analysis of Randomized Controlled Trials

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RATIONALE: The timing of the introduction of egg to infant’s diet is of current interest. Therefore, meta-analysis of the existing literature was conducted to evaluate whether the early introduction of egg to infants influences the development of egg allergy and whether dosage or nature of the allergen and atopy status can influence the results.

METHODS: Literature searches were conducted in MEDLINE, EMBASE and CENTRAL, and trial protocols were searched in Meta Register and OpenGREY. Only randomized controlled trials (RCTs) comparing early (between 3-6 months of age) egg introduction to no early introduction were included. The primary outcome was the development of egg allergy.

RESULTS: Of the 416 articles identified and screened, 6 RCTs met the eligibility criteria for data extraction. Allergic outcomes were evaluated in a total of 3032 participants. A moderate level of evidence showed a benefit of the early introduction of egg (relative risk [RR], 0.60; 95% CI, 0.44-0.82; P = .002; mild heterogeneity [I2 = 23%]). There were variable doses of egg protein exposure, with a median dose of 2800 mg/week (range 350–7500 mg/week). Consumption of <4000 mg/week of egg protein had a greater preventive effect than a higher dose.

CONCLUSIONS: This systematic review and meta-analysis showed an association between the early introduction of egg and a possible lower risk of egg allergy. Furthermore, the nature and dose of egg protein exposure may play a role. These findings should be addressed in the context of the primary studies.
819 Prevalence of Comorbidities with Peanut Allergy: Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial (PALISADE)

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RATIONALE: Peanut allergy (PA) is increasing in prevalence and seriously impacts quality of life for patients and caregivers. To better understand the burden of PA, we explored allergic comorbidities reported in the PALISADE study population.

METHODS: Study subjects were enrolled in PALISADE, a randomized, double-blind, placebo-controlled phase 3 trial of AR101 oral immunotherapy for PA. Eligible subjects were aged 4-55-years-old and tolerated ≤100mg peanut protein as determined by a double-blind, placebo-controlled food challenge. Comorbidities calculated in the primary analysis population (4-17-years-old) included asthma (baseline asthma control test [ACT] and lung function also captured), atopic dermatitis (AD), allergic rhinitis (AR), other food allergies (FAs), and history of peanut-related anaphylaxis.

RESULTS: 496 PA subjects aged 4-17-years-old enrolled in PALISADE (n=372 AR101-treated; n=124 placebo-treated). Median tolerated dose was 10mg peanut protein at baseline. Previous peanut-related anaphylaxis was reported in 72% (n=358) of subjects, with 30% of these experiencing ≥2 episodes. 95% of subjects reported other atopic disorders or allergic comorbidities in addition to peanut allergy, 66% of subjects reported FAs in addition to peanut. Overall, AD was reported in 62% (n=308) of subjects and AR was reported in 72% (n=356). Approximately half of the population had asthma (53%, n=263) which was well-controlled (ACT score ≥20) based on key inclusion/exclusion criteria. The distribution of these comorbidities was well-balanced between the AR101 and placebo groups.

CONCLUSIONS: PALISADE enrolled a highly sensitive peanut-allergic cohort with multiple atopic comorbidities, presenting allergists the opportunity to continually evaluate and manage these common comorbid conditions associated with PA.

820 Knowledge regarding epinephrine auto-injector use and peanut introduction among resident and staff pediatricians at an academic health center

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RATIONALE: Health care provider (HCP) knowledge on use of epinephrine auto-injectors (EAI) has not been widely studied. HCP awareness of peanut introduction guidelines can vary. This study assessed knowledge on EAI use and peanut introduction guidelines among residents and staff pediatricians affiliated with an academic medical center.

METHODS: Pediatric residents of different post graduate years (PGYs) and staff at Indiana University Health completed a 5-6 question survey on EAI use and peanut introduction, anonymously, from January to July 2018.

RESULTS: The overall pediatric resident response rate was 48% (n=95/198; new PGY1 [30/46; 65%]; middle PGY1 [25/45; 56%]; PGY2 [19/44; 43%]; PGY3 [17/43; 40%]; PGY4+ [4/20; 20%]). PGY4+ were less likely to respond than other PGYs (p=0.006). Forty percent of residents (n=38) did not know how to use an EAI, with no significant differences among PGY levels. Twenty one staff pediatricians were also surveyed. There were no significant differences between staff and PGYs, or among PGY levels, regarding correct responses to any of the five questions on peanut introduction (p-values 0.31-0.99, NS). The majority of residents (88%) and staff (90%) knew that early introduction to peanut reduces risk of peanut allergy development. The majority of residents (53%) and staff (81%) did not know the appropriate screening of infants at high risk for peanut allergy.

CONCLUSIONS: Forty percent of residents do not know how to use an EAI, emphasizing the need to improve EAI education. Pediatricians know the importance of early peanut introduction, but need further guidance.

821 Troponin C is the Major Shrimp Allergen Among Chinese Patients with Shellfish Allergy

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RATIONALE: Shellfish is a frequent cause of food allergy in Asia-Pacific. Tropomyosin is recognized to be the major shrimp allergen. However, little is known about the prevalence of shrimp allergen sensitization among the Chinese population. This study aimed to evaluate the IgE sensitization pattern to shrimp allergens among shellfish-allergic patients in Hong Kong.

METHODS: Chinese subjects with a history of shellfish allergy within five years and/or a positive skin prick test (wheat ≥3 mm) to shellfish mixture were recruited. Serum specific IgE (sIgE) levels to shrimp extract and tropomyosin tPen a1 were measured by ImmunoCAP. sIgE reactivity to seven recombinant shrimp allergens including tropomyosin (TM), arginine kinase (AK), myosin light chain (MLC), sarcoplasmic calcium-binding protein (SCP), troponin C (TnC), triosephosphate isomerase (TIM) and fatty-acid-binding protein (FABP) were measured by ELISA.

RESULTS: Among 74 shellfish-allergic subjects (54% male; median age = 25 years [2-58]), 38 (51.4%) and 16 (21.6%) had positive sIgE (≥0.35 kUA/L) to shrimp extract and tPen a1, respectively. Sensitization to multiple shrimp allergens was common among subjects with positive sIgE to shrimp (17/38; 44.7%). Patients who were sensitized to shrimp by sIgE more frequently recognized TnC (19/38; 50.0%), followed by TM (16/38; 42.1%), and AK and FABP (15/38; 39.5%).

CONCLUSIONS: Sensitization to multiple shrimp allergens was common in Chinese shellfish-allergic subjects, with TnC being the major allergen. Further studies need to examine the relationship between IgE sensitization pattern and clinical reactivity to shrimp. (Funding: Hong Kong Institute of Allergy Research Grant 2017; AXA Post-doctoral Fellowship)
**822 Omalizumab Gets Tolerance In Patients With Severe Food Allergy: A Real-Life Study**

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**RATIONALE:** The effects of Omalizumab on food allergy thresholds are poorly studied out of the context of Oral Immunotherapy. This real life study aims to assess the effect of Omalizumab on food tolerance in children treated for severe asthma.

**METHODS:** We review the food thresholds of patients with severe asthma and anaphylactic reactions to 2+ foods before and after a 4-month-long Omalizumab treatment. We also report their asthma control and quality of life, measured by PedSQL.

**RESULTS:** Fifteen children—allergic to 37 foods—got a threshold increase for milk, egg, wheat and hazelnut from 1221.1 ± 1736.7 mg to 8553.7 ± 8063.6 mg eliciting dose (p < 0.001). Patients reached full tolerance for 70.4% of the tested foods, which were re-introduced in the patients’ diet without necessity of oral immunotherapy procedures. The remaining foods were partially tolerated. The number of reactions to unintended ingestion of allergenic foods over 4 months dropped from 47 to two. The PedSQL increased from 60.47 ± 5.32 to 87.25 ± 7.33 (parental judgement; p < 0.001) and from 62.99 ± 7.39 to 89.71 ± 4.54 (patients’ judgement; p < 0.001). Omalizumab costed a mean of € 1,311.63 per month.

**CONCLUSIONS:** Food tolerance increased by 7 times during Omalizumab treatment for severe uncontrolled asthma. The patients’ quality of life increased, due to better asthma control and reduction of dietary restrictions. The cost/benefit ratio of such treatment for selected cases of severe food allergy remains to be evaluated.

**823 Baseline Scores On Food Allergy Quality Of Life Questionnaire (FAQLQ) And State/Trait Anxiety Inventory In Mothers Of Cows Milk Allergic Infants Recruited To A Randomised Controlled Trial Of Single Low Dose Challenges With Cows Milk.**

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**RATIONALE:** The Food Allergy Quality of Life Parent Form (FAQLQ-PF) questionnaire has proven a valid and reliable measure of change in randomised control trials in food allergy management (RCT). Single dose challenges are a novel method of assessing low dose reactivity in food allergic children. We report the baseline scores on QOL and maternal anxiety questionnaires at randomisation in an ongoing RCT of single dose challenges in cow’s milk allergic infants.

**METHODS:** FAQLQ-PF, the Food Allergy Independent Measure (FAIM) and the State/Trait Anxiety Inventory (STAI) questionnaires were used. Total STAI score (on a scale of 20 to 80) was categorised as severe anxiety ≥ 75th percentile; moderate anxiety 75th to 25th percentiles; and mild anxiety < 25th percentile.

**RESULTS:** To date mothers (mean age 37, 3.2) of 20 infants (mean age months 7.4, 1.9) have completed all measures at enrolment. Mean scores for FAQQLQ (3.0, 1.6) and FAIM (3.9, 1.6) were above norms for age. State anxiety was normally distributed (Shapiro-Wilk >0.05) and was positively associated with FAQQLQ (r=0.4, p=0.04), FAIM (r=0.63, p=0.001), and Trait anxiety (r=0.66, p=0.001).

**CONCLUSIONS:** The small standard deviations and normal distributions on all measures suggest an homogenous sample. There were significant associations found between anxiety, expectation of adverse outcome if an accident occurs for child, and parental perceived quality of life in infants at randomisation in an RCT of treating cows milk allergy in young infants.

**824 Perceived food allergy, sensitivity, or intolerance and its impact on breastfeeding practices**

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**RATIONALE:** The impact of suspected allergic disease on breastfeeding duration is not well defined. The purpose of this study was to examine the association of reported infant adverse reactions to food with breastfeeding duration and the impact of infant age and specific symptoms on this relationship.

**METHODS:** 2,586 breastfeeding mothers who participated in the Infant Feeding Practices Study completed surveys at 4, 9, and 12 months postnatally regarding breastfeeding duration and infants’ adverse food reactions. Four groups were considered: no food reactions (84.6%), reaction to something the infant ate (10.6%), reaction to a food the infant was exposed to via breastmilk (2.4%), and reaction due to both sources (2.4%). Kaplan-Meier survival curves were utilized to compare breastfeeding duration between groups using Logrank Tests.

**RESULTS:** Mothers who reported reactions due to food exposure, either alone (M=45.8 weeks) or in combination with food the infant ate (M=40.2 weeks), breastfed significantly longer than mothers who reported no reactions (M=32.0 weeks), and mothers who reported a reaction to a food the infant ate only (M=27.3 weeks); all p<.01. Later symptom onset (p=.03) and eczema with food issues (p=.06) were associated with longer breastfeeding duration. Similar associations were noted using Cox Proportional Hazards Models adjusted for race/ethnicity, income, and maternal age.

**CONCLUSIONS:** Mothers’ perceptions regarding infants’ adverse reactions to food appear to impact breastfeeding duration. Future work should explore how problems with food factor into mothers’ decisions about breastfeeding, their diet, and infant solid food introduction, especially in the context of allergen introduction in infancy.
Prevalence of Physician-Reported Food Allergy in Canadian Primary Care Practices

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RATIONALE: To date, prevalence data for food allergy (FA) in Canada is limited to self-report, with a previous survey documenting self-reported FA prevalence of 8.3%. Our study is the first in Canada aiming to determine the prevalence of physician-reported FA using Electronic Medical Record (EMR) data from providers participating in the Manitoba Primary Care Research Network (MaPReN). We expect a lower prevalence of FA compared to self-reported rates.

METHODS: An algorithm detecting FA documentation was constructed and validated, defining 2,817 of 4,488 possible allergy related chart entries as FA. The MaPReN repository contains 221,132 patients of all ages (52.4% females) receiving primary care in Manitoba, Canada. Patients with FA were identified by the constructed algorithm. Descriptive statistics assessed for FA prevalence and a multivariable logistic regression model determined the association with patient, provider and practice variables.

RESULTS: 1.4% of participants have a documented FA, of which 61.4% have one or more comorbidities (asthma, depression, diabetes, hypertension, autism, or ADHD). Of those with FA, 44.8% (P < 0.0001) and 34.3% (P < 0.0001) are diagnosed with asthma and eczema, respectively. Individuals with FA have 1.8 times higher odds of an eczema diagnosis (CI 1.47-2.11%) and 2.1 higher odds of having one or more comorbidities (CI 1.89-2.41) compared to non-FA patients.

CONCLUSIONS: EMR derived data revealed a lower prevalence of FA than previously determined based on patient self-report. The algorithm created in this study will be applied within the Canadian Primary Care Sentinel Surveillance Network (CPCSSN), to determine Canada’s national prevalence of FA and investigate geographical variation of FA prevalence.

Safety of single vs multiple food oral immunotherapy in a private practice setting

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RATIONALE: Oral immunotherapy (OIT) with single and multiple foods is increasingly used for treatment in community settings. Ascertaining the safety profile of such therapy is paramount.

METHODS: A retrospective chart review of 121 patients completing single or multiple food OIT was conducted. Data on number of treated foods, concomitant omalizumab administration, and adverse reactions was analyzed.

RESULTS: Sixty-three of 69 enrolled multiple food OIT patients and 51 of 52 enrolled single food OIT patients successfully completed OIT buildup. Twenty-four of the multiple food and 9 of the single food OIT patients used concomitant omalizumab.

In the multiple food OIT group, 29(42%) patients experienced cutaneous symptoms, 29(42%) respiratory, 53(76%) gastrointestinal, and 1(1%) cardiovascular during treatment. Twenty-seven (39%) patients had reactions requiring dose adjustment. Five of 24 omalizumab users versus 22 of 45 non-omalizumab users had reactions requiring dose adjustment (p=0.02). Epinephrine-requiring reactions occurred in 6(10%) of the single food OIT patients, none using omalizumab.

CONCLUSIONS: Adverse reactions, especially gastrointestinal, are common and similar in single and multiple food OIT when unadjusted for omalizumab use. Reactions requiring OIT buildup dose adjustment appear less common in the multiple food omalizumab group. Epinephrine-requiring reactions were similar between groups.

Chart Review to Evaluate Co-Sensitization Between Cashew and Sesame

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RATIONALE: In the USA, the diagnosis of tree nut and seed allergy appears to have increased in recent years. An association between tree nut and sesame allergy has been observed, and we noticed a particular association between cashew and sesame allergy. We sought to investigate this further.

METHODS: We reviewed electronic medical records for office visits between July 1-20, 2016 at our pediatric allergy practice. Patients with evidence of cashew sensitization, defined as skin prick test (SPT) wheal 3 mm greater than the negative control or cashew-specific serum IgE >0.35 kUA/L (ssIgE), who were avoiding cashew were identified. Demographic, clinical, and laboratory data were compiled.

RESULTS: We reviewed 214 visits and identified 100 patients with cashew sensitization including 57% males, 43% females, median age 7.6 years (range: 8 months-20 years). A history of a convincing allergic reaction to cashew was documented in 21 patients (21%). The median cashew-ssIgE was 7.8 kUA/L (Immunocap, range: <0.35->100 kUA/L), and the median SPT wheal diameter was 8 mm (range: 0-20 mm). Forty-one (41%) of cashew-sensitized patients were avoiding sesame, and of those, 16 (39%) patients had a history of a convincing allergic reaction to sesame. Three patients (3/21, 14.3%) had convincing allergic reactions to both cashew and sesame. The median sesame-ssIgE was 22.1 kUA/L (range: 0.38->100 kUA/L); the median SPT was 5 mm (range: 0-23 mm). Patients with higher cashew-ssIgE were more likely to avoid sesame (P = .02).

CONCLUSIONS: Cashew allergy is common in our practice, and there is a high rate of allergic co-sensitization between cashew and sesame.
828 Evaluation of Peanut Sublingual Immunotherapy for Peanut Allergy: A Pilot Study

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RATIONALE: To evaluate the safety of sublingual immunotherapy (SLIT) for peanut allergy using commercially prepared peanut cream.

METHODS: We enrolled children aged <15 years who were diagnosed with peanut allergy by an open oral food challenge (OFC) and who agreed to undergo peanut SLIT. Doses of peanut protein from commercially prepared peanut cream were gradually increased from 13.8 μg/day to 4600 μg/day over the study period. We evaluated adverse events during SLIT and changes in maximum tolerated OFC doses from initiation to 12 months.

RESULTS: Ten patients with a median age of 5.6 years (range: 5–13 years) were included in our study. One patient withdrew from the study; however, this was not due to an adverse event. Regarding adverse events, symptoms involving the oral cavity occurred in 7/10 cases (156/2045 dose times, 7.6%), and mild systemic symptoms occurred on an average at 0.1 times/case/year. The median maximum tolerated OFC dose increased significantly from 0.3 g (range: 0.1–0.5 g) to 0.4 g (range: 0.1–3.0) over 12 months (p=0.034). In addition, the skin prick test wheal size decreased significantly from 10±2.4 to 7.3±1.7 mm over 12 months (p=0.006). Conversely, median peanut-specific IgE levels were not significantly different at 12 months (13.6 UA/mL) compared to baseline (13.5 UA/mL) (p=0.43).

CONCLUSIONS: SLIT using commercially prepared peanut cream resulted in only a few, mild adverse reactions and may increase tolerance to peanuts. Further studies are needed to evaluate the effectiveness of peanut SLIT.

829 Institution of Clinic Scheduling Guidelines for Early Introduction of Peanut

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RATIONALE: The National Institute of Allergy and Infectious Disease (NIAID) published international consensus addendum guidelines on the early introduction of peanuts. One criticism of these guidelines is the shortage of allergists in the USA may prevent the practical institution of these guidelines. We designed a scheduling protocol to prioritize infants at high risk for peanut allergy.

METHODS: We flagged every referral for patients <12 months old as urgent, regardless of reason. Four new patient appointments and two challenge slots were reserved weekly for these patients. If appointment was not available within two weeks a physician would review case to assess urgency. Evaluation and treatment was at the discretion of treating physician. We took a retrospective review July 2016-September 2018.

RESULTS: 69 patients met criteria as “high risk” per NIAID guidelines and were evaluated in clinic on average 18.9 days (range 2-62 days) post referral. 31 patients were determined to need an in office peanut challenge for peanut introduction, with challenges happening on average 31.7 days (range 7-56 days) post referral. During this time period the 3rd next new patient slot for non-urgent appointments was on average 94.3 days.

CONCLUSIONS: By automatically flagging new referrals in all children <12 months old and reserving clinic and challenge appointments for these children, we were able to systematically evaluate these children 75.4 days sooner than general referrals. Our unique scheduling method allowed us to prioritize patients at high risk for peanut allergy and helped decrease the risk of developing a peanut allergy while on the appointment wait list.

830 Implementation of Early Peanut Introduction Guidelines Among Pediatricians

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RATIONALE: Expert guidelines recommending early introduction of peanut before 12 months of age to infants at high risk for developing peanut allergy were published in January 2017. Guideline implementation in the primary care setting is unknown.

METHODS: We conducted a retrospective chart review of infants with a suspected diagnosis of eczema or egg allergy that were seen for at least one well child visit between November 2017 and May 2018 within a large tertiary care medical center’s primary care network. Infants with non-eczematous dermatitis or mild eczema treated without prescription topical steroids were excluded. Records were reviewed for demographic information and details from each visit, including discussion of eczema and/or early peanut introduction. Allergy and dermatology visits were also reviewed, when applicable.

RESULTS: Among 577 initial infants, 167 were excluded due to mild eczema and 138 were excluded for non-eczematous dermatitis. Of the 272 patients included in the final analysis, 174 were male; 249 had eczema, 11 had egg allergy and 12 had both. Eczema skin care was discussed in 148/240 (61.7%) of 4-month, 154/238 (64.7%) of 6-month and 89/172 (51.7%) of 9-month visits. Discussion of early peanut introduction occurred in 3.3% of 4-month, 3.3% of 6-month and 3.0% of 9-month visits. Early peanut introduction was discussed at well child visits only 21 times in 17 (6.3%) unique patients and always involved a referral to allergy.

CONCLUSIONS: We identified very few instances of discussions about early peanut introduction in an at-risk population of infants seen in a large primary care network.
831 Importance of Peanuts Lipophilic Proteins on Diagnosis of Allergic Disease

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RATIONALE: Peanut allergy usually occurs during the first years of life and most allergic children do not overcome it when they reach the adult stage. The prevalence varies from 1.2% to 2% in children and from 0.6% to 8.0% in adults. The allergenic extracts that are currently used for the diagnosis and treatment of patients discard oil-body associated proteins (OAPs) during their manufacture, so many of potentially allergenic proteins are not included.

METHODS: We evaluated 30 children (median: 5 years old) with a convincing history of peanut ingestion related symptoms. Sensitizations to hydrosoluble and liposoluble proteins of peanut were determined through skin prick test (SPT), allergen-specific IgE antibodies (sIgE), Western blot (WB) and histamine release test (HRT).

RESULTS: 6 patients had a hydrosoluble fraction SPT negative (20%). 3 of them presented a liposoluble fraction SPT positive. 43.33% presented liposoluble fraction SPT positive. 90% presented skin symptoms, 40% respiratory and 33% digestive symptoms. 63% were sensitized to other nut (10 walnut, 3 cashew nut, 2 almond, 2 pistachio and 2 hazelnut). Hydrosoluble fraction sIgE: 1.83 kU/L and liposoluble fraction sIgE: 0.77 kU/L. Histamine release corresponding to hydrosoluble fraction was 21.9 ng/mL and 20.82 ng/mL to liposoluble fraction. Patients’ sera recognize several proteins between 10 and 75 kDa with different patterns in both fractions.

CONCLUSIONS: In our study we found a considerable number of patients had SPT and sIgE positive to liposoluble fraction. So, we demonstrated the importance of develop adequate extracts to be used in the diagnosis and treatment of patients.

832 Shy or fearful temperament not associated with IgE mediated food allergy in early childhood

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RATIONALE: Anxiety has been associated with food allergy in school age children. It is unclear whether that association is the consequence of or contributes to risk for food allergy. The Early Childhood Behavior Questionnaire (ECBQ) is a validated measure of toddler temperament that has been associated with subsequent childhood anxiety. We hypothesized that increased shyness and or fear as a toddler would be associated with food allergy.

METHODS: ECBQ was completed by a parent for 364 toddlers (median, 20 months) in a prospective infant cohort, 29 (8%) of whom have an IgE-mediated food allergy (overall rate 6%). Shyness and fear were measured on a likert scale. Wilcoxon rank sum and Pearson’s Chi-squared tests were used to evaluate for associations between ECBQ, food refusal and food allergy.

RESULTS: Shyness and fear measured by the ECBQ were correlated with each other (τ = 0.5, p < 0.01). The median shyness score among participants with food allergy was 3.25[2.5 – 4.2] versus 3[2.5 – 3.8] (p=0.16). There was also no significant difference in fear score [2[1.8 – 2.6] vs 2[1.6 – 2.7]; p=0.57. was a positive and significant association between parent reported food refusal (n =137) and shyness (p=0.014). Despite this association, cases of IgE-mediated allergy were no more frequent among those reporting food refusal (p=1).

