School-based self-management educational interventions for asthma in children and adolescents: A systematic review

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RATIONALE: Children with asthma are at risk of asthma exacerbations, unscheduled medical care and school absences. To date, the evidence for schools-based interventions for these adverse outcomes is unclear. We therefore performed a systematic review of the effectiveness of school-based self-management interventions on children’s asthma outcomes.

METHODS: We searched 19 databases to identify eligible students for inclusion. The review investigated studies across a range of population groups and environments, including primary/elementary and secondary/high schools. The inclusion criteria stated that interventions must be delivered to children with asthma, aged 5 to 18 years, within the school setting. Meta-analyses were conducted to evaluate the effectiveness of the interventions across 11 outcomes, compared with usual care.

RESULTS: 34 studies, from 7 countries, met the inclusion criteria for the review, and 24 were included in the meta-analyses. School-based interventions were effective in reducing hospitalisations (SMD -0.19, 95% CI -0.35 to -0.04) and emergency department visits (OR 0.71, 95% CI 0.53 to 0.95). Days of restricted activity also had higher levels of quality of life at follow-up (SMD 0.27, 95% CI 0.18 to 0.36). The effect of the intervention on school absences, day and night time symptoms, and the use of reliever therapies was less consistent.

CONCLUSIONS: School-based interventions for children with asthma are effective in improving a number of outcomes, including quality of life and healthcare use.

Comparative efficacy of daily inhaled fluticasone propionate and episodic inhaled combined salmeterol/fluticasone propionate in children with recurrent wheezing

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RATIONALE: Daily inhaled corticosteroid (ICS) is recommended by the world expert committee to treat patients with persistent asthma and tendency to have asthma as a controller. However, many children in Thailand tend to receive episodic inhaled corticosteroid due to their parents’ inconvenience. We compare efficacy of daily inhaled fluticasone propionate (IFP) and episodic inhaled combined salmeterol/fluticasone propionate (ISFP) in children with recurrent wheezing.

METHODS: Forty-four children aged 1 to 15, with recurrent wheezing and tendency to have asthma were recruited in our study. Participants were randomized to receive either daily IFP (N=24) or 14-day of ISFP started at the onset of symptoms of respiratory tract illness (N=20). The primary outcome was the percentage of exacerbations which needed systemic corticosteroid. The secondary outcome was the monthly height rate. Proportional-hazards regression model and ANOVA were used for statistical analysis.

RESULTS: At 6 months after the treatment, the percentage of exacerbations which needed systemic corticosteroid between 2 groups had no statistically significant difference (P=0.790) with hazard ratio of 1.224 (95% confidence interval (CI) 0.278 to 5.392). Monthly height rate also had no significant difference (P=0.869). 0.66 (95% CI 0.56 to 0.76) centimeters (cm) in daily IFP and 0.67 (95% CI 0.56 to 0.78) cm in episodic ISFP. Median cumulative ICS dose in daily IFP group (45,000 micrograms) and episodic ISFP group (5,250 micrograms) was significantly different (P<0.001). No adverse event was found in episodic ISFP group.

CONCLUSIONS: There were no significant difference in reducing exacerbation and height suppression between daily IFP and episodic ISFP in 6-month period.

Assessing the Relationship between Age and Clinical Outcomes in Adult Patients Using the ASTHMA-Educator, a Novel Smartphone Application

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RATIONALE: There is a lack of published literature regarding subpopulations that benefit from smartphone applications for asthma. This study examines the relationship between age, asthma knowledge, and clinical asthma outcomes in patients that used the ASTHMA-Educator mobile application.

METHODS: 25 adult patients (mean age 53 years) completed the ASTHMA-Educator program via tablet (iPad) at baseline, 2 months, and 4 months. At each visit, patients received the program and we administered the Asthma Knowledge Questionnaire (AKQ), Asthma Control Test (ACT), and Mini-Asthma Quality of Life Questionnaire (mini-AQLQ). Patients reported the time spent to complete the ASTHMA-Educator. We evaluated patient satisfaction with the application. We assessed relationships between age, AKQ, ACT, mini-AQLQ, and time spent to complete the program using the Pearson’s correlation.

RESULTS: We observed a significant negative correlation between age and patient satisfaction (r=-0.37, p=0.04). At 2 and 4 months, age negatively correlated with mini-AQLQ (r=-0.18, p=0.28; r=-0.33, p=0.11); at both time points, age positively correlated with time spent using the application (r=0.20, p=0.24; r=0.17, p=0.42). Patient satisfaction was positively associated with AKQ score (r=0.23, p=0.21) at 2 months. There were