CONCLUSIONS: Shy or fearful temperament were not cross-sectionally associated with presence of food allergies in toddlerhood. Previously observed associations between food allergy and anxiety may be more likely a consequence of food allergy than due to shared neurobehavioral underpinnings of the two conditions.

833 Successful Administration of Yellow Fever Vaccine in Egg-allergic Patients

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RATIONALE: The yellow fever vaccine (YFV) is recommended in endemic areas but represents a risk for egg-allergic patients, as it is cultivated in chicken embryos. This study aims to describe the outcomes of yellow fever vaccination in patients with confirmed egg allergy (EA).

METHODS: EA was diagnosed through oral food challenge (OFC) or recent history of anaphylaxis following egg contact. Skin prick test (SPT) with YFV was performed in all participants (starting at 1:10 dilution for patients with anaphylaxis history and full strength for all others). If negative SPT, an intradermal test (IDT) was performed at 1:100 dilution. If negative IDT, a full dose of YFV was administered, followed by an observation period of 2 hours. If positive skin test, the YFV was administered using a graded-dose protocol.

RESULTS: Twenty-five patients with IgE-mediated EA were studied (15M:10F, median age of 2.3y). Ten patients reported prior anaphylaxis, three of whom recently. The other 22 had a positive OFC. SPT with YFV was negative in all patients. IDT was negative in 20 patients, who received a full dose of YFV in usual manner, unequivocally. Five patients had a positive IDT and received the YFV in graded doses. Two patients presented a mild reaction controlled with antihistamines only and three patients received the vaccine without reactions.

CONCLUSIONS: In an appropriate setting, skin testing with vaccine and the use of a graded-dose protocol for high-risk patients allowed a safe administration of the YFV to egg-allergic patients, even with prior risk of anaphylaxis.
Low Dose Oral Immunotherapy In Children With Egg and Milk Allergies: A Retrospective Case Series Study

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RATIONALE: Low dose oral immunotherapy (OIT), which maintenance doses are lower than threshold doses diagnosed by oral food challenges (OFCs), is not evaluated the safety and efficacy.

METHODS: This was a retrospective case series study, evaluating patients who 1) tested positive on open OFCs with <10 g or ml of boiled egg white or milk from June 2016 to March 2017; 2) consumed the causative foods for one year as OIT, initiated at 1/100–1/10 and maintained at 1/10–2/3 of the total OFC doses; and 3) underwent OFCs after one year. We evaluated adverse events during low dose OIT and changes in tolerated OFC doses from initiation to 1 year.

RESULTS: Seventeen patients aged 1–9 years (10, egg; 7, milk; with duplication) were analyzed. Regarding adverse events, symptoms involving the oral cavity occurred with 11/17 cases, and systemic symptoms occurred 0.7 times/cases/year. Median (interquartile range; IQR) total tolerated OFC doses increased from 0.3 (0.3–1.0) to 3.0 g or ml (1.0–3.0) (p = 0.002). Median (IQR) ovomucoid-sIgE and milk-sIgE tended to decrease from 48.0 (33.8–64.2) to 29.1 UA/mL (17.0–39.4) (p = 0.20), 69.7 (48.6–100.0) to 24.2 UA/mL (17.8–100.0) (p = 0.36), respectively.

CONCLUSIONS: Adverse events occurred 0.7 times/cases/year. It might be necessary to implement lower doses in our protocol.

Clinical utility of serum specific IgE food testing in general practice: A tertiary care experience

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RATIONALE: Serum Specific IgE (SSIgE) testing is the preferred method for diagnosis of food allergy by Primary Care Physicians(PCPs). However, the diagnostic value of such tests, without a valid history, is questionable due to high false positive results. We tested the hypothesis that greater than 50% of positive food allergens according to Serum Specific Immunoassays do not correlate with a definitive food allergy.

METHODS: We performed a medical record review on 336 patients previously diagnosed with “food allergies” based on positive SSIgE ordered by PCPs. We compared these SSIgE results with an assessment from our tertiary care center Allergy specialists which included detailed history, skin prick testing and home/in office oral challenges.

RESULTS: The top 10 foods tested by PCPs were milk, peanut, wheat, shrimp, soybean, codfish, walnut, egg, sesame, and scallop. 167 (49.7%) subjects had positive skin testing to one or more foods. Only 41(12.20%) had positive oral food challenges. Average total serum IgE per patient was 581IU/ml (ref: 100-300IU/ml). SSIgE assay was obtained only on 71 subjects in 2008 compared to 240 in 2018.

CONCLUSIONS: False positive rate in our study is >80 % compared to >50% in the previous studies.A high average total serum IgE level/patient related to nonspecific IgE and cross-reactive but clinically irrelevant allergen SSIgE might be a reason for false-positive IgE values for the specific food allergen. A rising trend for indiscriminate ordering of SSIgE in the last 10 years has caused not only the over diagnosis of food allergy but also an unnecessary cost of evaluation.

Changing The Outcomes Of Peanut Oral Immunotherapy (POIT)

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RATIONALE: Previous reports of POIT demonstrate a desensitization success rate of ~80%. Between 01/01/09 and 06/30/18, we have treated 329 patients with POIT. The initial 270 patients have been reported. Based on our and others’ experience we have adjusted treatment age and the POIT process in an effort to increase the availability of POIT and improve the outcome. We contrast the outcomes of the initial and subsequently treated patients.

METHODS: Retrospective record review of patients receiving POIT approved by the North Texas IRB. POIT was administered according to modifications of previously reported protocols.

RESULTS: 99% of the initial patients and 50% of the recent patients were >5yo. 82% of the initial patients (excluding 8 [2.9%] who transferred care) and 94% of the subsequent 67 patients reached their target peanut protein dose (TPPD). Epinephrine treated reactions occurred in 24% of the initial but only 7.5% of the subsequently treated patients. 14% of the initially treated patients but only 7.5% of the recent patients experienced esophlagitis-like OIT-related GI symptoms. Among the recently treated patients there was no significant difference in adverse events between those <5yo and >5yo.

CONCLUSIONS: Changes in POIT protocols and management experience from treating >325 patients has increased the likelihood of desensitization and decreased the rate of serious GI and systemic adverse events requiring epinephrine. These improvements cannot be explained by the inclusion of younger patients.
Peanut Component Sensitization Patterns in Children in the Chicago Metropolitan Area

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RATIONALE: Peanut component test (PCT) results have been reported to vary geographically. The aim of this study was to describe PCT sensitization patterns in our patients undergoing assessment for peanut allergy.

METHODS: Retrospective review of clinical data in the electronic health records for all patients who were seen in our clinics and had PCT results from January 2012 to August 2017 was conducted. IgE to peanut component proteins (Ara h1,2,3 and 9) was measured. Sensitization was defined as IgE ≥ 0.35 kUA/L. PCT data were analyzed using descriptive statistics (mean ± standard deviation, frequency/percent, median [IQR]).

RESULTS: Among the 450 patients, h2 sensitization was most prevalent (58%). Sensitization to h1 was next highest at 42.4% followed by h3 (29.8%), h8 (13.8%) and h9 (9.8%). We observed higher proportions of PCT sensitization for all components in males. Sensitization to h2 was the most common in all age strata as follows: 0-3 (n=144), 3-6, (n=56), 6-9 (n=67), 9-12 (n=58), 12-15 (n=33), and 15-21 (n=23) with 56.9%, 56.0%, 59.7%, 63.8%, 54.6%, and 60.9% of participants sensitized, respectively. 109 (24.2%) patients were sensitized to Ara h1, h2 and h3. Ara h8 or h9 mono-sensitization was present in 25 (5.6%) individuals, with higher rates in the older strata: 12-15 (15.2%) and 15-21 (13.0%).

CONCLUSIONS: We found that h2 is the most common component associated with sensitization and did not vary by age in contrast to sensitization to Ara h8 and h9. Mono-sensitization to Ara h 8 and h9 was more common in older children.

Component Resolved Diagnostics in Patients with Peanut Allergy versus Peanut Sensitization

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RATIONALE: Peanut-specific-IgE(PN-sIgE) and peanut component diagnostics(CRD) are often ordered simultaneously in evaluating for peanut allergy. This study examined PN-sIgE and association with CRD in patients with and without history of clinical reactivity.

METHODS: A retrospective chart review of 196 children who had PN-sIgE and CRD testing in an outpatient setting, was performed. 98 patients had a history of an IgE mediated reaction to peanut and 98 did not. The Fisher’s exact test was used to assess the relationship between CRD(arah 1,2,3 and 9 <0.35kUA/L)and PN-sIgE at different cutoff levels(2kUA/L,5kUA/L and 14kUA/L).McNemar’s test was used to assess agreement between CRD and PN-sIgE. Logistic regression was applied to examine differences in the findings between patients with and without history of clinical reactivity.

RESULTS: CRD with arah1,2,3 and 9 <0.35kUA/L, regardless of arah 8, was significantly more likely to be associated with lower PN-sIgE levels at each cutoff point evaluated: PN-sIgE<2kUA/L versus ≥2kUA/L(30% vs. 4%, p<0.0004), <5kUA/L versus ≥5kUA/L(38% vs. 6%, p<0.0002), and <2kUA/L versus ≥2kUA/L(59% vs. 6%, p<0.0001). These findings were not significantly different between patients with and without a history of clinical reactivity.

CONCLUSIONS: CRD values correlate with PN-sIgE. Regardless of clinical history, if a CRD(arah 1,2,3 and 9) cutoff of <0.35kUA/L is used as a clinical decision point to assess risks of oral challenge, then a PN-sIgE>2kUA/L is unlikely to meet the cutoff. The decision to obtain peanut CRD should be made after evaluation of the total PN-sIgE. Larger studies are needed to identify optimal CRD cutoff points.
840 Predictive value of peanut SPT and sIgE in peanut allergic patients diagnosed of LTP-Syndrome

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RATIONALE: Patients sensitized to nsLTP comprise a heterogeneous group in terms of sensitization profile, symptom severity and complexity in diagnosis. The aim of this study is to compare sensitivity, specificity, positive and negative values (PPV and NPP) of skin prick test (SPT) and specific IgE (sIgE) in the diagnosis of peanut allergy in patients with LTP-Syndrome.

METHODS: We included 67 patients with confirmed peanut allergy. We performed peanut diagnosis based on positive SPT, sIgE and oral food challenge (OFC); except in those that presented ≥ 2 episodes of anaphylaxis in the previous two years.

RESULTS: After peanut intake, 30 patients (45%) presented symptoms and 9 (13%) tolerated. Twenty-eight patients (42%) avoid peanut intake because positive SPT and/or sIgE. After OFC, 26 patients (38.8%) were confirmed as allergic to peanut. From 41 (61.2%) who tolerated, 32 (78%) had positive SPT and/or sIgE. SPT and sIgE showed a moderate agreement level (kappa = 0.50). However, we found a fair level of agreement between SPT and OFC (kappa = 0.20), and sIgE and OFC (kappa = 0.21).

CONCLUSIONS: These data show the relevance of OFC for confirming the diagnosis of peanut allergy in patients with LTP-Syndrome regardless of the positivity of SPT/sIgE. Further investigations are warranted to clarify the role of LTP in allergy to other plant foods.

841 A Retrospective Study On High Risk Factors For The Development of Peanut Allergy

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RATIONALE: The Learning Early about Peanut Allergy (LEAP) trial demonstrated that early introduction of peanut products in high risk infants decreases the risk of peanut allergy by 5 years of age. High risk patients were defined as infants with severe eczema, and or egg allergy. In our study, we aimed to identify other high risk factors associated with the development of peanut allergy and thereby additional patient populations who may benefit from early introduction of peanut products.

METHODS: A retrospective chart review was performed on 103 patients ages 0-3 years old with either positive (≥3mm) skin test to peanuts or serum peanut immunoglobulin E (IgE) level greater than or equal to 1.0 kU/L. Clinical data from this subset of patients was analyzed for additional risk factors (i.e. other food allergies, family history of food allergy, parental asthma, etc.) that could lead to the development of peanut allergy using logistic regression analysis.

RESULTS: Parental asthma was found to be significantly associated with an increased risk of peanut allergy in the child (p = 0.0359, OR 2.743). Other concurrent food allergy to soy was also associated with a propensity for peanut allergy (p-value 0.0150, OR 6.344).

CONCLUSIONS: Patients with food allergy to soy or parental asthma should be further investigated as potential identifiers of patients at high risk of developing a peanut allergy.

842 Pru p3 sublingual immunotherapy and allergy to lipid transfer protein, a case report

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RATIONALE: Pru p3 belongs to the lipid transfer protein (LTP) panallergen family. LTPs are related with severe anaphylactic reactions after its ingestion. Pru p3 sublingual immunotherapy (Pru p3 SLIT) can increase allergen tolerance.

METHODS: Skin prick test (SPT) and serum specific IgE to Pru p3 (peach), peanut, nut, onion, tomato, Artemisia pollen. Oral food challenge to onion and tomato (raw and cooked).

RESULTS: We present a 54 y.o. women with a history of anaphylactic reactions with several foods (rosaceae fruit, nuts, tomato, onion and lettuce), including cross-contamination (fried food). She was on a very restricted diet with high impact on quality life. SPT were all positive, confirming the sensitization. Serum specific IgE were peach (Pru p 3; LTP) 3.47 Ua/mL, peanut 3.35 Ua/mL, nut 1.09 Ua/mL, onion 0.42 Ua/mL, tomato 1.73 Ua/mL, Artemisia pollen 5.50 Ua/mL. Risk and benefits were reviewed and discussed with patient and Pru p3 SLIT was started following standard recommendations and 4 days rush schedule. An excellent tolerance both, in the build-up and maintenance phases, was observed. After 6 months, upon request of the patient, oral food challenges to onion and tomato (raw and cooked) were carried out without reactions. She added both foods, widely used in Mediterranean diet, to her daily diet with good tolerance.

CONCLUSIONS: In this case, we evaluate the efficacy of Pru p3 SLIT in a 6-month period. Pru p3 SLIT can reduce accidental intake risk and improve quality of patient’s life.
Clinical and Epidemiological Features Of Children With Egg Allergy (EA) Followed In A Brazilian Referral Center Of Allergy

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RATIONALE: Egg is the second most common food allergen in childhood and the most important one in children with moderate-to-severe atopic dermatitis (AD). Despite this fact, few are the Brazilian data regarding epidemiology, clinical features and natural history of EA in our population. The aim of our study was to analyze clinical and epidemiological features of EA children.

METHODS: Review of electronic charts from patients followed from July, 2017 to July, 2018. Patients over 18 y/o were excluded from the study.

RESULTS: 135 children with food allergy (FA) were evaluated. Egg was the second most common food allergen in this population (36 patients, 26.6%), following cow’s milk (85%). EA was more prevalent in male sex (1,6:1). The mean age of onset of symptoms was 6 months and at diagnosis was 35 months (delta 29m). 50% of the patients presented with immediate IgE-related features, 11% presented with delayed reactions and 39% referred both symptoms. 33 (93%) of the patients have at least one other allergic disease (now called multimorbidity) and 86% have other FA. 9 patients (25%) developed tolerance during the year, with a mean age of 55 months, none of them had history of severe reactions. 27 (75%) persist with EA (mean age-76 months).

CONCLUSIONS: EA is the second most prevalent cause of FA in our population, following the data of most FA prevalence surveys. EA prognosis is considered good, and most children develop tolerance up to 60 months. High rates of multimorbidity and other FA were observed.

Molecular IgE reactivity pattern in Lipid Transfer Protein (LTP) allergy using a new multiplex diagnostic array.

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RATIONALE: Non-specific Lipid transfer protein (nsLTP) is the main cause of food allergy in the Mediterranean area.

- Aim: To describe the molecular IgE profile of LTP using AllergyExplorer® (ALEX), a macroarray containing 282 reagents (157 “whole” extractive allergens & 125 molecular components: 9 food LTPs; 2 pollen LTPs), and to compare it with ImmunoCAP® ISAC.

METHODS: 20 patients with history of plant food allergy and sensitization to Pru p 3 (peach LTP) by skin prick test were selected.

- Sera were assayed with ALEX® & ISAC® IgE reactivity to LTPs was compared between techniques:
  - Pru p 3 (peach), Ara h 9 (peanut), Cor a 8 (brazil nut), Art v 3 (Artemisia pollen), Par j 2 (Parietaria pollen) [ALEX® & ISAC®].
  - Mal d 3 (Apple), Vit v 1 (grape), Act d 10 (kiwi), Sola l 1 (tomato), Api g 2 (celery) [ALEX®].
  - Tri a 14 (wheat), Jug r3 (walnut), Pla a 3 (plane tree pollen), Ole e 7 (olive tree pollen) [ISAC®].

RESULTS:

- Number of LTP recognized: 1LTP(5%); 2LTP(10%); 3LTP(5%); 4LTP(5%); 5LTP(10%); 6LTP(10%); > 6LTP(55%).
- IgE reactivity pattern: Pru p 3 (85%); Mal d 3 (85%); Cor a 8 (70%); Ara h 9 (70%); Jug r3 (65%); Pla a 3 (65%); Act d 10 (50%); Api g 2 (50%); Vit v 1 (35%); Ole e 7 (30%); Tri a 14 (25%); Api g 6 (15%); Sola l 1 (10%).
- IgE reactivity correlation between the two tests: Cor a 8 (95%); Pru p 3 (90%); Ara h 9 (90%); Art v 3 (60%); Par j 2 (40%).

CONCLUSIONS: The majority of LTP allergic patients recognized more than 6 LTPs: being peach’s and apple’s the most frequently involved, followed by nut’s, kiwi’s and celery’s.

A consistent "shortage" of cases of the alpha-gal syndrome (AS) on the Gulf coast: possible relevance of fire ants as a predator of lone star ticks

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RATIONALE: Allergic reactions to red meat in patients with IgE to alpha-gal are common in the southeastern U.S., but appear less common on the Gulf coast and into much of Texas. This contrasts with the reported distribution of A.americanum (lone star tick). In addition, it has been known for many years that fire ants can kill ticks.

METHODS: We carried out a survey of the prevalence of AS in allergy practices in areas where the fire ant has been present since 1974 (n = 10), compared to areas of the Southeast without fire ants in 2000 (n = 23). In a subset of clinics we additionally assessed reports of fire ant anaphylaxis (FAA).

RESULTS: In keeping with the reported area of fire ants, few cases of FAA were reported in VA, KY, MO, OK, or northern AR. By contrast, there was a progressive increase in FAA cases through TN to the Gulf coast. A clinic in Montgomery, AL reported 100 cases of FAA and no cases of AS. A similar trend in reported FAA was identified in a north-south gradient from MO to TX. Cases of AS were much more common in clinics outside of the reported fire ant zone (χ² 10.5, P = 0.001).

CONCLUSIONS: The geographic distribution of cases of FAA coincided with the known distribution of fire ants and the unexpectedly low incidence of AS. The likely explanation is that the fire ants have decreased the population of lone star ticks so that tick bites and sensitization to alpha-gal are no longer common in these areas.
846 Gastric pH Modulation Increases Risk For Subsequent Prescription Of Anti-allergy Medication: Evidence From A Nationwide Cross-sectional Study

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RATIONALE: Anti-ulcer drugs, such as proton pump inhibitors (PPI), are widely prescribed and used in developed countries worldwide. Recently concerns about the promotion of allergic sensitizations following gastric pH modulation have been raised in mechanistic and observational studies. We aimed to assess the frequency of anti-allergic drug prescription following gastric acid inhibitors use in a population-wide study in Austria.

METHODS: In this cross-sectional study, age and gender controlled data from health insurance claim records between 2009 and 2013, covering 8.2 million subjects (approx. 97% of the Austrian population), were analyzed regarding prescriptions of i) gastric acid inhibitors (PPI, H2-receptor antagonists, sucralfate, prostaglandin E2) and anti-allergic medication (antihistamines, desensitization therapy). Other commonly prescribed drugs (lipid-modifying and antihypertensive substances) served as controls by Cox regression in a regional subgroup.

RESULTS: Prescription of anti-allergic drugs following gastric acid-inhibitors showed a rate ratio of 1.96 (95% CI: 1.95-1.97) in overall Austrian data and 3.07 (95%-CI:2.89-3.27) in the regional data set, which was more prominent in women (P<0.001). Age and gender adjusted hazard ratio was found to be 2.05 (95%CI:1.91-2.19), and was elevated independent of prescribed gastric acid-inhibiting substances. Further, rate ratios increased from 1.47 (95%CI:1.45-1.49) in subjects <20 years of age, to 5.20 (95%CI:1.5-5.25) in >60 year olds.

CONCLUSIONS: The increased use of anti-allergy medication subsequent to gastric acid suppression suggests an association with the occurrence of allergic symptoms. Prescription of anti-ulcer drugs should be restricted to cases with clear indication and adequate diagnosis to minimize the risk for allergic comorbidities.

847 Allergy, depression and quality of life among pregnant women in the Japan Environment and Childrens Study (JECS)

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RATIONALE: We aimed to investigate the association of maternal mental health, including depression, anxiety and quality of life, with allergic features during pregnancy.

METHODS: This is a cross-sectional study within a birth cohort. Lifetime prevalence of allergic disease was assessed on the basis of a self-reported doctor’s diagnosis from the questionnaire. Serum total and allergen-specific IgE titers were assayed by ImmunoCAP. Kessler’s K-6 Non-Specific Psychological Distress Scale (K-6) was used to evaluate maternal anxiety and depression. Health-related quality of life was measured using the Medical Outcomes Survey Short Form-8 questionnaire (SF-8).

RESULTS: We included 86,085 participants in this analysis. Der p 1 (adjusted odds ratio [aOR], 1.05; 95% CI, 1.02-1.08), asthma (aOR, 1.28; 95% CI, 1.22-1.34), rhinitis (aOR, 1.20; 95% CI, 1.17-1.24), and eczema (aOR, 1.17; 95% CI, 1.12-1.22) increased the risk of depression (K-6 scores ≥5). For PCS and MCS scores of the SF-8, allergic diseases such as asthma, rhinitis, eczema, and food allergy were negatively associated with PCS and MCS.

CONCLUSIONS: Our study suggests that allergy in pregnant women is associated with mental disorders, such as depression, and contributes to lower quality of life. Our results highlight the importance of addressing allergy and mental health comorbidity as a public health and clinical management priority, to improve overall health. (J Allergy Clin Immunol Pract. 2018 Jul-Aug;6(4):1421-1424)

848 The Association between “Hay-Fever” and Cancer Diagnoses in the National Health Interview Survey 2015

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RATIONALE: Studies suggest patients with atopic disease may have increased immune surveillance which may be protective against cancer(1)(2)(3). Our own large data study showed asthma to be protective against cancer diagnoses. This study aimed to examine association between personal histories of hay fever and cancer, as diagnosed by a physician, in the National Health Interview Survey (NHIS) from 2015.

METHODS: This is a cross sectional cohort study. NHIS data from 2015 was analyzed using bivariate analysis between demographic variables, Hay fever and cancer, defined as ever being told they had these conditions by a doctor or health care professional. Covariates included age, sex, race and obesity. Nested multivariate logistic regression model was conducted. All statistical analysis was done using SAS v9.4.

RESULTS: Data available for 33,672 adults. Odds of cancer diagnosis with a history of ever having Hayfever was 0.62 (95% CI 0.56-0.69), P<0.001. After adjustment for age, sex, race and obesity, the odds remained similar at 0.67 (95% CI 0.60-0.75) p<0.001.

CONCLUSIONS: This study found that a personal history of hayfever, a marker of atopy, was a strong and significant protective factor for cancer diagnosis, a finding in line with our previous finding that asthma was protective of cancers, suggesting an altered immune responses in atopics is protective against cancer.
Allergic rhinitis treatment preference, compliance and adherence in Thai children

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RATIONALE: Allergic rhinitis (AR) is a common disease in children; the main pharmacotherapy includes antihistamine and intranasal steroid (INS). Patient preference and compliance of treatment are ones of the key factors that contribute to the success of AR treatment.

METHODS: We conducted a cross-sectional questionnaire survey study in 250 children with AR aged between 1-18 years. The primary outcome was to study compliance and preference of treatment. The secondary outcome was to study adverse effects of pharmacotherapy.

RESULTS: 238/250 children (95.2%) had persistent AR which 156 (62.4%) were moderate-to-severe and 82 (32.8%) were mild. 114/250 (45.6%) preferred oral antihistamine (OAH), 66/250 (26.4%) preferred INS, and 67/250 (26.7%) preferred both. There was no significant difference in the preference of treatment by disease severity (p = 0.1348). However, significantly higher number of children with moderate to severe AR preferred INS with/without OAH to only OAH (91.64%) than those with mild persistent AR (35.45%), p-value = 0.0293. The compliance to oral antihistamine (72.8%) was better than INS (64.8%). Adverse symptoms of INS were reported in 65/243 children (26.7%) and 42/250 (16.8%) in OAH. The most reported adverse effect of INS was post nasal dripping (17.3%, 75% in budesonide) where drowsiness was the most common in OAH (8.8%). Interestingly, drowsiness was highly reported in second generation OAH: 33.3% in desloratadine, and 16.7% in loratadine.

CONCLUSIONS: Most children preferred OAH to INS, however, children with more severe AR preferred INS to OAH monotherapy as the main treatment. Drowsiness is commonly found in OAH even in new generation OAH.

Increasing Influenza Vaccination Rate with Institution-wide Mandatory Program and Allergy Evaluation

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RATIONALE: Mandatory influenza vaccination for all hospital employees is increasingly common, and was a policy at NYU Langone Health System (NYC, Winthrop, Lutheran) in 2017. Employees applied for exemption based on prior allergic reaction underwent evaluation by an Allergy Evaluation performed by an Allergy & Immunology Physician (NYC, Winthrop, Lutheran) in 2017. Employees applied for exemption based on prior allergic reaction underwent evaluation by an Allergy Evaluation performed by an Allergy & Immunology Physician (NYC, Winthrop, Lutheran) in 2017.

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CONCLUSIONS: Most children preferred OAH to INS, however, children with more severe AR preferred INS to OAH monotherapy as the main treatment. Drowsiness is commonly found in OAH even in new generation OAH.

Lactobacillus for Prevention of Pediatric Atopic Disorders: A Meta-Analysis of Randomized Controlled Trials

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RATIONALE: Several studies were designed to examine the efficacy of lactobacillus probiotics in the prevention of atopic disorders in pediatric population, which conveyed conflicting results. This review is to investigate whether lactobacillus probiotic supplementation prenatally and/or postnatally could reduce the risk of pediatric atopy.

METHODS: From PUBMED database, we searched and reviewed randomized controlled trials on the preventive effect of lactobacillus on pediatric atopic disorders from 2000 to 2016. Meta-analysis for the results of studies was performed using RevMan 5.0 and the co-effect was pooled by using random-effects model of relative risk (RR) ratios.

RESULTS: Ten trials published between 2000 to 2006 were included in the meta-analysis. The result showed that the preventive effect of prenatal and postnatal supplementation on pediatric atopic disorder was not significant with the RR=0.76 (95% CI: 0.44, 1.30). There was no evidence of significant publication bias by inspection of the funnel plot.

CONCLUSIONS: Present evidence cannot show in inconsistent terms that prenatal and postnatal lactobacillus probiotic supplementation will prevent pediatric atopic disorder.
All abstracts are strictly embargoed until the date of presentation at the 2019 Annual Meeting.

853 Lifetime Work Productivity Gains Among Patients with Chronic Rhinosinusitis with Nasal polyps (CRS年中国). Treated with EDS-FLU

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RATIONALE: Chronic rhinosinusitis with/without nasal polyps is a debilitating inflammatory disorder commonly diagnosed in working age adults, and is characterized by significant morbidity and poor outcomes with standard medical therapy. CRS affects approximately 15% of adults, generating $60B in lost productivity annually. In two randomized controlled trials in CRSwNP (NAVIGATE I/II), treatment with the exhalation delivery system with fluticasone (EDS-FLU; XHANCE®), was associated with a 52.7% improvement in self-reported work productivity. We model the long-term impact of EDS-FLU treatment on work productivity in specialist-treated CRSwNP patients from a societal perspective.

METHODS: Using the human capital approach, a 30-year Markov model was developed comparing EDS-FLU vs. standard medical therapy. Mean cohort age was 40 years. Health state transition probabilities and lost productivity associated with health state and sinonasal surgery were obtained from NAVIGATE I/II and published literature. Costs were discounted to 2018 dollars. A probabilistic sensitivity analysis was conducted.

RESULTS: Over 30 years, standard medical therapy was associated with 2.9 years with $134,823 in productivity losses per specialist-treated patient, while treatment with EDS-FLU was associated with productivity losses of 1.6 years, worth $74,978. If EDS-FLU replaced current medical therapy, the societal savings would be $19.5B. The model was most sensitive to health state transition probabilities, and the proportion of patients with severe disease at baseline.

CONCLUSIONS: In this model, EDS-FLU treatment was associated with 1.3 productive years gained per patient over 30 years vs. standard medical treatment, with estimated societal savings of nearly $20B.

854 Patterns Of Authorship In Allergy/Immunology By Women: 1997-2017

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RATIONALE: We reviewed authors’ gender in The Journal of Allergy and Clinical Immunology (JACI) and Annals of Allergy, Asthma and Immunology (Annals) from 1997-2007 to determine frequency and patterns of publication by gender.

METHODS: Data were collected in five-year intervals for articles from the USA and Canada, and analyzed by journal (JACI or Annals), article type (review, original investigation, guideline, editorial, case report), and year of publication. Logistic regression was used to analyze factors associated with first authors being women. We compared these patterns with frequencies of women in AAAAI and as fellows-in-training.

RESULTS: Women were first authors in 36.5% of publications, increasing from 26.6% in 1997 to 48.1% in 2017 (p<0.001). Original articles had the highest percentage of women as first authors (42.5%); editorials had the lowest (17.1%). Women as last authors increased from 18.1% in 1997 to 30.9% in 2017 (p=0.001). Males were more frequently (82.8%) sole authors (p<0.001). Articles with women as first authors were associated with women being last authors (OR = 3.1, p<0.0001), original investigations (OR=2.1, p<0.001) and more recent publication (OR=1.7, p<0.001). The increasing frequency of women first authors was correlated with increasing proportions of women as AAAAI members and fellows-in-training (Pearson correlation=0.96, p=0.01).

CONCLUSIONS: Our data demonstrate that authorship by women has become more frequent in JACI and Annals. The probability of women being first authors is statistically significantly more likely in articles with women as last authors — implying that mentorship of women by women may encourage women to become more active in research and publication.

855 Allergy/Immunology Electives Using the AAAAI Clinical Rotation Curriculum Are Highly Valued By Medical Trainees

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RATIONALE: Many early learners in the field of medicine have limited exposure to allergy/immunology (AI) during their training. The American Academy of Allergy, Asthma and Immunology (AAAAI) Clinical Rotation Curriculum (CRC) has provided online educational resources to support AI electives in the outpatient setting. We report the feedback received from medical students and residents who have completed this curriculum.

METHODS: The AAAAI CRC consists of a syllabus, online videos, journal articles, and pre- and post-test questions relevant to medical trainees rotating through an AI elective. The AAAAI also provided faculty development resources on office based teaching along with assessment and feedback. Trainees who participated in the curriculum were asked to complete a questionnaire to rate the quality of the AI elective, the preceptor, and the online curriculum on a 5 point scale, with 1 being “excellent” and 5 being “unacceptable.” Data from the students and residents who completed the survey from September 2013 to April 2018 was reviewed.

RESULTS: During the 5 year period of our review, a total of 185 faculty members and 754 learners participated in the program and 315 learners completed the questionnaire. Respondents gave high scores for course materials (1.6), clinical experiences (1.5), and clinical faculty members (1.4). Of note, 99% of students agreed that the elective “enhanced my medical education” and “would recommend this rotation to other medical students/residents.”

CONCLUSIONS: Students and residents who use the AAAAI CRC while on an AI elective highly rate their education during the rotation and would recommend it to other learners.
An Intramural Review to Support Research and Scientific Publication

Richard F. Lockey, MD, FAAAAI1, and Jennifer D. Newcomb, MS2; 1Division of Allergy and Immunology, Department of Internal Medicine, University of South Florida Morsani College of Medicine, Tampa, FL, 2University of South Florida, Tampa, FL. RATIONALE: Academic careers drive science through accurate and effective written communication of novel ideas and research findings. Publishing in high impact journals is one of the foundations for success. However, effective, scientific writing skills are rarely taught. Impact | An Intramural Review to Support Research and Scientific Publication is designed to provide support for scholarly writing at the University of South Florida (USF), a concept introduced by the USF Division of Allergy and Immunology. METHODS: Impact has two avenues to assist in writing abstracts, case reports, reviews, research articles, chapters for books, and to design posters: 1. an easy-to-navigate website (http://impact.health.usf.edu) housing many writing resources; and 2. a submission process for intramural peer review for which 87 volunteer faculty in the Colleges of Medicine, Nursing, Pharmacy, and Moffitt Hospital serve as editors. Instructions are provided to the editors for objective feedback on the quality, clarity and structure of a manuscript, its language, statistical analysis and conclusions. Two editors, preferably from outside of the author’s expertise, review submissions within three weeks. Anonymous follow-up is conducted to determine Impact’s effectiveness. RESULTS: Impact reviewed 76 submissions between February 2017 and July 2018, thirty-eight percent of which were published in peer-reviewed journals with an average impact factor of 5.07 (range: 1.15-24.01). The survey respondents were highly supportive of Impact. CONCLUSIONS: USF Health’s Impact fills a gap in education and promotes cooperation and collaboration in scientific writing and also helps educate tomorrow’s scientists and academicians.

Factors Influencing Show Rates at an Outreach Clinic in an Underserved Community

Sebastian Sylvestre, MD, Nancy Linebaugh, RRT, Tracy B. Fausnight, MD FAAAAA, and Doerthe A. Andreau, MD PhD; Penn State Hershey Medical Center, Hershey, PA. RATIONALE: Lack of patient adherence to medical appointment times leads to delayed or absent care, increased cost, and is detrimental to patients, physicians, and health care institutions. This study investigates interventions/factors influencing show rates at an underserved community pediatric Allergy/Immunology outreach clinic. METHODS: Over a 10 week period, 97 patient appointments were included in the analysis. For the final five weeks, all patients received personal reminder phone calls two days prior to appointment times. Additionally, the following factors were compared: new versus return appointment, morning versus afternoon appointment, distance to clinic, and type of insurance. RESULTS: Reminder phone calls increased patient show rates to 54.7% from 47.7% (p-value 0.498). In the total 10 week period, 55.0% of all return appointments showed as compared to 49.1% of new appointments (p-value 0.573). Afternoon appointments had a 56.3% show rate compared to the 46.9% of morning appointments (p-value 0.364). Patients traveling greater than five miles from home had a show rate of 59.1% as compared to 52.2% of those traveling less than five miles (p-value 0.515). Private insurance users had a show rate of 62.5% as compared to 51.1% for individuals who used other methods of payment (p-value 0.541). CONCLUSIONS: Factors that may influence show rates in this underserved patient population include being a return patient, having afternoon appointment times, living greater than five miles away from clinic, and/or having private insurance. In the time interval studied, a personal reminder phone call produced a 7.0% increase in show rates.

Evidence is Limited for the Efficacy and Safety of Corticosteroid Irrigation in Chronic Rhinosinusitis (CRS)

Jonathan A. Bernstein, MD FAAAAI1, John C. Messina, Jr, PharmD2, Harry J. Sacks, MD3, Per G. Djupesland, MD, Ph.D3, and Ramy A. Mahmoud, MD, MPH3, 1Bernstein Clinical Research Center LLC, Cincinnati, OH, 2OptiNose US, Inc., Yardley, PA, 3OptiNose AS, Oslo, Norway. RATIONALE: High-volume nasal irrigation has been shown to have benefits in CRS patients. Addition of high-dose corticosteroid to saline irrigations is increasingly common, though guidelines note inadequate evidence to confirm efficacy. We summarize existing evidence and usage trends. METHODS: Reviewed literature on corticosteroid irrigation in CRS. Budesonide claims data [2007-2016; Covance Inc] were evaluated for patients with a CRS-related diagnosis. RESULTS: Seventeen efficacy (15 budesonide; 1 mometasone; 1 fluticasone) and/or safety studies (3 weeks-22 months) were identified. Most were uncontrolled (n=12) versus randomized (n=5); small and underpowered (≤10 subjects: n=3; 11-49: n=5; 50-100: n=4; ≥100: n=1) and conducted in CRS sub-populations (eg, post-sinus surgery: n=9). The 3 which were generalizable (ie, n≥50) and controlled, failed to show a statistically significant difference versus control (saline irrigation). One small study (n=35) demonstrated benefit on imaging but mixed results on symptoms. Evidence of, or a trend toward, HPA axis suppression was apparent in 2/6 studies. Annual claims data showed increasing use of Budesonide Respules® with increased costs (mean prescription number=6 among patients with ≥1 prescription; mean cost=$210/prescription). Adherence was reported to be adversely affected by third party coverage and irrigation solution preparation time, and 2.5% ± 1.6% of irrigation doses are retained in the nose. CONCLUSIONS: Evidence for efficacy of adding corticosteroid to nasal irrigations is low-quality, with reported possible benefits limited to a sub-population with previous surgery. Adequate, well-controlled studies are needed to address dosing issues, efficacy, safety, adherence, and patient selection in order to understand the role of adding corticosteroid to nasal irrigations in CRS.
All abstracts are strictly embargoed until the date of presentation at the 2019 Annual Meeting.

**859 Evidence for Twice-Daily Nasal Steroids Versus Once Daily for Treatment of Chronic Rhinosinusitis with Nasal Polyps**

**Eric J. Schenkel, MD, FAAAAI**, Anju T. Peters, MD, FAAAAI, John C. Messina, Jr, PharmD, Harry J. Sacks, MD, FAAFP, and Ramy A. Mahmoud, MD, MPH
1 Valley Allergy Care, Bethel, PA; 2 Northwestern University, Chicago, IL; 3 OptiNose US, Inc., Yardley, PA.

**RATIONALE:** Nasal steroids are first-line treatment for chronic rhinosinusitis (CRS), with nasal polyps. Some physicians prescribe once-daily (QD) regimens and some twice-daily (BID) doses. This literature review compares once- vs twice-daily dosing.

**METHODS:** We reviewed select reasonably sized randomized controlled trials (RCTs) testing the efficacy of QD or BID nasal steroids vs placebo in reducing polyp burden.

**RESULTS:** Six RCTs exposing a total of 1,712 patients to conventional nasal steroid sprays or placebo were identified. In addition, two RCTs using a novel exhalation delivery system with fluticasone (EDS-FLU) were identified (N=643). In four RCTs (N=142, 310, 354, 748), mean total bilateral polyp grade (polyp grade) was significantly reduced with BID nasal steroid vs placebo. In contrast, three RCTs (N=104, 142, 310) found that polyp grade improvement was not significantly better with QD nasal steroid compared to placebo. Only one large RCT (N=354) showed significant reduction in polyp grade with QD treatment, while one additional very small RCT (N=54) reported reduction in polyp volume with a nonstandard scale. Notably, efficacy with mometasone nasal spray using BID dosing was replicated in 2 independent registration studies, but not with QD dosing. Both RCTs with EDS-FLU (NAVIGATE I/II) studied BID showed significant symptom reduction of comparatively large magnitude and statistically significant polyp grade reduction vs placebo.

**CONCLUSIONS:** Evidence suggests that twice-daily treatment with topical corticosteroid is likely to offer more reliable efficacy than once-daily treatment for patients with moderate-to-severe CRS with nasal polyps.

**860 Nasal challenge with ketorolac: utility and safety in clinical practice**

**Marta Sanchez-Jareño, MD**, Pilar Barranco, MD PhD, Magdalena Lluch-Bernal, MD PhD, Valentín López-Carrasco, and Santiago Quirce, MD PhD; 1 Hospital Universitario La Paz, Madrid, Spain; 2 Allergy Department, Hospital La Paz Institute for Health Research (IdiPaz), Spain; 3 Cleveland Clinic, Cleveland, Ohio; 4 CIBERES, Madrid, Spain; 5 Allergy Department, Hospital La Paz, Madrid, Spain; 6 Allergy Department, Hospital La Paz Institute for Health Research (IdiPaz), Madrid, Spain.

**RATIONALE:** Nasal ketorolac challenge (NKC) has been proposed as a diagnostic test for patients with aspirin exacerbated respiratory disease (AERD) with predominantly nasal symptoms. The aim of this study is to evaluate the clinical outcome of NKC with 16.38mg in everyday clinical practice.

**METHODS:** Adult patients with symptoms of AERD who underwent NKC at Hospital La Paz from 2009 to 2016 were included. NKC was performed by intranasal increasing doses of ketorolac every 30 minutes up to a maximum accumulated dose of 16.38 mg. Negative NKC was followed by oral challenge (OC). We collected data as clinical characteristics, baseline nasal examination, peak nasal inspiratory flow rates, forced expiratory volume in 1 second (FEV1), blood eosinophils baseline levels and IgE levels. Data were analyzed with SAS 9.3 (SAS, Institute, Cary, NC, USA).

**RESULTS:** NKC was performed in 19 patients (mean age 45 ± 15 years), 10 were males. Six NKC were negative (32%). Five patients experienced rhinitis, 4 bronchial symptoms (decrease FEV1 > 15%) and 3 anaphylaxis occurred (2 with 16.38mg and 1 with 8.82mg). No significant differences were found between these 3 patients and the other 10 patients with a positive NKC. Negative NKC were followed by OC: 4 resulted negative, 1 showed bronchial symptoms and 1 urticaria. PNK with 16.38mg showed a sensitivity of 67%, specificity and positive predictive value of 100% and negative predictive value of 67%.

**CONCLUSIONS:** NKC with 16.38mg is a useful method for diagnosis of AERD although it is not as safe in everyday clinical practice as previous publications.

**861 Nasal Sinus Surgery Improves Lower Airway Reactivity during Aspirin Desensitization for AERD**

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**RATIONALE:** Aspirin desensitization and initiation of high-dose aspirin is an effective means of controlling symptoms in patients with aspirin-exacerbated respiratory disease (AERD). In practice, desensitization is often performed after sinus surgery, although the benefit of this has not been proven. We hypothesized that sinus surgery prior to aspirin desensitization would be associated with less severe aspirin-induced lower respiratory reactions during desensitization.

**METHODS:** In this retrospective case series, adult subjects with AERD were identified who had undergone two aspirin desensitizations at Brigham and Women’s Hospital, one within 60 days after sinus surgery and one in the absence of recent surgery. Subjects with incomplete spirometry data or whose desensitizations were aborted due to nonmedical reasons were excluded. Spirometry data were compared, and paired student’s T-tests were used for analysis. Pretreatment with montelukast was controlled for by subgroup analysis.

**RESULTS:** Fifteen subjects met inclusion criteria. Recent sinus surgery within 60 days was associated with significantly reduced decline in FEV1 during aspirin desensitization (mean FEV1 decrease of 0.28 L/min vs 0.50 L/min, p=0.014, n=15). Five of the 15 subjects (33%) who had significant aspirin-induced decrease in FEV1 prior to surgery (FEV1 decrease >15%) had no lower airway reaction during aspirin desensitization after sinus surgery (FEV1 decrease <15%). When subjects on montelukast postoperatively but not nonoperatively were excluded, a similar trend was observed but was less significant (mean FEV1 decrease of 0.35 L/min vs 0.56 L/min, p=0.057, n=11).

**CONCLUSIONS:** In patients with AERD, aspirin desensitization following a recent sinus surgery is associated with decreased aspirin-induced lower airway reactivity and improved safety.
862 Objective study of sleep disruption in Chronic Rhinosinusitis (CRS) by polysomnography

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RATIONALE: It is well established that most patients with chronic rhinosinusitis(CRS) suffer from poor sleep, which is associated with impaired quality of life. However, this has not been studied objectively and the risk factors for sleep disruption in CRS remain unknown. This prospective study aimed to investigate the extent of disturbances and breathing disorders during sleep by using polysomnography (PSG).

METHODS: Thirty randomly selected CRS patients underwent overnight PSG and completed 2 sleep-related questionnaires including the Pittsburgh Sleep Quality Index (PSQI) and Munich Circadian Rhythm. CRS characteristics including presence of nasal polyps, sinus tissue histopathology, Lund-Mackay Score (LMS), sinonasal outcome test scores (SNOT-22) and comorbid diseases (asthma, aspirin exacerbated respiratory disease, allergic rhinitis and gastroesophageal reflux (GERD)) were also investigated. PSG results were recorded and compared in association with these variables.

RESULTS: Overall, 58.6% of the patients had apnea-hypopnea index above 5 indicative of obstructive sleep apnea (OSA): 27.6% mild, 13.8% moderate and 17.2% severe. 68% of patients had hypoxemic episodes during sleep. The mean ± SD O2 nadir was 77.5 ± 23.0% in the whole series. Male gender and GERD were associated with OSA, after adjusting for BMI. Patients with nasal polyph had a trend toward increased supine AHI (adjusted p = 0.09). OSA was associated with poor sleep quality measured by PSQI and circadian rhythm disruption measured by Munich.

CONCLUSIONS: Our prospective study screening with PSG showed that more than half of the CRS patients have OSA, which suggests that all CRS patients potentially need to be screened using PSG, especially male patients and those with comorbid GERD. Further research on cost effectiveness is warranted.

863 Aspirin-Exacerbated Respiratory Disease: Association of Sinus and Asthma Morbidity

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RATIONALE: The association between sinonasal symptoms and pulmonary function in aspirin-exacerbated respiratory disease (AERD) is not fully established. The aim of this study was to determine if sinonasal symptomatology predicts asthma severity.

METHODS: Prospectively collected enrollment and follow-up data from an AERD registry was included from 2013-18. Sino-Nasal Outcomes Test (SNOT) 22-item scores were the predictor variable, with Asthma Control Test (ACT) scores and percent predicted forced expiratory volume in one second (FEV1%) as primary outcome variables. All instances of paired data on the same date were used. ACT was also evaluated with FEV1% as the outcome. Mixed effects regression was completed with SAS 9.4.

RESULTS: 1071 AERD patients were in the registry (mean age 47.5y, SD 13.06, 61.9% female, 28.1% male, 10.0% not stated). Mean SNOT-22 score was 42.2 (SD = 24.2, n = 1281 observations from 845 patients), mean ACT score was 19.4 (SD = 5.1, n = 1435 observations from 863 patients), and mean FEV1% was 82.9 (SD 19.8, n = 746 observations from 298 subjects). SNOT-22 significantly predicted ACT scores (p < 0.0001, 1173 observations from 828 subjects) and FEV1% (p = 0.011, 473 observations from 242 subjects). Any ten-point increase in SNOT-22 was associated with a 0.87 decrease in ACT and a 0.82 decrease in FEV1%. ACT significantly predicted FEV1%; any one-point increase in ACT was associated with a 0.991 increase in FEV1% (p < 0.0001, 599 observations from 260 subjects).

CONCLUSIONS: SNOT-22 scores significantly predict ACT scores and FEV1%. ACT scores also significantly predicted FEV1%. This study demonstrates a significant association between rhinosinusitis symptom severity and subjective and objective measures of asthma severity.

864 Age-related B Cell Inflammatory Changes in Nasal Polyps

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RATIONALE: B cell activation markers are upregulated in nasal polyps (NP). However, age-related B cell inflammatory changes in NP are not well understood.

METHODS: Sinonasal tissues and nasal lavage fluids (NFL) from young (18-49), mature (50-64), and elderly subjects (≥65) with NP, and age-matched healthy controls were collected. Affymetrix microarray assays were performed using NFL and uncinate tissues, and the expression of B cell activation markers was examined. A murine model of NP was generated in 3 age groups: young (2 months), middle-aged (12 months) and old-aged (20 months). Levels of B cell activating factor (BAFF) and anti-dsDNA antibody were measured by ELISA and CD138 (plasma cell marker) was examined using immunohistochemistry.

RESULTS: There was increased BAFF protein levels in NFL in mature adults (50-64) with NP compared to controls (75.5 vs 17.2 pg/ml, p = 0.0198). Levels of anti-dsDNA antibody were significantly increased in older subjects with NP compared to controls (68.8 vs 7.9 IU/ml, p = 0.003). CD138 staining was greater in NP subjects than controls without age differences. The microarray analysis revealed that gene expressions of TNFRSF13C (BAFF receptor), CD19(B-cell marker), MS4A1(CD20; B-cell marker), SDC1(CD138; plasma cell marker) and TPSB2 (MCP-6; mast cell marker) were significantly higher in elderly NP subjects vs elderly controls. In the murine model of NP, BAFF protein levels were significantly increased in NFL compared to controls in the middle-aged NP group (299.2 vs 29.4 pg/ml, p = 0.007), demonstrating a similar pattern in human NP.

CONCLUSIONS: This study demonstrates age-related differences of B-cell inflammatory responses in human NP and a murine NP model.
Age-related Gene Expression and Histologic Changes in Human Nasal Polyps

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RATIONALE: An unbiased investigation of age-related gene expression changes in nasal polyps (NP) may provide new treatment targets, especially for the elderly.

METHODS: Affymetrix microarrays using NP tissues and control uncinate tissues (elderly, age ≥65 vs non-elderly, age 18-49; n=4 each group) were performed and differentially regulated genes were analyzed with a cutoff p value < 0.05 and a cutoff gene expression change >2-fold. Real-time PCR (qRT-PCR), immunohistochemistry (IHC), periodic acid-Schiff (PAS) and trichrome staining were used to validate the microarray results.

RESULTS: Microarray analysis identified genes regulated differentially by disease and age: 340 in NP vs controls, 446 in elderly controls vs non-elderly controls, 45 in elderly NP vs non-elderly NP, 320 in non-elderly NP vs non-elderly controls, and 190 in elderly NP vs elderly controls. qRT-PCR confirmed downregulation of PLAT (tissue-plasminogen activator-1, tPA), upregulation of SERPINE1 (plasminogen activator inhibitor-1, PAI-1) and SERPINB2 (PAI-2), and downregulation of submucosal gland-related genes such as SCGB1D2, SCGB2A2, MUC7 and LPO (lactoperoxidase) in NP vs controls. SERPINE1 expression was significantly increased in elderly NP compared to elderly controls and PLAT expression was downregulated in non-elderly NP compared to non-elderly controls. IHC confirmed significantly reduced expression of anti-microbial proteins, MUC7 and lactoperoxidase, in NP. There was age-related reduction of serous submucosal glandular cells and relative increase of PAS-stained mucous glandular cells. Trichrome staining showed increased collagen deposition with age.

CONCLUSIONS: This study demonstrates age-associated dysregulated genes in human NP. PAI-1 and tPA, which can be potential treatment targets, especially in the elderly.

Strong Dose-response Using a Conjunctival Provocation Test During a Phase II Allergen Immunotherapy Study With Subcutaneously Administered Tyrosine Adsorbed Modified Grass Allergen + MPL

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RATIONALE: This Phase II study [EudraCT 2017-000333-31] evaluated the dose response relationship for a modified grass subcutaneous immunotherapy (SCIT) product with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants for allergic rhinoconjunctivitis (ARC) due to grass pollen.

METHODS: In total 447 patients were enrolled in this randomized, double-blind, placebo-controlled, parallel group study. Patients were randomized to one of five dose regimens of 5100, 14400, 27600 and 35600 SU and placebo. The primary endpoint was the total symptom score (TSS) as measured during a conjunctival provocation test (CPT). Three dose response models were predefined: an Emax, logistic, and linear in log-dose model. MCP-Mod was used to characterize a dose response relationship.

RESULTS: For all three individual pre-specified dose response models a highly statistically significant dose-response (p<0.0001) was shown for the range of cumulative doses from 5100 SU to 35600 SU. The dose reaching at least 50% of the full CPT effect size over placebo (ED50) was approximately 2900 SU, in support of the currently marketed cumulative dose of 5100 SU in Europe, which is almost 2-fold higher. All doses evaluated were well tolerated.

CONCLUSIONS: This study demonstrates a clear and statistically significant dose response on TSS following CPT after an ultra-short course of 6 injections with allergoid grass SCIT treatment with adjuvants MATA and MPL. Both the cumulative 27600 SU and 35600 SU doses showed a similarly optimal risk/benefit profile. Either dose may therefore be selected for further investigation in pivotal phase III studies.

A Pooled Post-Hoc Analysis of Pre-Treatment Allergen Specific IgE and SLIT-Tablet Efficacy

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RATIONALE: Specific IgE sensitization is a common inclusion criteria in clinical trials evaluating sublingual immunotherapy (SLIT) tablets. Our aim was to evaluate the impact of pre-treatment specific IgE levels on clinical efficacy.

METHODS: Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass). Data from 8 placebo-controlled phase III SLIT-tablet clinical trials (allergens: house dust mite, grass, ragweed, tree) were used in the analysis. In two trials, clinical effect was assessed in environmental exposure chambers, remaining trials were confirmatory clinical trials (allergens: house dust mite, house dust mite, grass, tree, grass).
Effect of House Dust Mite SLIT-tablet Treatment on Quality of Sleep in Allergic Rhinitis Patients

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RATIONALE: House dust mite (HDM) SLIT-tablet (12 SQ-HDM, ALK, Denmark) has been shown to be effective in treating HDM allergic rhinitis and asthma in DBPC trials. This post-hoc analysis investigates effect of treatment with SQ-HDM SLIT-tablet on sleep in HDM allergic rhinitis.

METHODS: Subjects from a Phase III trial (EudraCT: 2011-002277-38; placebo: N=338, 12 SQ-HDM: N=318) with moderate-severe HDM allergic rhinitis were treated for up to 1 year (Demoly et al. 2016;JACI;137:444-51). At baseline and during the course of the trial each subject filled-in the Juniper's RQLQ. 3 sleep parameters (DIFFICULTY getting to sleep, WAKE up during night. LACK of a good night’s sleep) were scored from 0 (not troubled) to 6 (extremely troubled). For the purpose of this analysis, scores <3 were categorized into “mildly affected” and >=3 into “moderately/severely affected”.

RESULTS: Of those moderately/severely affected at baseline (62-72% of the population) only 7-10% remained in that category following treatment with the SQ-HDM tablet. This improvement was significantly better than that observed following treatment with placebo (LACK: 12 SQ-HDM: 10.1%; Placebo: 27.5%; p<0.001; WAKE: 12 SQ-HDM: 8.4%; Placebo: 23.0%; p<0.001; DIFFICULTY: 12 SQ-HDM: 7.3%; Placebo: 17.2%; p=0.006). For those starting in the mild category, only 1-7% shifted to the moderate/severe category at end-of-treatment with no difference between placebo and 12 SQ-HDM groups.

CONCLUSIONS: Treatment with 12 SQ-HDM significantly improved quality of sleep for the group of patients who were affected by poor sleep at the start of the trial.
**871** Association Between Baseline Specific IgE Levels and Adverse Events with Sublingual Immunotherapy Tablets

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**RATIONALE:** Adverse events (AEs) associated with sublingual immunotherapy (SLIT)-tablets used to treat allergic rhinoconjunctivitis and/or asthma occur at a rate of approximately 57%-83%, most of which are mild-to-moderate. Biomarkers that could identify patients at risk of more severe reactions would be useful. Baseline specific IgE data from 11 trials of timothy grass, ragweed, house dust mite (HDM), and tree SLIT-tablets were evaluated for associations with frequency and severity of first-reported AEs.

**METHODS:** Specific IgE (kUA/L) was divided into Class 0/1/2 (<3.5), Class 3 (3.5-17.4), Class 4 (17.5-49), Class 5 (50-99), or Class 6 (≥100). Patients’ first-reported AEs were classified as none, mild, moderate, or severe.

**RESULTS:** Overall, 9,187 AEs were reported with SLIT-tablet treatment (n=5,296 patients). The percentages of patients with any AE were 51.7%, 62.4%, 64.4%, 64.9%, and 67.5% for baseline IgE Classes 0/1/2, Class 3, Class 4, Class 5, and Class 6, respectively. Most AEs were mild. The percentages of patients with moderate/severe AEs were slightly higher for Classes 5 (11.7%) and 6 (10.6%) versus lower Classes (5.1%-7.9%). Patterns of slightly increasing AE frequency with increasing IgE levels were observed for seasonal SLIT-tablets, whereas AE frequencies with HDM SLIT-tablet were comparable among IgE classes. AE frequency decreased over time, with approximately 80% of AEs occurring by week 5.

**CONCLUSIONS:** The magnitude of baseline specific IgE corresponds with the frequency of AEs and appears to be a class effect of seasonal SLIT-tablets. The majority of AEs are mild and high IgE is not clearly associated with severe AEs. AE frequency decreases over time.

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**872** Improving Allergy Skin Testing Proficiency

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**RATIONALE:** In 2006, Oppenheimer and Nelson have proposed a method to determine Skin Prick/Puncture Testing (SPT) proficiency. However, the certification and recertification process is not widely practiced. Based on a hypothesis that SPT proficiency correlates with hands-on allergy experience, the objective was to gain insight into training requirements of staff and fellows in an academic practice.

**METHODS:** Twenty allergy staff and physicians (9 RN, 2 NP, 9 MD/DO) used the Quintip® device to perform 10 repetitions of positive (histamine) and negative (diluent control) SPTs on the forearms, for practical purpose, after discontinuing antihistamines for a minimum of five days. Resulting orthogonal wheal diameters were recorded in mm in the presence of an independent observer. Mean histamine wheal diameters were used to determine SD. These values were used to calculate Coefficient of Variation (CV x100=CV%). Professional degree earned, postgraduate years, and years of hands-on allergy clinic experience were also documented. Prism GraphPad software was used for non-parametric Spearman correlation analyses.

**RESULTS:** Seven subjects passed at the first attempt to achieve CV < 30% (median: 2; maximum: 3). Increased hands-on experience was associated with decreased histamine CV% (n = 32, p = 0.0381). Subjects with less than 4 years of allergy experience as a group had wider variability of CV% (15.9-89.0%), regardless of professional degree. Intra-subject variability in one subject was 26% over 12 days.

**CONCLUSIONS:** Hands-on experience in the allergy clinic inversely correlates with histamine CV%. This study highlights the importance of implementing systematic SPT proficiency certification and recertification.

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**873** Withdrawn

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**874** Increased Runx2 expression in chronic rhinosinusitis with neo-osteogenesis

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**RATIONALE:** There is increasing evidence supporting the impact of neo-osteogenesis in the pathophysiology of chronic rhinosinusitis (CRS), especially in the recalcitrant group of patients. Although Runt-related transcription factor 2 (Runx2), a member of Runx family, controls osteoblast differentiation and bone formation, the role and regulation of Runx2 in CRS with neo-osteogenesis patients remains unclear.

**METHODS:** Sinonasal bone and overlying mucosa samples were obtained from patients with CRS with and without evidence of neo-osteogenesis and healthy controls. Immunofluorescence, immunohistochemistry, and immunoblotting were performed to evaluate Runx2 expression in CRS patients with and without neo-osteogenesis. In addition, osteogenic capacity of proinflammatory cytokines were examined by alkaline phosphatase activity (ALP) and bone mineralization assay in vitro.

**RESULTS:** Runx2 expression was increased in CRS patients with neo-osteogenesis compared with tissue from control subjects and those with CRS without neo-osteogenesis (P<.01). Runx2 expression was detected in osteoblast cells around new bone surfaces in CRS sinonasal specimens. Moreover, mucosal extracts from CRS with neo-osteogenesis patients increased Runx2 expression in C2C12 cells, whereas those from patients without neo-osteogenesis did not.

**CONCLUSIONS:** Taken together, these findings suggest that Runx2 may regulate a new bone formation in CRS patients through its effect on the activity of osteoblasts. Thus Runx2 need to be considered as a novel target for preventing neo-osteogenesis in CRS patients.
Evidence for a role of ST6GAL1 in goblet cell hyperplasia in allergic rhinitis patients

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RATIONALE: Mucus hypersecretion with goblet cell hyperplasia is one important feature of allergic rhinitis (AR). However, the mechanisms underlying the remodeling of nasal epithelium in AR are not well understood. β-Galactoside α2,6-sialyltransferase (ST6GAL1) is widely expressed in epithelial cells and participates in the regulation of cell signaling, proliferation, differentiation and apoptosis through processing the sialylated N-glycosylation of proteins. However, the role of ST6GAL1 in AR has been barely studied.

METHODS: The protein and mRNA expression levels of ST6GAL1 in nasal tissue biopsies and nasal epithelial cells were detected by immunohistochemistry, western blotting, and real-time PCR analysis. Human nasal epithelial cells (HNECs) scraped from control subjects were cultured in an air-liquid interface (ALI) condition and transfected with or without ST6GAL1 overexpression plasmid vector. After transfection, cells were treated with or without IL-13. HNECs were then stained with Sambucus nigra lectin (SNA)-FITC and evaluated by flow cytometry.

RESULTS: Immunohistochemistry showed that the expression of ST6GAL1 was up-regulated in nasal mucosa from AR patients particularly in nasal epithelial cells. RT-PCR and western blotting analysis confirmed the up-regulation of ST6GAL1 in nasal epithelial cells from AR patients compared with controls. After IL-13 stimulation, the mRNA levels of goblet cell hyperplasia markers, including MUC5AC and FOXA3 besides ST6GAL1 were elevated in HNECs, and this elevation was more compared with controls. After IL-13 stimulation, the mRNA levels of goblet cell hyperplasia markers, including MUC5AC and FOXA3 besides ST6GAL1 were elevated in HNECs, and this elevation was more prominent in cells with ST6GAL1 plasmid transfection than those without transfection. IL-13 receptor α2 (IL-13Rα2) of HNECs exhibited increased α2,6-sialylation on N-glycans after overexpression of ST6GAL1.

CONCLUSIONS: ST6GAL1 might promote goblet cell hyperplasia induced by IL-13 in AR patients.

Association of L-plastin Expression With Recalcitrant Nasal Polyps In The Patients With Aspirin-Exacerbated Respiratory Disease

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RATIONALE: Nasal polyps from patients with aspirin-exacerbated respiratory disease (AERD) are defined by a predominant Th2 inflammation environment, and AERD nasal polyps are much more likely to have rapid relapse postoperatively. However, little is known about the specific cellular and molecular mechanisms contributing to the pathogenesis of nasal poly development in patients with AERD are not present.

METHODS: We collected nasal polyp tissue from patients with AERD and from patients with chronic rhinosinusitis with nasal polyps (CRSwNP). Protein profiles were analyzed by 2-dimensional electrophoresis and identified several proteins, including L-plastin, as highly expressed. We examined L-plastin and tissue factor (TF) expression by immunohistochemical and immunofluorescence analyses. To examine the role of L-plastin in eosinophils, we knocked down L-plastin expression in Eol-1 cells by using siRNA transfection.

RESULTS: L-plastin protein levels in nasal polyp tissue were increased in patients with AERD relative to those in patients with aspirin tolerant CRSwNP. Immunofluorescence analysis revealed that L-plastin was dominantly expressed in eosinophils and L-plastin and TF were co-expressed in eosinophils in AERD nasal polyp tissue. Silencing of L-plastin in Eol-1 cells disrupted the cell surface distribution of TF by stimulation with granulocyte macrophage colony-stimulating factor. We also found that L-plastin knockdown attenuated transmigration of Eol-1 across the endothelium, and decreased cytokines release.

CONCLUSIONS: The expression of L-plastin by eosinophils may contribute to abnormal fibrin deposition through TF translocation to the eosinophil cell surface in AERD nasal polyp tissue, which in turn may contribute to the pathogenesis of AERD.

Urine eosinophil-derived neurotoxin declines following mepolizumab treatment in subjects with Eosinophilic Granulomatosis with Polyangiitis

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RATIONALE: Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a vasculitic disorder associated with elevated blood and tissue eosinophilia. Attempts to define biomarkers that predict disease activity or relapse in EGPA have proven difficult, and blood absolute eosinophil count (AEC) may not accurately reflect tissue eosinophilia. Although blood and urine levels of eosinophil granule proteins (EGP) correlate with markers of eosinophil activation in other eosinophilic disorders, little is known about their utility in monitoring disease activity in EGPA.

METHODS: Urine and plasma were obtained at fixed time points from 55 patients with relapsing or refractory EGPA enrolled on a Phase 3 double-blind, placebo-controlled (NCT02020889) study of mepolizumab (300mg every 4 weeks). Concentrations of major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil-derived neurotoxin (EDN) and eosinophil peroxidase (EPO) were measured using a suspension array multiplex immunoassay.

RESULTS: Plasma EDN (pEDN) and urine EDN (uEDN) levels decreased significantly in the first sample collection following initiation of mepolizumab (pEDN baseline vs. week 4 (V9)) p<0.0001; uEDN (baseline v. week 24 (V9)) p=0.0002), but not placebo. pEDN correlated positively with AEC (R=0.57, p<0.0001 [0.33, 0.74]) and inversely with GC dose. uEDN was not correlated with either parameter. Samples collected within 10 days of a relapse showed higher uEDN concentrations than those collected at the prior visit (GM 1420 vs. 958 ng/mg Cr; p=0.01).

CONCLUSIONS: In this preliminary analysis, uEDN concentrations declined following mepolizumab treatment, increased with relapses, and were less affected by GC dosing than pEDN, suggesting that uEDN may be a useful biomarker of disease activity in EGPA.
**878 Exploring a relationship between B cells and eosinophils**

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**RATIONALE:** Recent data supports an important regulatory role for eosinophils in maintaining homeostasis. Consequently, increasing use of eosinophil-targeted therapies in allergic disease has raised concerns about the effects of eosinophil depletion on the numbers and function of other immune cells. Whereas studies in murine models suggest that eosinophils regulate bone marrow and peripheral B lymphocytes, but there is limited evidence of this relationship in humans.

**METHODS:** (1) Retrospective analysis of clinical and laboratory data from healthy volunteers and subjects enrolled on a clinical protocol to study unexplained eosinophilia which included those ultimately diagnosed with hypereosinophilic syndrome (HES) (2) In vitro assessment of B cell proliferation, measured by CFSE dye dilution, in response to eosinophil-conditioned media.

**RESULTS:** Peripheral B cell counts and serum immunoglobulins (IgG and IgM) were positively correlated with absolute eosinophil count (AEC, r = 0.22-0.26; p < 0.05) in untreated eosinophilic subjects (AEC > 1000 cells/mm³, n = 107) but not in healthy volunteers (n = 44). The correlation between AEC and B cell count was greatest in patients with myeloid HES (MHS) (r = 0.62, p < 0.05), and B cell numbers decreased in the setting of eosinophil reduction by imatinib in treatment-responsive patients with MHS (n = 17). B cells from healthy volunteers demonstrated increased proliferation 4 days in media containing culture supernatants conditioned by purified eosinophils from MHS patients (n = 4).

**CONCLUSIONS:** The current study confirms a correlation between AEC and peripheral B cell counts in patients with eosinophilia and suggests that soluble factors from activated eosinophils may play a key role in this process.

(NCT00001406, NCT00044304)

**879 Eosinophil Subtypes Defined by Distinct Gene Expression and Function**

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**RATIONALE:** Eosinophils are evolutionarily conserved granulocytes typically associated with parasite killing or allergic diseases. Although eosinophils are traditionally characterized as destructive and cytotoxic cells with the main activity being degranulation (releasing toxic proteins), we and others are identifying eosinophils as immune regulatory cells in health and disease. We hypothesize that there are many subtypes of immune polarized tissue infiltrating eosinophils that are disease/issue specific and can be used as a diagnostic/prognostic indicator of health and disease. In particular, we propose type 1 and type 2 immune environments induce specific gene expression and functions of eosinophils.

**METHODS:** Blood-derived eosinophils were purified from IL-5 over expressing mice (NJ 1638) and cultured for 18 hours with type 2 cytokines IL-33/GM-CSF/IL-4 or type 1 cytokines IFNγ/TNFα to generate E2 and E1 eosinophils respectively. RNAseq was completed with confirmation RT-PCR. Cell surface markers were assayed by flow cytometry. Viability was compared with and without corticosteroids. Proteins were assayed by multiplex assay and degranulation by eosinophil peroxidase (EPX) ELISA.

**RESULTS:** RNAseq analysis showed E2 as compared to E1 had 371 upregulated and 407 downregulated genes and E1 as compared to E2 had 386 upregulated and 107 downregulated genes. Released proteins were unique between subtypes. Characteristic cell surface markers of E2 include C1q Hb3 and CD69α while E1 include Ly6Cδ. E1 eosinophils had reduced viability with and without corticosteroid treatment as compared to E2 eosinophils. E2 eosinophils released significantly more EPX upon culture.

**CONCLUSIONS:** The cytokine environment induces differential activation of eosinophils resulting in unique gene expression and functional activities.

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**RATIONALE:** Innate type 2 lymphoid cells (ILC2s) recruit and accumulate in the lung in response to type 2 inflammation. This coincides with production of IL-5 and IL-13 from ILC2s and pulmonary eosinophils. Although ILC2s have been shown to modulate eosinophil activities, the role of eosinophils in regulating ILC2 responses is less well defined and may represent a novel regulatory feedback pathway.

**METHODS:** Type 2 pulmonary inflammation was induced by either intratracheal cytokine administration (e.g., IL-33) or using models of ovalbumin or house dust mite allergen sensitization/challenge. Eosinophils were specifically depleted immediately prior to instillation or challenge using inducible eosinophil-deficient mice (iPHIL) mice to determine the role of eosinophils on pulmonary ILC2s in these type 2 inflammation models. Lung-derived ILC2s were cultured with eosinophils to define ILC2 and eosinophil interactions. Activation and chemotaxis of ILC2s were assessed in vitro.

**RESULTS:** Depletion of eosinophils in all type 2 models of respiratory inflammation resulted in a significant reduction of total and activated pulmonary ILC2s. For example, lung IL-13+ILC2s were significantly reduced in IL-33 treated eosinophil-depleted iPHIL, mice (236,018±42,307 vs 106,220±26,617 IL-13+ILC2s (p<0.05)). Baseline and saline treated animals had comparable pulmonary ILC2 numbers (<20,000 ILC2s (p>0.05) between eosinophil-proficient and deficient mice. In vitro IL-33 activated eosinophils released chemotactic factors for ILC2s and induced activation of ILC2s through cell-cell contact.

**CONCLUSIONS:** Our data demonstrates an underappreciated and significant role for eosinophils in recruitment and activation of ILC2s. These data suggest a reciprocal role for eosinophil-ILC2 interactions in amplification of the type 2 pulmonary inflammatory response.
**AB290**

**Analysis of the causative factors of hypereosinophilia in an inner city population**

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**RATIONALE:** Hypereosinophilia (HE) is a persistent absolute eosinophil count (AEC) > 1500 cells/µL. The World Allergy Organization (WAO) recommends several diagnostic tests for HE patients. We analyzed utilization of WAO recommendations among patients from a large inner-city population.

**METHODS:** A retrospective chart review was conducted on HE patients from 2013-2016. Several laboratory, histopathological tests and ICD-9 diagnoses were recorded.

**RESULTS:** 290 patients with HE were identified with a mean AEC of 2300 cells/µL (±159). Most patients were male (56%) of Hispanic origin (50%), with a mean age of 62 years (±18.3). Only 23 patients (8%) had total serum IgE tested (mean level 1292 IU/ml±18.3, range 6.5-5822 IU/ml). Cortisol level was checked in 59 patients (13.4%) (mean level 17 µg/dL ±13.7) and trypstatin in 10 patients (3.4%) (mean level 5.4 ng/mL ±2.7, range 2.0-11.0 ng/mL). Strongyloides, toxocara and trichinella serologies were negative for the remaining parasites tests were negative.

Stool test for ova and parasites was checked in 35 patients (12.1%) and bone marrow biopsy was performed in 12 patients (4.2%). Asthma was diagnosed in 101 patients (35%), and 5 patients (2%) were diagnosed with nasal polyps. A complete WAO HE work-up was not performed in any of these patients.

**CONCLUSIONS:** Asthma & strongyloidiasis were the most common causes of HE. HE was not thoroughly evaluated as recommended by WAO. Better evaluation of HE patients is beneficial, especially to identify treatable & potentially dangerous conditions.

**882 Transgenic Expression of a Novel Secreted and Active Form of IL-33 Promotes Tissue Eosinophilia in a Mouse Model of Eosinophilic Esophagitis**

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**RATIONALE:** Eosinophilic esophagitis is characterized by eosinophilia in conjunction with IL-33 expression. IL-33 is a proinflammatory cytokine that induces eosinophils and other cells to produce type 2 cytokines, such as IL-13. IL-33 is produced in an inactive form and stored in the cell nucleus presenting hurdles for transgenic studies of IL-33 activity. We hypothesized that transgenic expression of a secreted/active form of IL-33 would overcome these hurdles and promote eosinophilic inflammation.

**METHODS:** We generated a secreted/active mouse IL-33 fusion gene by combining the IL-2 secretory signal peptide gene sequence with that encoding an active IL-33 fragment (a.a. 109-266). Fusion gene function was examined *in vitro* with a tetacycline-inducible system transduced into HEK-293 cells, and by culturing eosinophils with the HEK-293 cell culture supernatants and assessing IL-13 production by ELISA. IL-33 activity was examined *in vivo* by transgenic expression from the esophageal epithelium using an Epstein-Barr virus promoter (ED-L2). Mice were subjected to OVA sensitization/gastric challenge. Eosinophil densities were compared based on eosinophil peroxidase immunohistochemistry.

**RESULTS:** Fusion gene transfected HEK-293 cells secreted an active form of IL-33 that induced eosinophils to produce IL-13. Expression of IL-33 by the esophageal epithelium resulted in increased esophageal eosinophilia relative to wild type in an OVA sensitization/challenge eosinophilic esophagitis model.

**CONCLUSIONS:** Fusion of the IL-2 secretory signal peptide sequence with that encoding an active IL-33 fragment generated secreted/active IL-33. The ability to express secreted/active IL-33 in a cell/tissue-specific manner will facilitate studies examining IL-33 activities and mechanisms of diseases.

**883 Identification of reactive oxygen production site in Siglec-8 induced eosinophil death**

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**RATIONALE:** Siglec-8 is expressed on the surface of eosinophils and induces cell death. This function is paradoxically enhanced by co-stimulation with IL-5, an activation/survival factor for eosinophils. We previously reported that this cell death was dependent on intracellular reactive oxygen species (ROS) unlike ETosis, which require extracellular ROS. Here we conducted functional analysis of NAPDH oxidase (NOX) and mitochondria to identify the source of intracellular ROS production in Siglec-8 induced cell death.

**METHODS:** Human peripheral blood eosinophils were purified and stimulated by anti-Siglec-8 monoclonal antibodies (as ligand) simultaneously with IL-5, or by Ca++ionophore A23187 as ETosis inducer. Then we evaluated (1) phosphorylation of p40(phox)/p47(phox)(NOX cytosolic subunits) by Western Blotting and phopho-flow, (2) cell surface expression of gp91(phox)(a NOX membrane subunit) by flow cytometry, (3) mitochondrial membrane depolarization and its ROS production using fluorescent indicators JC-1 and MitoSOX Red, respectively.

**RESULTS:** Phosphorylation of p40(phox) was observed with both Siglec-8 and A23187 stimulation, with the latter showed more prominent change. Interestingly, cell surface expression of gp91(phox) was not changed by Siglec-8, contrary to the significant increase by A23187. In mitochondrial analysis, mild depolarization but no ROS production was detected in Siglec-8 stimulated cells.

**CONCLUSIONS:** NOX was turned out to be the predominant source of intracellular ROS in Siglec-8 mediated cell death. The difference in surface expression of gp91(phox) may explain the difference in ROS production by Siglec-8 and ETosis stimuli, proposing previously unrecognized property of eosinophil NOX.
**884** NEIL2 protects against cat dander-induced eosinophilic airway inflammation

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**RATIONALE:** Nei-like 2 (NEIL2) is a DNA glycosylase enzyme that can excise oxidized DNA bases like 5-hydroxycytosine. NEIL2-null mice show more innate inflammatory response in the lungs stimulated by oxidative stress-inducing challenges. Here we hypothesized that NEIL2 regulates cat dander extract (CDE)-induced allergic airway inflammation and sensitization.

**METHODS:** Wild-type (WT) and Neil2 KO mice were sensitized with 5 intranasal doses of CDE and challenged with CDE to elucidate allergic airway inflammation. Allergic airway inflammation and the lung mRNA expression of 84 genes known to be associated with allergic-inflammation were quantified.

**RESULTS:** Multiple challenge with CDE in WT mice induced allergic inflammation characterized by an increase in eosinophilic airway inflammation, stimulation of mucin in airway epithelial cells, and levels of cat dander specific IgE in serum at 72-hours post challenge. Multiple CDE challenges in Neil2 KO mice enhanced these increases observed in WT mice. PCR array and qPCR identified Ccl11 and Il5ra as two eosinophilia-associated genes that were higher 4 h-post challenge in Neil2 KO mice.

**CONCLUSIONS:** These observations indicates that NEIL2 suppresses CDE-induced eosinophilic airway inflammation. NEIL2 may be a novel target for attenuating eosinophilic airway inflammation and antigen-specific IgE.

**885** Improved esophageal barrier function following treatment with TLR2 agonists

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**RATIONALE:** Eosinophilic esophagitis (EoE) is a multifactorial, chronic esophageal disorder characterized by epithelial barrier dysfunction and eosinophil-predominant allergic inflammation. The precise mechanisms that sustain epithelial barrier dysfunction and inflammation in EoE are poorly understood. The esophageal epithelium expresses functional Toll-like receptors (TLR), which are a family of Pattern recognition receptors (PRR). The objective of these studies was to investigate the effect of TLR2 agonist treatment on esophageal epithelial barrier function.

**METHODS:** Immortalized human esophageal epithelial cells were stimulated with TLR2 agonists in an in vitro air-liquid interface (ALI) epithelial model system. We then used transepithelial electrical resistance (TEER) and permeability to FITC-labeled dextran were used to assess membrane barrier function following TLR2 stimulation.

**RESULTS:** Primary and EPC2-hTERT esophageal epithelial cells express high levels of TLR2 and TLR3. TLR2 stimulation led to increased transepithelial electrical resistance (1.4-fold) and decreased paracellular permeability to FITC-Dextran. ALI cultures treated with zymosan have altered epithelial architecture. TJ-proteins are specifically induced after treatment with TLR2 agonist zymosan, with induction of claudin-1 (3.9-fold) and zonula occludens 1 (2.7-fold) gene expression. Chromatin immunoprecipitation analysis demonstrated significant increase in H4ac at the CLDN1 enhancer and promoter following stimulation of EPC2-

**886** Steroid-Dependent Episodic Angioedema with Eosinophilia (Gleich Syndrome) in a Patient with Rheumatoid Arthritis

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**RATIONALE:** Episodic angioedema with eosinophilia, or Gleich syndrome, is a rare disorder characterized by periodic episodes of angioedema and leukocytosis with marked eosinophilia. Symptoms resolve spontaneously or are treated with corticosteroids as first-line therapy. Treatment of patients unresponsive to or dependent on corticosteroids is poorly defined. Several rheumatologic diseases, including rheumatoid arthritis (RA), can also present with elevated eosinophilia in blood or tissue. Here we present a case of steroid-dependent Gleich syndrome complicated by concurrent rheumatoid arthritis.

**METHODS:** A retrospective chart review of a patient with Gleich syndrome at a university hospital-based Allergy/Immunology outpatient clinic in Kansas City, KS.

**RESULTS:** This patient with seropositive RA had multiple episodes of angioedema with eosinophilia and associated dyspnea. Labs showed absolute eosinophil count of 12.9 K/UL and WBC 25.51 K/UL. Tryptase was elevated at 26.1 ug/L. CT neck showed subglottic swelling. Further workup included normal ACE and Cl esterase inhibitor levels and negative ANCA serologies. Bone marrow biopsy showed hypercellular marrow and normal cytogenetics. A diagnosis of Gleich syndrome was suspected. She was initially treated with glucocorticoids but with attempts at weaning experienced recurrent pharyngeal swelling and increase in serum eosinophilia. She was then started on rituximab for RA and hypereosinophilia with decrease in eosinophil count and ability to tolerate further steroid tapers.

**CONCLUSIONS:** To our knowledge, this is the first reported case of Gleich syndrome in a patient with RA. Rituximab therapy has been described in hypereosinophilic syndromes but not reported specifically for Gleich syndrome, demonstrating the importance of recognizing alternative therapies for complex, steroid-dependent disease.
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RATIONALE: Hypereosinophilic syndromes (HES) are challenging heterogeneous disorders.

METHODS: We describe two cases of uncommon HES, treated with the monoclonal anti-IL-5 antibody mepolizumab.

RESULTS: Patient 1, a 34-year-old man, and patient 2, a 57-year-old woman, referred to our Center complaining about recurrent episodes of edema of the extremities, with significant weight gain, partial functional defect and severe weakness. Marked hypereosinophilia was repeatedly detected. The autoimmunity panel, IgE, C4 resulted normal. The evaluation for hematologic, allergic, infectious diseases including bone marrow biopsy with cytogenetic analysis-immunophenotyping, viral panel, prick/patch tests and imaging provided inconclusive results. Interestingly, the exams of patient 1 showed hyper-IgM. IgM monoclonal components and IgM-cryoglobulinemia. The diagnosis of Gleich syndrome was suggested.

In both cases IL-5 and eosinophil cationic protein (ECP) were elevated: IL-5 264.2 and 84.10 pg/ml, mv < 7.8; ECP 192 and 171 mcg/l, mv < 15 respectively. Off label mepolizumab was started, with subcutaneous administrations twice a month.

Both patients initially showed clinical-laboratory improvement (from 27970/mm3 to 10171/mm3 eosinophils in patient 1, from 6340/mm3 to 850/mm3 eosinophils in patient 2). Steroids were tapered, mepolizumab dose was increased (200 mg in patient 1, 300 mg in patient 2 twice a month). Patient 1 experienced minor recurrences and, also due to the lack of compliance, mepolizumab was withdrawn. Patient 2 developed mild erythematous lesions. Punch biopsy revealed a diffuse eosinophilic infiltration.

CONCLUSIONS: Biologics targeted to eosinophilic growth factors open a new area of intervention for HES, potentially allowing steroid sparing strategies. Further investigation is needed to evaluate the correct treatment regimens.
**Cysteinyl Leukotriene Receptor 2 Drives IL-33-Mediated Aspirin Sensitivity Through A Platelet Dependent Mechanism**

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**RATIONALE:** Cysteinyl leukotrienes (cysLTs) facilitate mucosal type 2 (eosinophilic) immunopathology, especially in aspirin-exacerbated respiratory disease (AERD), by incompletely understood mechanisms. Leukotriene C4 (LTC4) acts at platelet- and epithelial-associated type 2 cysLT receptors (CysLT1R, CysLT2R) to modulate eosinophilic airway inflammation. Because platelets constitutively express IL-33 protein, which is essential to the induction of type 2 immunopathology and aspirin sensitivity, we sought to determine whether platelets, activated through CysLT2R, cause IL-33-dependent immunopathology.

**METHODS:** Prostaglandin E2 synthase deficient (Ptges−/−) mice were primed with house dust mite extract, and then were challenged with lysine aspirin (Lys-ASA) for lung function and mediator measurement. Lung IL-5, IL-13, and IL-33 were measured by ELISA. Intrapulmonary platelet recruitment was determined by histological staining and western blotting for CD41.

**RESULTS:** Challenges of AERD-like Ptges−/− mice with inhaled Lys-ASA elicited LTC4 synthesis and caused rapid intrapulmonary platelet recruitment, accompanied by rapid increases in lung IL-33, IL-5, and IL-13. Platelet depletion and blockade of CysLT2R eliminate all manifestations of Lys-ASA challenges, including mast cell activation, changes in airway resistance, and increases in IL-33, IL-5, and IL-13.

**CONCLUSIONS:** Platelets are essential to the CysLT1R-driven type 2 respiratory immunopathology and IL-33-dependent aspirin sensitivity. Antiplatelet medications may be useful to treat AERD and other disorders associated with type 2 immunopathology.

**The effect of muscarinic M3 receptor blockade in development of M2 macrophages in allergic inflammation**

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**RATIONALE:** We have reported that muscarinic M3 receptor antagonists (tiotropium) inhibit the allergic airway inflammation in murine model of asthma. However, the mechanism is still unclear. The purpose of this study is to investigate the effect of muscarinic M3 receptor blockade in development of M2 macrophages in allergic inflammation.

**METHODS:** Balb/c mice were sensitized and challenged with OVA to develop the mouse model of asthma. During the challenge phase, mice were treated with/treated without tiotropium. Twenty-four hours after the last challenge, lung cells were isolated from the lung. The lung cells were gated by CD68 positive cells, and analyzed the expression of Relm-a and Arginase-1 (M2 macrophage markers) by flow cytometry. Additionally, mouse bone marrow cells derived macrophages (mBMMacs) and also human peripheral blood mononuclear cells (PBMCs) derived macrophages were stimulated with IL-4 and treated with muscarinic M3 receptor antagonist in vitro.

**RESULTS:** The number of total cells and eosinophils, and the levels of cytokines (IL-5 and IL-13) in BALF were significantly decreased in asthma group treated with tiotropium compared to untreated asthma group. The expression of Relm-a and Arginase-1 in macrophages was significantly reduced in asthma group treated with tiotropium compared to untreated asthma group, suggesting that the development of M2 macrophages was inhibited by muscarinic M3 receptor blockade. The blockade of muscarinic M3 receptor in vitro, significantly inhibited the development of M2 macrophages in both mBMMacs and PBMCs derived macrophages.

**CONCLUSIONS:** These results suggest that the blockade of muscarinic M3 receptor inhibits the development of M2 macrophages and prevent the allergic airway inflammation.

**P2Y6 Signaling Controls an Innate Alveolar Macrophage-NK Cell Axis That Dampens Type 2 Lung Immunopathology**

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**RATIONALE:** Type 6 purinergic (P2Y6) receptors are high affinity G protein-coupled receptors (GPCRs) for uridine diphosphate (UDP). We found that P2Y6 receptor expression during the sensitization phase plays a critical role in preventing sensitization to the allergen. In this study, we sought to identify key steps and cell types response for the protective effect of P2Y6 receptors.

**METHODS:** p2ry6(flox/flox);rosa26creER/+ and p2ry6(flox/flox);+/+ controls were treated with tamoxifen starting either 10 days before the initial sensitization. The mice were sensitized with an extract from Dermatophagoides farinae (Df) intranasally on days 0 and 1. We examined BAL fluid from P2ry6flox/flox/Cre/+ mice and +/+ controls for Th1 cytokines by alveolar macrophages, as well as the NK cell activation, during the sensitization phase.

**RESULTS:** BAL fluid levels of IL-12p40, expression of IFNγ, and M1-cytokine/chemokine transcripts by BAL fluid cells increased sharply in response to 2 sensitizing doses of Df in +/+ but not in P2ry6flox/flox/Cre/+ mice. Alveolar macrophages were the dominant source of P2Y6 receptor-dependent IL-12p40 expression, driving IFNγ production by NK cells. The IL-12-restored P2ry6flox/flox/Cre/+ mice showed significantly increased expression of IFNγ at day 2 and decreased BAL fluid eosinophils at day 16, compared to the Df-treated +/+ controls. Antibody depletion of NK cells before sensitization abolished the protective effect of P2Y6 receptors.

**CONCLUSIONS:** Alveolar macrophages use UDP-P2Y6 signalling to drive an innate IL-12/NK cell axis that strongly influences the outcome of respiratory allergen exposure.
**893** Macrophage Response to Particulates Plays a Pivotal Role in Development of Allergic Immune Response to Airborne Pollens

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**RATIONALE:** Innate immune responses in respiratory mucosa, such as those mediated by airway epithelial cells, likely play pivotal roles in development of type 2 immunity to inhaled allergens. The goal of this project was to investigate the roles for another innate immune cell type, namely airway macrophages, to induce allergic sensitization to pollens by using mouse models.

**METHODS:** Naïve BALB/c mice were exposed intranasally (i.n.) to ragweed pollen particles or ragweed extract twice a week for up to 3 weeks. Development of allergic immune responses was examined by analyzing sera and by challenging the animals i.n. with ragweed extract. The roles for macrophages were examined by in vitro culture and by depleting them in CD169-DTR transgenic mice. Clodronate liposome particles were used to characterize macrophage responses.

**RESULTS:** Mice developed allergic immune responses to ragweed, including increased serum levels of IgE antibodies and airway eosinophilia, when exposed to ragweed pollen particles but not to ragweed extract. Pollen particles showed adjuvant activities to promote development of follicular helper T cells and allergen-specific IgE antibodies. Isolated airway macrophages produced IL-1α in response to pollen particles or clodronate liposome particles, but not to ragweed extract, in vitro. IL-1α and clodronate liposomes showed similar adjuvant activities as ragweed pollen particles to promote allergic immune responses in vivo. Finally, depletion of airway macrophages in CD169-DTR mice abolished IL-1α production and development of allergic immune response to ragweed pollens.

**CONCLUSIONS:** Airway macrophages play a pivotal role to promote development of allergic immune responses to inhaled allergen particles.

**894** Distinct Enteric Microbiota Perturbations Exist in Atopic Adults With or Without Asthma.

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**RATIONALE:** Growing evidence indicates that early life gut microbiome perturbation and associated metabolic dysfunction precede the development of childhood allergy and asthma. However, the extent of microbiota restructuring and its relationship to clinical and inflammatory features of established atopic asthma in adults remains largely unexplored.

**METHODS:** Bacterial and fungal communities in stool samples collected from 36 atopic adults with mild asthma (AA), 20 atopic adults without asthma (ANA) and 19 non-atopic healthy controls (HC), were profiled by 16S rRNA and ITS biomarker sequencing, respectively. Statistical analyses were performed in Qime and R environment.

**RESULTS:** Bacterial gut microbiota in AAs was compositionally distinct from both ANAs and HC subjects (weighted UniFrac; PERMANOVA R²=0.033, p=0.050 and R²=0.035, p=0.045, respectively) and associated with predicted %FEV1 (R²=0.037, p=0.005). Variance in fungal gut microbiota composition was associated with bronchial hyperresponsiveness (Bray Curtis; PERMANOVA R²=0.050, p=0.011) and atopic status (R²=0.074, p=0.001). Allergic adults in this study (both AAs and ANAs) harbored less diverse (Shannon index; Welch’s t-test p=0.041) and less even (Welch’s t-test p=0.016) gut fungal communities compared to HC subjects.

**CONCLUSIONS:** Imbalance in both fungal and bacterial gut microbiota is a signature of established atopic asthma, and features of these communities are associated with clinical markers of the disease. Perturbations to fungal community composition in the adult gut appear to be associated with atopy, with or without coincident asthma.

**895** Hizikia fusiformis Ameliorates Allergic Inflammation in an Ova-induced Allergic Rhinitis Mouse Model.

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**RATIONALE:** Recently, several studies have reported that extract of Hizikia fusiformis (HF) shows the immune-modulatory, anti-cancer, anti-atoric and anti-oxidant activities. The anti-inflammatory activity of HF suggests applications for diverse disorders including allergic and auto-immune, and sinonasal relative disease. We hypothesized that HF would alleviate the allergic rhinitis inflammation.

**METHODS:** After establishment of allergic inflammation with OVA albumin in 4-week-old BALB/c mice, HF was administered intraperitoneally 5 times per week for one week during nasal challenging period in one group. The other group received additional HF intraperitonnely 3 times during sensitization period. To compare its anti-inflammatory effects, triamcinolone acetone (TAC) was utilized as a control drug. Histopathologic changes were evaluated using H&E stain for eosinophilic infiltration. The levels of IgG1, IgG2, Total IgE, ova-specific IgE was assessed. The levels of cytokines in the nasal mucosa were measured by Real-Time PCR. The levels of cytokines in spleen cell culture supernatant, including TNF, interleukin (IL)-4, IL-5, and IL-13, IL-10, IL-17 were assessed by ELISA.

**RESULTS:** The allergic symptom score, ova-specific IgE, IgG2 level were lower in HF treated group compared to the TAC-treated or OVA (+) group, which was more obvious in the mice group received HF during sensitization and nasal challenge period. The cytokine IL-4,5,13 and IL-17 were significantly lower in the HF treated group compared with OVA (+) group. The degree of eosinophilic infiltration was significantly decreased by instillation of HF; the potency being greater than TAC.

**CONCLUSIONS:** This study demonstrated that HF can suppress Th2 and Th17 responses in an AR murine model.
Effect of CysLTR1 blockade on allergen challenge induced CD49d expressing neutrophil recruitment to the nasal lavage

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RATIONALE: We demonstrated CD49d expressing neutrophils (CD49d+ PMN) accumulate in human nasal lavage with cold symptoms or following allergen challenge. Both human and mouse CD49d+ PMN express cysteinyl leukotiene receptor 1 (CysLTR1). In mice, CysLTR1 blockade increased CD49d+ PMN apoptosis and prevented post-viral atopic disease. This study evaluated whether CysLTR1 blockade prevents human nasal lavage CD49d+ PMN accumulation post allergen challenge.

METHODS: Subjects (n=25; 13 female; 32(25-58) years old, median(range)) were randomized to receive placebo or 10mg montelukast daily for 1 week. After skin testing, a nasal lavage was performed, then an allergen challenge, with a repeat lavage 6 hours later. Subjects were then crossed-over to the other treatment for a week, and repeat challenge/lavages performed. Number of CD49d+ PMN in nasal lavage determined by flow cytometry.

RESULTS: CD49d+ PMN counts trended to increase with allergen challenge on placebo (930±230-1945 to 1255±552-5084; p=0.19; n=13; median±IQR number of CD49d+ PMN in nasal lavage pre to post challenge), while there was no increase with montelukast (443±216-1246 to 792±156-1559; p=0.72; n=14). Interestingly, the montelukast effect was greatest in subjects who were given the drug during the first week (494±328-746 to 444±116-1131; p=0.55; n=8) compared to the second week (249±123-11030 to 1706±396-2970; p=0.84, n=6).

CONCLUSIONS: There was a trend for increased CD49d+ PMN in the nasal lavage of allergic subjects treated with a placebo. CysLTR1 blockade with montelukast prevented a significant increase in nasal lavage CD49d+ PMN with allergen challenge, although an allergen challenge one week earlier seemed to blunt this prevention.

Butyrate and propionate regulated proliferation and activation of human group-2 innate lymphoid cells (ILC2s)

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RATIONALE: Commensal intestinal microbiota are thought to play fundamental roles in the induction, training and regulation of the human immune system, at least in part through innumerable microbial products such as short-chain fatty acids (SCFAs). We hypothesized that SCFAs such as butyrate, propionate and acetate directly affect group-2 innate lymphoid cell (ILC2) functions and regulate allergic inflammation. To test this hypothesis, we determined the effects of SCFAs on human ILC2s in vitro.

METHODS: Human ILC2s were sorted from peripheral blood lymphocytes (PBMC) of healthy donors and expanded in the presence of feeder cells and recombinant IL-2 for 3-4 weeks. After confirming their purity, the ILC2s were cultured with IL-2 and IL-33 in the presence and absence of such SCFAs as butyrate, propionate and acetate. Then the cells’ viability, proliferation and cytokine/chemokine production were determined.

RESULTS: We found that butyrate and propionate suppressed the ILC2s’ production of such type 2 cytokines/chemokine as IL-5, IL-9, IL-13 and IL-8 . Butyrate and propionate also induced apoptosis and suppressed proliferation of the cells through downregulation of IL-2Rα. Conversely, acetate showed none of those effects on the cells.

CONCLUSIONS: Butyrate and propionate, but not acetate, produced by the intestinal microbiota may play important roles in regulating the proliferation activation and cytokine/chemokine production profiles of ILC2s, thereby leading to regulation of allergic inflammatory diseases.

The Effect of Hydroxytolans on Macrophages

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RATIONALE: A group of hydroxytolans were previously found capable of suppressing tumor cell growth. The most current study further evaluated their regulatory effects on inflammation, a common factor in many diseases including cancer, arthritis and cardiovascular disorders.

METHODS: The study focused on macrophages, an immune cell type responsible for chronic inflammation. Cell viability assays were conducted to assess the effect of hydroxytolans, at various concentrations for 24h, on murine macrophage cell line RAW 264.7, compared to murine fibroblast L929 cells. Quantitative RT PCR analysis was conducted to detect activation of inflammatory genes (TNFα, IL-1, IL-6 and iNOS) in response to LPS stimulation (2.5 µg/mL, 2h) after hydroxytolan treatment (50 µg/mL, 0.5h). NF-kB activation is one of the underlying mechanisms for LPS-induced inflammation, and its regulation was investigated by using a luciferase assay on RAW 264.7 cells following hydroxytolan treatment (50 µg/mL, 0.5h) and LPS stimulation (2.5 µg/mL, 6h). In addition, phosphorylation of JNK, one of the key molecules driving the signal pathway for induction of pro-inflammatory cytokine was assessed by Western blot analysis after hydroxytolan treatment (50 µg/mL, 0.5h) and LPS stimulation (2.5 µg/mL, 0.5h).

RESULTS: RAW 264.7 macrophages were more susceptible to 4,4’-dihydroxytolan in terms of cell viability, compared to non-macrophage L292 cells. Pre-treating RAW 264.7 with both 4,4’-dihydroxytolan and 3,4’-5-trihydroxytolan attenuated LPS-induced expression of cytokines and iNOS, NF-kB activation, and JNK phosphorylation. CONCLUSIONS: Together our data implicated that these drug candidates exhibited an inhibitory effect on macrophages, suggesting a therapeutic potential of hydroxytolans for the treatment of macrophage-medicated inflammatory diseases.
Location of Pulmonary Mast Cells Predicts Asthma Outcomes

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**RATIONALE:** Pulmonary mast cells (MC) have been associated with asthma pathogenesis. We have previously shown differences in MC phenotype by location in the lung (submucosa and epithelium) [Balogh, AJRCCM, 2011]. Little is known regarding the relative importance of luminal MCs to asthma. We hypothesized that distal/luminal MCs would better predict more severe clinical outcomes than proximal/epithelial MCs.

**METHODS:** In 102 University of Pittsburgh asthmatics enrolled in NHLBI trials, bronchial epithelial brushings, bronchoalveolar (BAL) cells and fluid were obtained at bronchoscopy. Expression of the MC protease tryptase mRNA was determined by qRT-PCR. Using the median tryptase mRNA values for epithelial brushings and BAL cells, subjects were classified as proximal and distal MC "Hi" or "Lo." Regression analysis was performed to assess the effect of MC "Hi" on the outcomes of history classified as proximal and distal MC signature or FeV1% predicted and FeV1/FVC. Results: Distal MC asthma significantly predicted decreased FEV1% predicted and FEV1/FVC (OR = 3.6, p = 0.004), while proximal MC asthma did not (OR = 1.7, p = 0.2). Distal MC asthma negatively associated with baseline FEV1% predicted [Beta = -12.5, p = 0.006, R2 = 0.07] and baseline FEV1/FVC [Beta = -0.06, p = 0.019, R2 = 0.05]. This relationship was not seen with proximal MC asthma [p for FEV1% predicted = 0.6, p for FEV1/FVC = 0.8].

**CONCLUSIONS:** In matched samples from asthmatic subjects, the distal/BAL cell MC signature better predicted asthma exacerbation, lower FEV1%predicted and decreased FEV1/FVC than the proximal/epithelial MC signature. In asthma, this suggests an important difference in MC function based on the location in the lung. Use of distal MC biomarkers should better identify more clinically severe asthma.

Association study in African-admixed populations across the Americas recapitulates asthma risk loci in non-African populations

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**RATIONALE:** Asthma is a complex disease with striking disparities across racial and ethnic groups. Despite its high burden, representation of African ancestry individuals in asthma genome-wide association studies (GWAS) has been inadequate to date, and true associations in these underrepresented minority groups may have been missed. Here, we report the largest asthma GWAS to date from the Consortium on Asthma among African Ancestry Populations (CAAPA).

**METHODS:** CAAPA participants (7009 asthmatics, 7645 controls) were genotyped using the African Diaspora Power Chip (ADPC), an array designed to complement existing genome-wide array data, as well as Illumina’s Multi-Ethnic Genotyping array. Genotypes were imputed using the CAAPA whole-genome-sequence reference panel. Logistic mixed effects models were used to test for association between allelic dosage and asthma, separately for each study. Results were meta-analyzed using a meta-regression approach that accounts for heterogeneity in allelic effects among ethnic groups.

**RESULTS:** We identified two novel loci that may be specific to asthma risk in African ancestry populations (lead SNP rs13277810, intronic to LOC101927815, p = 3E-8; lead SNP rs114647118, intronic to TATDV1, p = 3E-7). We found strong evidence for association at four previously reported asthma locus whose discovery was driven largely by non-African populations (p < 0.05/810 candidate SNPs investigated), including the chr1q21.3 region, a novel locus identified by the Trans-National Asthma Genetic Consortium (TACG) that has previously not been replicated.

**CONCLUSIONS:** We report two associations that may be specific to asthma risk in African ancestry populations. Our results also suggest some asthma risk loci discovered in non-African populations are relevant in African ancestry populations.
Spirometry and Impulse Oscillometry Trajectories in an Inner-City Longitudinal Birth Cohort at High Risk for Asthma.

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RATIONALE: Assessment of lung function is an essential component for understanding lung development. We sought to determine trajectories of lung function in a high-risk, urban longitudinal birth cohort.

METHODS: The Urban Environment and Childhood Asthma (URECA) birth cohort study had spirometry and impulse oscillometry (IOS) measures taken at repeated intervals between ages 3-10 years in urban-residing children (n=434). Latent class mixed models identified age-related trajectories of the FEV1/FVC ratio and the area of reactance (Xa) with each exhibiting parallel age-related reductions over time. Xa values at age 10 for the groups were mean (SD) Xa=1.10 (n=52), 0.98 (n=50), and 0.94 (n=52) respectively. The differences among these trajectories were statistically significant (p<0.05). We also identified high, intermediate, and low trajectory subgroups with greater odds of having more severe and persistent asthma, and to predict responses to emergency treatment.

RESULTS: We identified 3 age-related trajectories for FEV1/FVC, with the largest group (n=305, 70%) consistently having high values (age 3 [mean±SD] 0.94±0.05; age 10, 0.86±0.04), a second group (n=62, 14%) with consistently lower values (age 3 0.82±0.10; age 10, 0.86±0.04) and a third group (n=67, 15%) that had comparatively high values at age 3 but subsequently developed airways obstruction (age 3 0.95±0.04; age 10, 0.76±0.05). We also identified high, intermediate, and low trajectory patterns for Xa with each exhibiting parallel age-related reductions over time. Mean (SD) Xa values at age 10 for the groups were 2.61±1.10, 1.70±0.52, and 1.11±0.47 respectively.

CONCLUSIONS: Our results demonstrate that children in an urban birth cohort at high risk for asthma have 3 different trajectories of lung function. Notably, there is one group with a high initial FEV1/FVC but develops airways obstruction over time. Additional analyses are required to determine whether there are specific early life exposures or other factors that are associated with progressive airway obstruction.

Characterization Of Allergen Sensitization Patterns In Canadian Preschool Children With Severe Wheezing.

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RATIONALE: Preschool children with uncontrolled asthma remain a challenge for clinical management and risk stratification due to the large overlap between transient and persistent wheezing phenotypes originating from various triggers, including allergenic sources. Extensive allergen sensitization profiling in this preschool cohort may help identify different subgroups with greater odds of having more severe and persistent asthma, and to predict responses to emergency treatment.

METHODS: Eighty-seven preschool children (3-5 years) who presented with wheezing in the SickKids Emergency Department were enrolled and assessed at baseline (within 120hrs of discharge) and 3 months later. Clinical workup, symptom scoring, and lung function testing was performed on both visits, and allergic sensitization was tested on the follow-up visit (Skin prick testing to 14 allergenic sources; specific IgE to 157 allergen extracts and 125 components (Allergy Explorer, Macroarray Dx, Vienna)). Hierarchical clustering was performed to find correlations between sensitizations.

RESULTS: Sixty-seven percent were sensitized to at least one allergen, with sensitization to peanut (36%) seed storage proteins (Ara h 1,2,3,6), their cross reactive counterparts (Cor a 9,11, Gly m 6, Jug r 2), as well as cat and dog (Fel d 1, Can f 1) being the most frequent and most strongly associated with baseline oral corticosteroid (OCS) usage, number of ER visits, and reduced respiratory control (TRACK score) 12 months prior to enrollment.

CONCLUSIONS: Sensitization to seed storage proteins, Fel d 1, and Can f 1 are associated with increased frequencies of OCS usage, number of ER visits, and reduced respiratory control in a high-risk preschool asthma cohort.
903 Novel Plasma Metabolite Markers From Arachidonic Acid Pathway For Distinguishing Refractory Asthma.

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RATIONALE: Eicosanoids are fatty acid oxides which are metabolized from arachidonic acids by oxidase such as cyclooxygenase (COX), lipoxigenase (LOX), and epoxysgenase, and it has been known that the abnormal activation of arachidonic pathway is association with the occurrence of asthma. We aimed to identify novel effective metabolite marker that distinguish refractory asthma and find out the etiology of refractory asthma.

METHODS: Peripheral blood was obtained from 4 subjects of control group, 56 subjects with non-refractory asthma, and 48 subjects with refractory asthma. Refractory asthma was defined as asthma that requires treatment with high dose inhaled corticosteroids to control, and when patients had two or more acute exacerbations within 12 months, or persistent decreased lung function (predicted value of forced expiratory volume in 1 second<80%). Simultaneous measurements of 43 multiple eicosanoid biomarker panels were performed using liquid chromatography(LC)-mass spectrometry(MS)/MS analysis.

RESULTS: Among 42 eicosanoids, the mean levels of PGJ2 (p = 0.035), LTB4 (p = 0.009), SSHETE (p = 0.002), 5-oxo-ETE (p = 0.005), 12-oxo-ETE (p = 0.006) and LXA4 (p = 0.008) were significantly increased in refractory asthma group than in non-refractory asthma group. Among 48 refractory asthmatics, 36 showed frequent exacerbations and 26 showed airway remodeling. The former 6 eicosanoids were increased in frequent exacerbation group, while patients with airway remodeling showed no difference in any eicosanoid. In non-refractory asthma group, the presence of atopy increased the level of 6 eicosanoids.

CONCLUSIONS: Eicosanoids metabolized by LOX and COX pathway were increased in refractory asthmatics, especially in frequent exacerbators. Increased eicosanoids in non-atopic asthmatics may be a predictor of frequent exacerbation.

904 Administration of anti-IgE to pregnant mice caused IgE-class-specific immunosuppression in offspring

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RATIONALE: Accumulating evidence suggests that environmental experiences in the first months of life may lead to progression of various allergic diseases through sensitization to Aeroallergens as well as food allergens. Prevention of IgE sensitization in this period is therefore theorized to reduce the future risk of allergy development. We aimed to clarify whether administration of anti-IgE to pregnant mice can prevent allergic sensitization in offspring.

METHODS: Pregnant mice were injected intravenously with 100 μg of anti-mouse IgE or isotype control at embryonic 12.5 days (E12.5) and E18.5. OVA emulsified with alum was injected intraperitoneally to offspring beginning on postnatal day 2 (PND2), 16, 30 and 44, twice with a one-week interval, and sera were collected 14 days after the second immunization. Spleen cells from the offspring were cultured with OVA for 3 days. The levels of OVA-specific immunoglobulins in the sera and cytokines in the culture supernatants were determined by ELISA. Each mouse was intraperitoneally challenged with OVA, and the body temperature was measured.

RESULTS: When pregnant C57BL/6 mice were administered anti-IgE, production of OVA-specific IgE antibodies was suppressed even in offspring immunized at PND44. In BALB/c mice, suppression was seen in offspring immunized at PND2, but not at the later ages. In both mouse strains, the manifestations associated with antigen challenge of sensitized infants were ameliorated by the treatment. However, the serum levels of IgG-class antibody and cytokine production from spleen cells in the offspring were not altered.

CONCLUSIONS: Administration of anti-IgE to pregnant mice suppressed allergic sensitization in their offspring.

905 Distinct innate immune cell maturation during the first year of life is associated with farm exposure

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RATIONALE: Early life farm exposure is associated with protection against development of atopic disease and severe respiratory infections. However, the impact of early life farm exposure on immune cell profiles and antiviral maturation on respiratory viral burden remains poorly characterized. We hypothesized that early life farm exposure is associated with differences in the innate immune cell signatures.

METHODS: Longitudinally collected blood mononuclear cells from cord (n = 108; [non-farm=64;farm=44]) and 1-year old (n = 91; [non-farm=50;farm=41]) animal farm-exposed and non-farm rural infants enrolled in Wisconsin Infant Study Cohort were stimulated with rhinovirus A16 (RV) or lipopolysaccharide (LPS) and analyzed with two multiparameter flow cytometry panels. Statistical analysis was performed using Prism 7, SPICE v6, and Qlucore Omics Explorer v3.4.

RESULTS: Using principal component analysis, significant age-related differences were seen with both RV and LPS stimulation at 1-year of age compared to cord blood (71 variables and 70 variables, respectively, q-value <0.05). Monocyte cytokine responses to LPS had a higher frequency of single and dual cytokine producing cells in farm-exposed children compared to non-farm children at 1-year of age (p=0.024). In contrast, RV-induced plasmacytoid dendritic cell function was similar between farm and non-farm infants irrespective of age.

CONCLUSIONS: Innate immune cell responses exhibit maturational changes during the first year of life and early life farm exposures are associated with increased monocyte multifunctionality at 1-year of age. Studies are ongoing to elucidate innate immune signature associations with specific farm-related early life exposures, atopic disease and respiratory viral disease burden.
906 Evaluating the Effects of Farm Exposure on Infant Gut Microbiome

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RATIONALE: Farm exposure in infancy is associated with a decreased risk of atopic disease, possibly due to different patterns of microbial colonization. We hypothesize that the gut microbiome of infants raised on farms will differ from the gut microbiome of infants not exposed to farms.

METHODS: In the Wisconsin Infant Study Cohort (WISC), stool specimens were collected at age 2 months from 94 infants from farm families and 110 infants from non-farm families. High-quality 16S rRNA biomarker profiles were obtained from 89 farm and 102 non-farm infants and statistical analyses were performed in R.

RESULTS: Gut microbiota of infants raised in farming versus non-farming environments differed significantly but explained only a small proportion of microbiota compositional variance (Unweighted UniFrac: R² = 0.008, p = 0.003). Consistent with this observation, six bacterial taxa were differentially enriched (FDR adjusted p < 0.2). Clostridiaceae, Akkermaniaceae, and Blautia members were increased in relative abundance in the stool of farm infants, while Veillonellaceae, Bifidobacteriaceae, and Clostridium members were relatively increased in non-farm infants.

CONCLUSIONS: The gut microbiota of infants raised on a farm have specific distinct taxonomic features. Members of the bacterial genera Akkermansia and Clostridia enriched in farm infants are also enriched in urban infants at lower risk of atopy and asthma development. They are known to reduce inflammation via gut microbiome restructuring and, in the case of Clostridia, via short chain fatty acid production. The differences in neonatal gut microbiome warrant further investigation to delineate how specific early life exposures might modulate the gut microbiome to reduce atopic disease.

907 Distinct patterns of bacterial vertical transmission from the maternal vaginal tract to infant gut microbiota

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RATIONALE: Infants born to mothers with allergic asthma possess a distinct gut microbiota at birth and experience delayed diversification of their bacterial microbiota over the first year of life. We hypothesized that there are distinct patterns of bacterial vertical transfer exist in mother-infant dyads.

METHODS: Bacterial composition of infant stool collected at 1, 2 or 3 months of age and maternal vaginal or vaginal/rectal swabs were profiled (16S rRNA) from two distinct birth cohorts within the Children’s Respiratory Research and the Environment Workgroup (CREW): The Microbes, Allergy, Asthma and Pets (MAAP) cohort in the greater Detroit metropolitan area, and the Wisconsin Infant Study Cohort (WISC) in Central Wisconsin. We utilized 442 high-quality bacterial profiles (WISC: n = 154 vaginal swabs, n = 195 2-month stool; MAAP: n = 33 vaginal/rectal swabs, n = 31 1-month stool, n = 29 3-month stool) for this study.

RESULTS: Consistent with previous studies, infant stool microbiota composition differed by age (Generalized Estimating Equations: Bray-Curtis, P = 0.011). Taxa shared between vaginal and stool microbiota of mother-infant dyads included Bifidobacterium, Lactobacillus, Staphylococcus, and Enterobacteriaceae. A total of 37 of 133 (28%) mother-infant dyads exhibited no evidence of bacterial vertical transmission, a finding that did not differ by infant age (Chi-Square P = 0.21) or cohort (Chi-Square P = 0.13).

CONCLUSIONS: Bacteria detected in the peri-natal maternal vaginal microbiota are also detected in infant stool until at least 3 months of age. However, a substantial proportion of infants exhibit no evidence of bacterial vertical transmission. Ongoing analyses aim to determine factors that govern microbial inheritance and its relationship to risk of allergic asthma in childhood.

908 Can Obesity Alter the Immune Response to Childhood Vaccinations?

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RATIONALE: Obesity is a major health issue in children. It is associated with increased risk of infections and infectious morbidity. Previous studies found a decrease in protective antibody titers to hepatitis B and influenza in obese adults after vaccination. Less is known about antibody responses to routine childhood immunization in obese children.

METHODS: Children (8-18 yr.) who had completed routine childhood immunization were recruited. Serum samples were tested by ELISA method for antibody levels to Diphtheria, Tetanus, Haemophilus influenzae type B and Streptococcus pneumoniae, along with serum HbA1c levels. BMI% and HbA1c levels were used as a continuous variable versus antibody titer levels. Spearman rank correlation, Fisher-exact test were used for statistical analysis.

RESULTS: 43% of the children had BMI≥95% (n = 69). There was an overall negative correlation between BMI and pneumococcal, diphtheria and tetanus titers, with significant correlation with S. pneumoniae serotype P3 titer (p = 0.037). There was an even stronger overall negative correlation between HbA1c and pneumococcal, diphtheria, tetanus and haemophilus type B tilters, with significant correlation with S. pneumoniae serotype P9N (p = 0.035), P4 (p = 0.002), P8 (p = 0.043), P12F (p = 0.002), P19F (p = 0.037), tetanus (p = 0.006) and Haemophilus type B (p = 0.001) titers. Obese children had impaired pneumococcal titers (7/14 serotype titers <0.2) when compared to non-obese children (p = 0.014).

CONCLUSIONS: In our study, increasing BMI% and HbA1c levels is associated with overall lower vaccine titers. Obese children (BMI≥95%) were more likely to have impaired pneumococcal titers when compared to non-obese children (BMI 25-94%) in a prospective, population-based cohort study.
909 A game of cat and mouse: cat ownership and the relationship between mouse exposure and respiratory outcomes among dual-sensitized inner-city children with asthma

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RATIONALE: Exposure to mouse allergen may worsen respiratory disease among sensitized-and-exposed children with asthma. Families may use cats for mouse control, but whether this benefits or harms children sensitized to both cat and mouse is unknown.

METHODS: We evaluated inner-city children sensitized to both cat and mouse and exposed to mouse infestation in the Mouse Allergen and Asthma Cohort Study (MAACS). We conducted longitudinal data analysis—adjusted for age, sex and allergic sensitizations—for symptom outcomes and ED use across 5 visits over 12 months. We evaluated the association with these outcomes for mouse allergen and cat ownership, then tested cat ownership as an effect modifier.

RESULTS: Sixty-two (42%) of 149 children were sensitized to both cat and mouse, 35 (23%) to cat but not mouse, 15 (11%) to mouse but not cat, and 36 (24%) to neither. Mouse infestation was observed for 37 of the 62 dual-sensitized children. Mouse allergen and cat ownership typically were non-significantly associated with worse respiratory outcomes. Cat ownership modified the association with mouse allergen for five of eight respiratory outcomes; e.g., among children without a cat, each log10 increase in mouse allergen was associated with 44% elevated odds of having a general symptom-day in the prior two weeks. For children with a cat, it was associated with 52% lower odds (interaction p<0.003).

CONCLUSIONS: Cat ownership may modify the relationship between mouse allergen exposure and respiratory outcomes for dual-sensitized children in mouse-infested homes. However, professional pest management is recommended for rodent control since exposure to cats may worsen asthma.

910 Rhinovirus Infection Does Not Alter Bronchodilation in Human Precision Cut Lung Slices from Asthma Donors.

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RATIONALE: Rhinovirus (RV) infection is present in 60-80% of children with asthma exacerbations in the emergency department. Recent studies suggest that during asthma exacerbations, children with RV are less likely to experience treatment failure than those with other viruses. We hypothesized that despite enhancing contraction in precision cut lung slices (PCLS) from asthma donors, RV does not affect the ability of these slices to bronchodilate.

METHODS: PCLS were prepared from asthmatic (n=6) and non-asthmatic (n=14) donor lungs. Baseline photomicrographs measuring airway cross-sectional area were taken before and after exposure to carbachol (2 μM), isoproterenol (4 μM), and forskolin (4 μM). PCLS were infected with RV39 for 48h or treated with 10mL/mL IL-25 for 24h. After treatments, slice responses to carbachol, isoproterenol, and forskolin were measured again. The percentage of bronchodilation for each slice was calculated using the percent difference in the airway area after exposure to carbachol and isoproterenol. Bronchodilation was compared pre- and post-treatments.

RESULTS: PCLS from asthma donors retained their ability to bronchodilate after isoproterenol despite RV infection (pre- 55.67%, post- 61.09%; p=ns), while PCLS from non-asthma donors had reduced bronchodilation post-infection (pre- 63.33%, post- 56.67%; p<0.05). PCLS treated with IL-25 bronchodilated more post-treatment in the asthma lungs (pre- 37.86%, post- 66.65%; p<0.05).

CONCLUSIONS: Although RV infection of PCLS causes airway hyper-responsiveness to carbachol in donors with history of asthma, it does not alter the ability of the airways to bronchodilate in response to isoproterenol. PCLS treated with IL-25 bronchodilated more post-treatment, suggesting that IL-25 enhances contraction, but does not affect bronchodilation.
Relation of serological reactivity to cytoplasmic extracts from spores of *Ganoderma applanatum* and commercial extracts of indoor, mitosporic fungi, and farm animal allergens among Puerto Rican subjects

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Rationale: Fungal spores with allergenic potential are a predominant biological component in the atmosphere of Puerto Rico. Spores of basidiomycete fungi, such as *Ganoderma spp*, often outnumber the atmospheric concentration of mitosporic fungi and pollen from trees and grass. Nevertheless, extracts from basidiomycete fungi are not currently used for serological testing and knowledge of the relationship of reactivity with commercial extracts is limited.

Methods: Spearman correlation matrices were generated, on an archived dataset, to identify relationships between reactivity to *G. applanatum* spore’s cytoplasmic extracts tested in ELISA (crude) and Western blot (19, 24, 33, 45, 56, 75, and 81 kDa) with reactivity to indoor, pests, farm animals, and pollen allergens commercial extracts. Also, principal component analysis was employed to identify clusters of variables explaining inter-subjects variabilities in reactivities.

Results: Only the reactivity to dog danger was highly correlated with the crude extract (r = 0.48, p < 0.001), but the 45 and 75 kDa polypeptides were correlated with reactivities to mitosporic fungi (*Alternaria, Aspergillus, Fusarium, Cladosporium*, Mucor, pests (American cockroach, mouse, rat), and farm animal danders (chicken, horse) (r = .30 to 57, p = 0.04 to < 0.001). *G. applanatum* polypeptides (except the 19 kDa) clustered together in explaining 21% of the variability among the subjects’ reactivities.

Conclusions: These results suggest that reactivity to mitosporic fungi, indoor allergens, and allergens from farm animals pose a respiratory health risk from exposures to *G. applanatum* fungal spores. Our findings also further support the relevance of *G. applanatum* as an important outdoor allergen among the Puerto Rico population.

A Combined Epidemiologic and Mechanistic Study of Endotoxin and Food Allergen Sensitization

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Rationale: Household endotoxin levels have been variably associated with asthma and atopy. We present a combined epidemiologic and mechanistic study of the relationship between endotoxin and food allergen sensitization.

Methods: Logistic regression models were built using data from the 2005-2006 National Health and Nutrition Examination Survey (NHANES, n = 6963), a large cohort representative of the US population, to test for associations between house dust endotoxin (log-transformed) and sensitization to specific foods (milk, egg, and peanut). To characterize inflammatory responses to endotoxin in individuals with vs. without food allergen sensitization, peripheral blood mononuclear cells (PBMCs) were collected from 21 children mono-allergic to milk, egg, or peanut and non-allergic controls. Following stimulation with endotoxin, cytokines were measured using the Luminex platform.

Results: Among NHANES subjects, the geometric mean endotoxin level was 15.5 EU/mg (SE 0.5). Prevalence of food allergen sensitization (sIgE ≥0.35 kU/L <SUB>≤</SUB>A <SUB>C</SUB>IL) varied by food: milk 5.7%, egg 4.0%, and peanut 7.9%. Household endotoxin level was associated with sensitization to milk (OR 1.7, 95% CI 1.2-2.1) and egg (OR 1.4, 95% CI 1.01-1.9), but not peanut (OR 0.98, 95% CI 0.8-1.2) in models adjusted for confounders. Interferon-gamma levels of endotoxin-stimulated PBMCs from individuals allergic to milk (mean 104.3 pg/ml) or egg (mean 44.4 pg/ml) but not peanut (mean 240.8 pg/ml) were significantly lower on day 5 compared to controls (mean 536.1 pg/ml) (P-values 0.007, 0.018, and 0.058, respectively).

Conclusions: Higher household endotoxin is associated with higher odds of milk and egg sensitization. Altered responsiveness to endotoxin is also observed in PBMCs from individuals with milk and egg allergy.

Management of Chronic Urticaria in a Pediatric Population

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Rationale: Data is sparse regarding omalizumab role’s in the management of Chronic Urticaria (CU) in children. We aimed to evaluate management of CU and assess the effect of omalizumab in children.

Methods: Children with CU were prospectively recruited from the Montreal Children’s Hospital from April 2013 to August 2018. Data were collected on demographics, co-morbidities, and management through a standardized questionnaire. Patients completed a weekly aggregated Urticaria Activity Score (UAS7). Tryptase, total IgE, C-reactive protein, and CD63 levels on basophiles were determined at study entry. Patients with suboptimal control of hives with up-dosing of antihistamines were treated with omalizumab.

Results: Over 5 years, 197 cases of CU were recruited, of which 50.8% were males and median age was 9.2 years. One-fifth of cases (20.8%) were diagnosed with physical urticaria and 12.7% were diagnosed with cholinergic urticaria. Autoimmune disease was reported in 7.1% of patients, mainly thyroiditis (2.5%). The most common antihistamines used were cetirizine (47.7%) and desloratadine (25.9%). Sixteen patients (8.1%) required treatment with omalizumab. Among these 16 patients, 56.3% were male with a median age of 11.6 years. Thirteen patients (81.3%) responded to our follow-up, of which 53.8% received 150 mg, 23.1% received 300 mg, and 15.4% received 450 mg of omalizumab. Following treatment, 69.2% reported complete resolution of hives, 23.1% reported fewer hives, and 7.7% found no effect. Of the 6 patients who stopped omalizumab, 4 reported recurrence of symptoms.

Conclusions: Omalizumab can contribute to better management of CU in children but recurrence will occur in the majority of cases on cessation.
915 Strategies for Discontinuing Omalizumab in Patients with Chronic Urticaria: Real-World Findings
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RATIONALE: Omalizumab is an effective treatment for chronic urticaria. However, discontinuation often results in relapse. Questions remain regarding possible benefits of tapering omalizumab doses after achieving satisfactory response.
METHODS: Electronic health records of 110 patients with encounter diagnosis ICD-10 code L50.x and documented omalizumab prescriptions at a tertiary medical center between 7/1/2014-6/30/2018 were reviewed. Sixty-eight patients were included in the final analysis after excluding 20 who did not start omalizumab and 22 with incomplete records.
RESULTS: At time of review, urticaria was well-controlled or in remission in forty-four (65% [44/68]) patients, with twenty-four (35% [24/68]) experiencing ongoing symptoms. Starting doses ranged from 150 milligrams to 600 milligrams every two to four weeks. Twelve (27% [12/44]) patients were in remission for a median of 17 [5-40] months following omalizumab discontinuation. Of those, 75% [9/12] were not tapered and remained symptom-free after 18 [5-40] months and 25% [3/12] were tapered by decreasing frequency to 9 weeks (n = 1) and 6 weeks (n = 2) before discontinuation.
CONCLUSIONS: Findings suggest that symptom remission occurs after omalizumab discontinuation regardless of discontinuation method. Tapering may be of most benefit to determine lowest dose and frequency required for symptom-free maintenance.

916 Deciphering the microbiome and virome composition of patients with Atopic Dermatitis and Eczema Herpeticum (ADEH+)
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RATIONALE: A subset of Atopic Dermatitis (AD) patients are susceptible to cutaneous viral infections, including eczema herpeticum (ADEH+). ADEH+ is associated with increased Staphylococcus aureus colonization and the skin microbiome may alter viral immune responses. The major objective of the current study was to compare the skin microbiome and virome of ADEH+, ADEH, and nonatopic (NA) participants.
METHODS: Skin swabs were collected from 40 subjects (15 ADEH+, 12 ADEH-, and 13 NA). For AD patients, swabs were collected from lesional and nonlesional skin. 67 shotgun metagenomic libraries were generated to investigate the microbiome and virome profile.
RESULTS: Lesional skin from ADEH+ showed significant microbial diversity reduction compared to lesional skin from ADEH- (p<0.05). Similar results were observed when nonlesional skin from ADEH+ and ADEH- was compared to NA skin. Decreased diversity was associated with increased relative abundance of S. aureus on lesional skin of ADEH+ compared to ADEH- subjects. ADEH+ subjects carried an increased viral load on lesional and nonlesional skin. While herpes simplex virus (HSV) showed similar relative abundance in all groups, human papillomavirus (HPV) and bacteriophages were significantly increased in lesional and nonlesional skin of ADEH+ (p<0.01).
CONCLUSIONS: ADEH+ subjects showed an increased relative abundance of pathogenic bacteria, such as S. aureus, and viruses and a reduction of commensal bacteria. Increased HPV load was previously associated with warts, another viral complication of AD. This study indicates that ADEH+ is associated with other forms of microbial infection beyond HSV and provides new mechanistic insight into viral skin infections in AD.

917 IL-17A and IL-4/IL-13 Exert Distinct Changes in Skin Lipids
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RATIONALE: IL-17A and IL-4/IL-13 are involved in the pathogenesis of inflammatory skin diseases. Their role in regulation of skin barrier lipid metabolism is unknown.
METHODS: Cu2+-differentiated primary human keratinocytes were grown with and without IL-17A or IL-4/IL-13 and lipids were analyzed by targeted liquid chromatography tandem mass spectrometry (LC-MS/MS). Stable isotope pulse-labeling was employed to define changes in sphingolipid metabolism in IL-17A, IL-4/IL-13 vs. sham-treated keratinocytes. Skin barrier function and lipid profiles were determined in skin tape strips of mice induced to express IL-17A after treatment with topical imiquimod application.
RESULTS: In contrast to IL-4/IL-13, IL-17A significantly increased ceramide production in keratinocytes. This effect of IL-17A was explained by the upregulation of serine palmitoyltransferase subunit-1 (SPT1) expression and SPT activity, resulting in increased sphingolipid biosynthesis as shown by U-[13C,15N]-serine pulse-labeling experiments. IL-4/IL-13 inhibited SPT1 expression and activity and suppressed de novo sphingolipid biosynthesis. The effects of IL-17A were inhibited in keratinocytes transfected with TRAF3IP2 siRNA, an adaptor protein associated with IL-17A receptor heterodimer. In mice, imiquimod treatment induced psoriasis and upregulated skin levels of IL-17A. In addition, imiquimod-treated mice had a substantial increase in skin transdermal water loss, disproportionate upregulation in non-hydroxy fatty acid sphingosine (NS)-ceramides and reduced EOS- ceramide levels as compared to vaso-line-treated mice.
CONCLUSIONS: IL-17A increased the expression and activity of SPT1 and significantly enhanced ceramide production by keratinocytes. IL-4/IL-13, however, inhibited SPT1 expression and activity and suppressed de novo ceramide biosynthesis. IL-17A-induced increase in keratinocyte ceramide production was abolished in keratinocytes with inhibited TRAF3IP2 expression.
918 Nonlesional Atopic Dermatitis Skin Shows Alterations in Langerhans Cells in Close Proximity to Tight Junction Fragmentation

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RATIONALE: Disruption of epidemial tight junctions (TJs), is thought to promote immunological responses to epicutaneous antigens. The Atopic Dermatitis Research Network performed a cross-sectional study to visualize TJs and Langerhans cells (LCs) in the skin of atopic dermatitis (AD) and nonatopic (NA) controls.

METHODS: Epidermal sheets were isolated from nonlesional, upper extremity skin taken from 8. aureus colonized (ADStaph+), 10 non-colonized (ADStaph−) AD subjects and 9 NASTaph+. These whole mounts were stained for the TJ protein (occludin) and markers of LCs/dendritic cells (DCs) (CD207 [Langerin] and HLA-DR). Images were captured with a confocal microscope and analyzed in a blinded manner using Imaris software.

RESULTS: Greater than 97% of epidermal DCs were LCs, with no differences observed between AD and NA. More epidermal LCs (HLA-DR+/CD207+) were present in AD skin (33.2±1.8 per 0.04mm²), compared to NA skin (26.3±2.8 per 0.04mm², p=0.043). The occludin staining could be categorized into four distinct patterns with the fragmented pattern observed more commonly in AD (49%) vs NA (20%). Notably, LCs clustered in the immediate region around the fragmented TJs, expressed high levels of HLA-DR and had greater dendricity. Staph colonization did not significantly affect these observations.

CONCLUSIONS: LCs are more numerous in nonlesional AD skin. This is the first demonstration that even the nonlesional skin of AD subjects frequently has an abnormal TJ appearance and that this is spatially associated with greater number of activated LCs. These findings suggest that LCs from nonlesional AD skin behave as though they are reacting to TJ disruption.

919 The Protective Effects of Eosinophilia and High IgE on Cancer Diagnoses in the National Health and Nutrition Examination Surveys (2005-2016)

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RATIONALE: Limited studies have examined the association between eosinophils, IgE levels and cancer prevalence using national data in the United States. This study examined the association between blood eosinophils, serum IgE levels and physician-diagnosed cancer in the National Health and Nutrition Examination Surveys (NHANES) 2005-2016.

METHODS: Bivariate analyses between demographic variables, IgE levels, eosinophil levels and cancer (physician-diagnosed) were conducted. IgE data available from the NHANES 2005-2006 required logarithmic transformation due to non-normality. Nested multivariate logistic regression models were then conducted. All statistical analyses were weighted and run using SAS v9.4.

RESULTS: Out of 60,936 adults included in this study, we found a significant decrease in cancer diagnoses in patients with eosinophilia vs. normal levels (>500 vs ≤500 cells/µL), 0.9% vs. 3.1%, p<0.0001. Similar decreases were observed in patients with high vs. low-IgE (>100 vs ≤100 kU/L), 0.6% vs. 2.2%, p<0.0001. HighIgE was also significantly negatively associated with cancer diagnoses in unadjusted regression models, OR=0.65 (95% CI 0.49-0.86), p<0.0001. A similar effect was obtained after adjustment for age, sex, race, body mass index, insurance and smoking status, OR=0.73 (95% CI 0.53-1.02) p=0.059. Eosinophilia was also significantly negatively associated with cancer diagnoses, adjusted OR=0.94 (95% CI 0.91-0.96), p<0.0001.

CONCLUSIONS: Higher eosinophil counts and IgE levels were strong protective factors against cancer diagnoses in this multi-year, nationally representative sample of US adults; suggesting that IgE-mediated eosinophil responses are important in the body’s defense against cancer.

920 Incidence of Hypersensitivity to Cetuximab

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RATIONALE: Cetuximab is a monoclonal antibody to epidermal growth factor receptor primarily used as adjunctive treatment of metastatic cancers. Hypersensitivity reactions, including anaphylaxis, and especially in the southeastern part of the United States, are one of the most well-known adverse effects of cetuximab. The aim of this meta-analysis is to gain better insight into the overall incidence of cetuximab-induced hypersensitivity reactions.

METHODS: Databases including PubMed, EMBASE, the Cochrane library, American Society of Clinical Oncology, and Web of Science were searched to identify relevant studies. Eligible studies identified were randomized to prospective comparator phases II and III trials of patients with cancer treated with cetuximab. The primary endpoint was the incidence of hypersensitivity reactions.

RESULTS: Fourteen studies were identified, including a total of 6047 patients available for analysis. 2,991 patients received cetuximab, and 3,056 patients did not. The risk ratio of grades 3 or 4 hypersensitivity reactions was found to be 2.45 (95% CI; 1.85-3.24). There were 154 grade 3 or 4 hypersensitivity reactions in the cetuximab group, and 61 grade 3 or 4 hypersensitivity reactions in the non-cetuximab group. The risk ratio of any hypersensitivity reaction (Grades 1-4) was 5.47 (95% CI; 3.80-7.87) with 337 hypersensitivity reactions in those treated with cetuximab, and 96 in those not treated with the drug.

CONCLUSIONS: Treatment regimens that include cetuximab are associated with a significant risk of hypersensitivity reactions including grade 3 and 4 hypersensitivity reactions. Pretreatment with anti-cetuximab antibody titers should be considered before starting this medication.
**921 Re-evaluation of Need and Tapering of Omalizumab in Chronic Idiopathic Urticaria**

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**RATIONALE:** Despite the known spontaneous remission of chronic idiopathic urticaria (CIU) over time, there are no clear guidelines on how long omalizumab treatment should be maintained or how to initiate tapering.

**METHODS:** We reviewed 162 patients treated with omalizumab for CIU between 2015-2017 to determine response to treatment and whether tapering had been initiated in complete responders. Using this data, a protocol for monitoring response and initiating tapering was established.

**RESULTS:** Of the 162 patients treated with omalizumab for CIU, 43% (74 patients) had complete response to 300mg every 4 weeks with no hives reported. 39% (29 patients) continued on treatment without tapering. 54% (40 patients) were tapered with 40% (16 patients) experiencing flare that resolved when dosing was returned to every 4 weeks. 15% (6 patients) discontinued omalizumab without any flare. Using this data, a standardized tapering protocol was developed. Patient response to medication was evaluated at each visit using the Urticaria Control Test (UCT). Once a threshold score was met on 3 consecutive visits, the tapering protocol was initiated automatically by nursing staff. Initial data showed an increase in patients initiating tapering without increase in flares.

**CONCLUSIONS:** Patients with CIU who respond to omalizumab can be successfully tapered using an established protocol, leading to decreased cost and risks associated with medication use.

**922 Optimizing Approaches to Drug Allergies in the Pediatric Inpatient Setting**

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**RATIONALE:** Inaccurate drug allergy designations in the adult population have been shown to increase broad-spectrum antibiotic use, medical costs, and morbidity. We hypothesized that the recording of drug allergies in the pediatric population is also imprecise and sought to assess the steps involved in recording drug allergies in a pediatric inpatient unit.

**METHODS:** A prospective chart review of all patients admitted to a pediatric inpatient unit was conducted over a 4-week period. Data recorded for each patient included: demographics, drug allergy details, provider involved in recording drug allergies in a pediatric inpatient unit.

**RESULTS:** A total of 145 patients were admitted to the unit. The inpatient physician and registered nurse reviewed the allergy section for only 60/145 (41.4%) patients. Total antibiotic allergies recorded were 9/145 (6.2%) patients, including 6/9 (66.7%) penicillin, 2/9 (22.2%) cephalosporin, and 1/9 (11.1%) sulfa allergies. Of the 9 patients with antibiotic allergies, reactions included “hives” (6/9, 66.7%), “unknown” (2/9, 22.2%), and “allergy” (1/9, 11.1%) without additional details. Notably, 2/145 (1.4%) patients had incorrectly labeled drug allergies in the emergency department amended during the admission process.

**CONCLUSIONS:** Drug allergies are inconsistently reviewed by physicians and nurses during the hospital admission process. As a consequence, medical errors are likely to increase when medications are prescribed. To overcome this flawed process, and promote judicious use of antibiotics, accurate allergy labeling and mandatory reconciliation prior to admission should be required. Future studies are needed to assess best approaches at antibiotic stewardship in the inpatient pediatric population.

**923 Impact of electronic health record transition on drug allergy labels: gains, losses, alterations and learning opportunities**

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**RATIONALE:** Maintenance of accurate drug allergy labels is critical to the safety and efficacy of future treatment choices. We assessed the accuracy and quality of drug allergy label transfer during the implementation of a simultaneous inpatient and outpatient electronic health record (EHR) transition.

**METHODS:** A retrospective review of 511 random patients seen in an outpatient drug allergy clinic from March 5, 2014 to November 1, 2017 was performed to assess the accurate transfer of revised drug allergy labels between EHRs.

**RESULTS:** A total of 114 label discrepancies were identified for 79/511 (15.4%) patients. Of these 114 labels, 40 (35%) suggested potentially severe reactions, and were either removed or downgraded in severity. Eight of the 28 patients with potentially severe reactions had an encounter in the new EHR. Seven patients who had been “de-labeled” in the 6 weeks prior to the EHR transition reverted back to their pre-testing drug allergy label following the EHR transition, including 9 penicillin, 4 sulfa, 1 fluoroquinolone and 1 cephalosporin labels. Re-labeling notably occurred with 19 medications post-transition compared with 14 pre-transition.

**CONCLUSIONS:** Using a drug allergy clinic population with frequent label changes, we identified several deficits and discrepancies in drug allergy documentation that occurred during an EHR transition that potentially threatens patient care and safety. There was wide variability in documentation, differentiation of allergy versus intolerance and a significant risk of re-labeling patients as allergic, particularly for penicillin (45%). Given the significant threat to patient safety, urgent reform is required to standardize drug allergy documentation and prevent labeling errors.
924 Sublingual Immunotherapy Tablets Do Not Alter Skin Prick Responses During Treatment

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RATIONALE: Unlike conventional immunotherapy, there is no dose escalation when using sublingual immunotherapy tablets. It is unknown if this immediate exposure to target doses of allergen would induce desensitization of mast cells. Inhibition of mast cell degranulation upon provocation with specific allergen is a indicator of desensitization. We hypothesized that desensitization of cutaneous mast cells occurs during Timothy grass or Short Ragweed SL (sublingual) immunotherapy.

METHODS: Eighteen adult patients with confirmed sensitization to Timothy grass or Short Ragweed pollen were recruited. These subjects were randomized to receive placebo or either Timothy grass or Short Ragweed allergen extract tablets (depending on their sensitivity). Randomization was performed in a double-blinded manner. Titration skin testing to Timothy grass or Short Ragweed, to one additional allergen to which the subject was sensitive, and to codeine (positive control) was performed before treatment initiation and 2 and 8 weeks after initiation. Skin prick test responses during this treatment were analyzed with repeated measures ANOVA.

RESULTS: No statistically significant differences were seen in the PC3 values before and after treatment with SL immunotherapy to Short Ragweed or Timothy grass vs. placebo at any time point during the study.

CONCLUSIONS: Lack of significant change in skin testing results suggests that desensitization of mast cells does not occur during SL tablet immunotherapy. Other mechanisms may facilitate the clinical response to these allergens during this treatment.

926 Improved Tolerance Of Subcutaneous Immunotherapy in Pediatric Patients Through The Use Of Comfort Devices: A Quality Improvement Project

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RATIONALE: Pain and swelling are common adverse reactions of allergen subcutaneous immunotherapy (SCIT) and can affect its tolerability in many children.

METHODS: We conducted a quality improvement project with the use of pain control interventions (Buzzy® vibratory device and ice packs) with SCIT. We administered patient/parent surveys to pediatric SCIT patients prior to SCIT to assess for history of pain or swelling with SCIT and the child’s current level of coping with SCIT (0= coped very poorly, 5= coped very well) and after 30 minutes of SCIT.

RESULTS: Fifteen parents/patients completed pre and post-SCIT surveys from June-August 2018. Baseline pre-SCIT surveys revealed a history of pain and swelling with SCIT in 27% (4/15) and 40% (6/15) children, respectively. 80% (12/15) used the offered comfort devices. The 3 patients who declined comfort measures reported tolerating SCIT without pain or swelling. Half (6/12) of patients who received comfort measures had a history of pain or swelling. 75% (9/12) used ice, 17% (2/12) used ice and the vibratory device, and 8% (1/10) used the vibratory device. Comfort measures improved pain and swelling in 92% (11/12) and 100% (12/12), respectively. All (66) patients with a history of pain or swelling with SCIT reported improved comfort measures. There was significant improvement in parental anxiety with comfort measures (P<0.001).

CONCLUSIONS: The majority of pediatric patients tolerate SCIT well. Those with a history of pain or swelling with SCIT had improvement with the use of non-pharmacologic comfort measures. Increasing awareness of comfort measures will improve SCIT tolerability.
927 Strong Dose-response On Immunoglobulin Makers During a Phase II Allergen Immunotherapy Study With Subcutaneously Administered Tyrosine Adsorbed Modified Grass Allergen + MPL

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RATIONALE: The results of this Phase II study [EudraCT 2017-000333-31] evaluated the dose response relationship for a modified grass allergen subcutaneous immunotherapy (SCIT) product (1.0 ml) with modified allergen tyrosine adsorbate (MATA) and monophosphoryl lipid A (MPL) adjuvants for the treatment of allergic rhinoconjunctivitis (ARC) due to grass pollen.

METHODS: In total 447 patients with grass pollen-induced ARC were enrolled in this randomized, double-blind, placebo-controlled, parallel group study. Patients were randomized to one of five dose regimens of 5100, 14400, 27600 and 35600 SU and placebo. As a secondary endpoint the immunoglobulin markers (total IgE, grass-specific IgE, grass-specific IgG4 and specific IgE/total IgE ratio) were evaluated.

RESULTS: For all immunoglobulin markers a strongly statistically significant dose-response was shown for a wide range of cumulative doses from 5100 SU to 35600 SU. Grass-specific IgE, grass-specific IgG4 and specific IgE/total IgE ratio demonstrated statistically significant increases compared to placebo for all cumulative doses (P<0.01), including the currently marketed dose of 5100 SU in Europe.

CONCLUSIONS: An ultra-short course of 6 injections with allergoid grass SCIT treatment with adjuvants MATA and MPL is associated with significant increases in immunoglobulin markers for a wide range of cumulative dose levels indicating a strong therapeutic response.

928 Experience with Pharmacist Prepared Pre-filled SCIT Dosing in an Urban Allergy Clinic

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RATIONALE: In the U.S., subcutaneous immunotherapy (SCIT) doses are typically prepared by medical staff removing a given volume from an extract vial at a patient’s injection visit. We report a novel methodology using pharmacist-prepared individual SCIT doses at an urban county hospital.

METHODS: SCIT extracts are prepared by a pharmacist using dosing recommendations in the U.S. practice parameters. Individual SCIT doses are prepared by a pharmacist prior to a patient’s appointment based on the patient’s dosing schedule. Doses are placed in labeled syringes in patient-specific baggies. Nurses administer the pre-filled syringes to patients at their appointment. We analyzed data from January 2014 to July 2018 using this methodology.

RESULTS: A total of 4203 doses were prepared: 3811 (90.6%) injections were given and 54 doses were held (1.2% of doses prepared). There were a total of 2323 patient appointments and 191 missed appointments (8% of total appointments). There were a total of 36 systemic reactions (0.9% of injections given) ranging from grade 1a to 2, with no grade 3-5 reactions. This rate of systemic reactions per injection is similar to what has been reported in the published literature of approximately 0.2% (Cox et al., 2010), and also comparable to previously reported incidences of non-fatal SCIT systemic reactions in two large cohorts.

CONCLUSIONS: We describe a unique approach to delivering SCIT doses yielding a low rate of systemic reactions per injection and minimizing dosing errors. This method may be appropriate for multidisciplinary clinics with frequently changing staff to enhance patient safety.

929 OBESITY DYSREGULATES IMMUNOMETABOLIC STATUS IN ASTHMA AND IMPACTS VACCINE RESPONSES

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RATIONALE: Asthma and obesity are two of the most significant chronic childhood diseases in the US and both are increasing in prevalence worldwide. As body mass index (BMI) increases, so does asthma risk, pointing to a pathophysiological link. However, while these diseases are common and severe, it remains unclear how they converge to affect pediatric immune function and increase infection severity.

METHODS: Prospective systems immunometabolic study of pediatric asthma and obesity: obese asthmatics (OA), non-obese asthmatics (A), obese non-asthmatics (O) and non-obese and non-asthmatics (HC). Asthmatics were robotic patients recruited from Allergy clinic, with deep clinical characterization including sensitization and spirometry. To assess the underlying mechanisms of immune dysfunction we used peripheral blood mass cytometry (CyTOF), serum metabolomics, serum cytokine analysis and high dimensional systems immunology analytics to combine the deep immunometabolic profiling with clinical immunological and metabolic data on these patients.

RESULTS: Pediatric atopic OA patients demonstrated alterations in T cell differentiation including increased CD8 T cell exhaustion. They also demonstrated altered serum metabolites including increased glutamate, which may underlie some of the immune dysfunction. Finally, altered vaccine responses were also connected to underlying immunometabolic dysregulation in obesity.

CONCLUSIONS: These insights into the mechanistic links between metabolic disturbances and immune dysfunction in OA may improve understanding of the severe asthma exacerbations with viral upper respiratory infections seen in OA. We are currently focused on testing these mechanisms in mouse models of disease. Ideally, this will lead to identification of novel therapeutic targets for this challenging to manage patient population.
930 Sleeve gastrectomy surgery reduces airway resistance and inflammation in chronically allergen-challenged obese mice

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RATIONALE: Obesity increases asthma severity. Weight loss in bariatric surgery improves asthma symptoms and reduces airway hyperresponsiveness. We hypothesized that vertical sleeve gastrectomy (VSG), a model of bariatric surgery, would reduce airway pathology in allergen-challenged obese mice.

METHODS: Five-week old C57BL/6 mice were fed a high fat diet (HFD - 45% kcal fat) or normal chow and concurrently challenged with intranasal house dust mite (HDM) allergen (25 µg) or saline 3 days/week for 8 weeks. These challenged mice immediately underwent VSG or sham surgery, or no surgery (NS) as control (n = 5 per group). After one-week recovery, mice were returned to HFD and HDM challenges for four weeks. Twenty-four hours after the final HDM challenge, the mice were tested for airway responsiveness to increasing doses of methacholine delivered intravenously, and lung mechanics were evaluated using Flexivent (SciReq). Blood and bronchoalveolar lavage (BAL) with saline were collected. Harvested lung slices were stained with Masson’s trichrome, Periodic acid Schiff or hematoxylin and eosin stains. Percent trichrome staining was quantified using Image J (NIH). Interleukin (IL) -13, IL-5, glucagon-like peptide-1, transforming growth factor-beta, insulin and leptin were measured in blood and/or lavage fluid using ELISA.

RESULTS: VSG induced significant weight loss and reduction of plasma leptin levels (p < 0.05). Airway reactivity to bronchoconstrictor, airway tissue inflammation and percent BAL eosinophils (13.3% NS, 4.7% sham, 0.8% VSG) were reduced in HFD-fed, HDM-challenged mice following VSG compared to sham or NS (p < 0.05).

CONCLUSIONS: Weight loss surgery in obese, chronically allergen-challenged mice induces metabolic changes associated with improved airway inflammation and resistance.

931 Therapeutic effects of pravastatin on asthmatic airway inflammation in high fat diet induced obese mouse model

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RATIONALE: Obesity is one of factors associated with severe, uncontrolled asthma. Th17 signaling pathway is known to be associated with obese asthmatics, however effect of pravastatin on obese asthmatic airway inflammation has not been evaluated.

METHODS: C57BL/6 mice were fed with high-fat diet (HFD) to induce obesity with or without ovalbumin (OVA) sensitization and challenge. Pravastatin was administered intraperitoneally during the OVA treatment. Airway inflammation, airway hyper-responsiveness (AHR) were analyzed and lung tissues were examined to evaluate the change of bronchial inflammation by pravastatin in obese asthma mice. The changes of MAPK, STAT3 and PI3K/Akt signaling pathways which were known to be stimulated by leptin were measured in lung tissues.

RESULTS: HFD exacerbated eosinophilic airway inflammation and increased AHR. Pravastatin successfully alleviated the airway inflammation and AHR in HFD+OVA mice as well as OVA challenged mice. The levels of cytokines examined in bronchoalveolar lavage fluid (BAL) revealed that expression of IL-4, 5 and IL17 were more elevated in HFD+OVA mice than OVA mice reflecting both Th2 and Th17 pathways were stimulated by HFD induced obesity and OVA challenge. Leptin/ adiponectin ratio was elevated in HFD+OVA mice, decreased with pravastatin administration. Treatment of pravastatin suppressed expression of IL-4, 5 and IL-17 in obese OVA mice. Moreover, phosphorylation of p38 and ERK 1/2 in lung tissues were significantly decreased in HFD+OVA mice.

CONCLUSIONS: Pravastatin treatment in obese asthmatic mouse showed anti-asthmatic effect by inhibition of Th2 and Th17 associated signaling pathways, decreasing the leptin expressions and downstream MAPK signaling pathways.

932 Glucose metabolism dictates murine eosinophil differentiation, chemotaxis, and IL-4 expression

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RATIONALE: Eosinophils express multiple hormone receptors and emerge as critical in the regulation of fat homeostasis and systemic metabolism. However, phenotypic and functional responses of naïve eosinophils to metabolic change are poorly understood. Here, we determined the acute and chronic effects of energy metabolism disruption on murine eosinophil differentiation and function

METHODS: To study differentiation, murine bone marrow-derived eosinophils were cultured in normoglycemic [6 mM] or hyperglycemic [20 mM] conditions for 13 days in the presence of IL-5. To assess plasticity in phenotype and function, mature differentiated eosinophils were treated with glucose [20 mM], insulin [633.6 mcIU/ml] or GLUT4 glucose transport inhibitor indinavir [200 uM] for 24 hours. Multi-panel flow cytometry and qPCR were used to quantify eosinophil phenotypic markers (Lin, Sca1, Siglec-F, CD11c, CD34, ST2) and cytokines (IL-4, IL-5, IL-10). We also quantified eosinophil chemotaxis in different glycemic conditions.

RESULTS: Terminal IL-5-driven eosinophil proliferation, differentiation, and maturation were suppressed in hyperglycemic conditions. IL-4 expression was significantly induced in eosinophils in both acute and chronic hyperglycemia, but acutely suppressed in insulin- and indinavir-treated cells. Siglec-F expression was significantly reduced in mature indinavir-treated eosinophils compared to controls (from an average of 76% to 50%). Moreover, hyperglycemia significantly suppressed eosinophil chemotaxis to eotaxin (CCL11).

CONCLUSIONS: Differentiation, chemotaxis, and IL-4 expression in eosinophils are all sensitive to glucose levels in the environment. Disrupted glucose metabolism may be a linking factor for eosinophil responses in obesity, asthma, and inflammation.
**933** Eosinophils Display Subtype-specific Metabolic Profiles

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**RATIONALE:** Under homeostatic conditions and in disease progression eosinophils have a variety of effector functions regulating Local Immunity And/or Remodeling/Repair (LIAR hypothesis). These activities are manifestations of different eosinophil subtypes, which, in turn, depend on the cytokine milieu of the tissue microenvironment. Eosinophil subtypes are characterized by expression of specific genes and we hypothesize that their functions are supported by a distinct metabolic phenotype. The goal of this study was to examine relationships between Th1 or Th2 cytokine-dependent gene expression and parameters of energy metabolism in mouse eosinophils.

**METHODS:** Eosinophils from IL-5 overexpressing transgenic mice (N1638) were purified to >98% purity and cultured in cytokine cocktails typical for Th1 or Th2 environment to polarize the cells to their subtypes (E1 and E2). RNA was extracted for RNA-seq transcriptome analysis and mitochondrial function was assessed by measuring the relative uptake of MitoTracker Orange (potential independent) to MitoTracker Far Red (potential dependent). Rates of oxygen consumption and extracellular acidification were directly assessed in polarized eosinophils using a Seahorse XFe96 Analyzer.

**RESULTS:** RNA-seq analysis showed elevated expression of genes present in mitochondrial respiratory chain in Th2 compared to Th1 cytokine treated eosinophils. Consistent with these observations E2 eosinophils had a higher inner mitochondrial membrane potential. E2 eosinophils had significantly higher maximal respiratory capacity and rate of media acidification compared to E1 eosinophils.

**CONCLUSIONS:** Our studies showed an overall elevated metabolic rate in Th2 cytokine treated eosinophils (E2 eosinophils), suggesting a link between eosinophil subtypes and parameters of their energy metabolism.

**934** Efficacy of RPC4046, an Anti-Interleukin-13 Monoclonal Antibody, in Patients With Active Eosinophilic Esophagitis: Analysis of the Steroid-Refractory Subgroup From the HEROES Study

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**RATIONALE:** The HEROES study evaluated RPC4046 in adults with active eosinophilic esophagitis (EoE). We conducted pre-specified and post-hoc analyses to assess RPC4046 in steroid-refractory subjects.

**METHODS:** Adults with EoE (n=99) were stratified by steroid-refractory status (determined by prior corticosteroid use and investigator judgment) and randomized 1:1:1 to RPC4046 360 mg (n=17), 180 mg (n=14), or placebo (n=16) weekly for 16 weeks. The primary endpoint was change from baseline in mean esophageal eosinophil counts at week 16. Secondary endpoints included mean change from baseline to week 16 in EoE Endoscopic Reference Score (EREF), improvements in dysphagia (Daily Symptom Diary [DSD]), Eosinophilic Esophagitis Activity Index (EESAI) score, and EoE histology scoring system (EoEHSS) per grade and stage.

**RESULTS:** At week 16, compared with placebo, each dose group showed significant improvements in mean esophageal eosinophil counts (P<0.0001), EREFS (P<0.005), and histology (EoEHSS) (P<0.05), and a significantly greater proportion of patients had peak eosinophil counts <15 per high-power field (P<0.01). In the 360 mg group, compared with placebo, symptom severity (EESAI) improved (P<0.05), while the mean change in DSD composite score approached significance (P=0.055). The most frequently reported adverse events in the overall study were headache, upper respiratory tract infection, arthralgia, nasopharyngitis, diarrhea, and nausea.

**CONCLUSIONS:** Compared with placebo, RPC4046 improved mean and peak eosinophil counts, histopathologic parameters, endoscopic features, and symptoms in steroid-refractory EoE patients, providing support that, in this subpopulation, RPC4046 markedly improves multiple measures used to evaluate EoE. In the overall study population, RPC4046 was generally safe and well tolerated.
The 1-Hour Esophageal String Test: A Non-Endoscopic Minimally Invasive Test to Accurately Detect Disease Activity in Eosinophilic Esophagitis

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Rationale: Eosinophilic esophagitis (EoE), a chronic allergic disease, lacks sensitive and specific peripheral biomarkers. We hypothesized that concentrations of EoE-related biomarkers captured using a 1-hour minimally invasive Esophageal String Test (EST) would correlate with mucosal eosinophil counts and tissue concentrations of the same biomarkers. We aimed to determine if a 1-hour EST accurately distinguishes active from inactive EoE.

Methods: In a prospective, multi-site study, children and adults (ages 7-55yrs) undergoing a clinically indicated esophagogastroduodenoscopy performed an EST with an esophageal dwell time of 1-hour. Subjects were divided into 4 groups: 1) active EoE, 2) inactive (treated) EoE, 3) GERD and 4) normal esophageal mucosa. Eosinophil-associated proteins were compared between EST effluents and esophageal biopsy extracts. Statistical modeling was performed to select biomarkers that best correlated with eosinophilic inflammation.

Results: 143 subjects (96 children, 47 adults) with active EoE (n=62), inactive EoE (n=37), GERD (n=9) and normal esophagus (n=35) completed the study; no serious adverse events were recorded. EST-captured eosinophil-associated proteins were significantly correlated with peak eosinophils/HPF, endoscopic visual scoring (EREFs), and the same proteins extracted from mucosal biopsies. Statistical modeling, using combined eotaxin-3 and MBP-1 concentrations, led to the development of EoE scores that distinguished between subjects with active EoE compared to inactive EoE in subjects with an EoE diagnosis, and compared to subjects with inactive EoE, GERD or normal esophagi.

Conclusions: The 1-hour EST can be used to accurately distinguish active from inactive disease in children and adults with EoE and facilitate monitoring of EoE disease activity in a safe, minimally invasive fashion.

Effect of a 4-Food Elimination Diet and Omeprazole in Children with Eosinophilic Esophagitis – A Randomized, Controlled Trial

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Rationale: The present trial assessed whether a 4-food elimination diet (4-FED), in combination with proton pump inhibitor (PPI) treatment, is superior to PPI monotherapy in children with eosinophilic esophagitis (EoE).

Methods: After a baseline gastroscopy, patients with histologically proven EoE ≥15 eosinophils per high power field (HPF) were randomized to omeprazole 1mg/kg twice daily (max. dose 20mg b.i.d.) plus a 4-FED (cow’s milk, soy, egg, wheat) vs omeprazole monotherapy. A second gastroscopy was performed after 8-12 weeks. Complete mucosal remission was defined as eosinophils <5/HPF, and partial remission as <10/HPF on repeat biopsy.

Results: Of 64 patients (median age 9.1 yrs) with EoE, 32 were randomized to PPI+4-FED, and 32 to PPI only. There was a higher rate of non-completers in the diet group (5/32 vs 1/32; NS). At baseline, median eosinophil counts were similar between groups (PPI 44.5 [IQR 24-82] vs PPI+4-FED 37 [IQR 21.5-57]; p=0.24). At 8-12 weeks, participants in the PPI+4-FED group had lower median mucosal eosinophil counts, compared to the PPI group (2.5 [IQR 0.5-19] vs 12 [IQR 0-37]; p=0.11). Eosinophil counts were significantly different only in the lower esophagus (PPI+4-FED 2 [IQR 0-18] vs PPI 24 [IQR 5-43]; p=0.003). On per-protocol analysis, at least partial remission (<10 eosinophils/HPF) was significantly more likely for PPI+4-FED vs PPI (88% vs 45%; p=0.002), with borderline significance on intention-to-treat analysis (PPI+4-FED 69% vs PPI 44%; p=0.054).

Conclusions: This is the first randomized clinical trial demonstrating that a 4-FED combined with PPI is significantly more effective than PPI monotherapy in children with EoE.
Esophageal Eosinophilia is Present in Some Peanut Allergic Patients

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RATIONALE: Oral immunotherapy (OIT) desensitization is an emerging treatment for food allergy. Despite attempts to minimize adverse events during desensitization, many participants still experience gastrointestinal symptoms and some develop eosinophilic esophagitis (EoE). It is unclear whether these subjects have subclinical esophageal eosinophilia (EE) at baseline. We evaluated the presence of EE in subjects with food allergy before peanut OIT.

METHODS: Baseline esophageagogastroduodenoscopies (EGD) were conducted with 21 adults before peanut OIT. Endoscopic findings were assessed using the Esophagastroduodenal Endoscopic Reference Score (EREFS), and biopsies were obtained from the proximal, middle, and distal esophagus. Esophageal biopsies were evaluated using the Esophageal Histologic Scoring System (EoEHSS). Hematoxylin and eosin stains of each biopsy were assessed for eosinophil density. Automated image analysis of eosinophil peroxidase (EPX) immunohistochemistry was also performed to assess eosinophil degranulation.

RESULTS: All subjects were asymptomatic at enrollment. Pre-existing EE was present in 5 participants (24%), 3 (14%) of whom had >15 eosinophils per high-power field (eos/hpf) associated with mild endoscopic findings (edema, linear furrowing, or rings; median EREFS=0, IQR 0-0.25). Some subjects also demonstrated basal cell hyperplasia, dilated intercellular spaces, and lamina propria fibrosis of the esophageal mucosa. EPX deposition (EPX/mm²) correlated with eos/hpf (r=0.53, p<0.0001) and identified a majority of subjects with EoE with high diagnostic accuracy [EPX/mm² (biopsy), AUC=0.88 (0.8, 0.96 95% CI), p<0.0001 and EPX/mm² (Cytosponge), AUC=0.83 (0.74, 0.93 95% CI), p<0.0001].

CONCLUSIONS: EE was present in 5 participants (24%), 3 (14%) of whom had >15 eosinophils per high-power field (eos/hpf). EPX deposition (EPX/mm²) correlates strongly with eos/hpf (biopsy) and EPX (Cytosponge) strongly correlated with eos/hpf (biopsy) (r=0.81, (0.7, 0.88 95% CI), p<0.0001) and identified a majority of subjects with EoE [AUC=0.9 (0.83, 0.97 95% CI), p<0.0001].

Image Analysis of Esophageal Biopsies and Cytosponge Specimens Stained for Eosinophil Peroxidase Identifies Subjects with Eosinophilic Esophagitis

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RATIONALE: Diagnosis and treatment of eosinophilic esophagitis (EoE) requires multiple endoscopic biopsies. The Cytosponge is a minimally invasive method to sample the esophageal epithelium. As tissue eosinophils undergo degranulation in EoE, we hypothesized that eosinophil peroxidase (EPX) deposition would correlate with eosinophils per high power field (eos/hpf) and enhance the diagnostic accuracy of the Cytosponge.

METHODS: Matched biopsies and Cytosponge specimens obtained in a previously conducted prospective study (n=72 from 60 patients) were stained for hematoxylin and eosin (H&E) and EPX. 43 were graded as active EoE (≥15 eos/hpf). EPX stains were digitized and analyzed for EPX-positive pixels (area=0.307 mm²). EPX/mm² (biopsy and Cytosponge) was compared to H&E eos/hpf (biopsy) to assess correlations (Spearman’s rho) and ROC curves were generated.

RESULTS: EPX/mm² from both the biopsy and Cytosponge specimens correlated strongly with eos/hpf (H&E eosphageal biopsy) [r=0.75, (0.62, 0.83 95% CI), p<0.0001 and r=0.72, (0.59, 0.82 95% CI), p<0.0001, respectively]. Each identified subjects with active EoE with high diagnostic accuracy [EPX/mm² (biopsy), AUC=0.88 (0.8, 0.96 95% CI), p<0.0001 and EPX/mm² (Cytosponge), AUC=0.83 (0.74, 0.93 95% CI), p<0.0001]. The point of optimal sensitivity (76.7%) and specificity (79.3%) corresponded to an EPX density of 16,403 pixels/mm² (Cytosponge). As previously reported, eos/hpf (Cytosponge) strongly correlated with eos/hpf (biopsy) [r=0.81, (0.7, 0.88 95% CI), p<0.0001] and identified a majority of subjects with EoE [AUC=0.9 (0.83, 0.97 95% CI), p<0.0001].

CONCLUSIONS: EPX/mm² (biopsy and Cytosponge) correlates strongly with eos/hpf (biopsy). Minimally invasive assessment of EPX/mm² and eos/hpf identify subjects with EoE with comparable diagnostic accuracy.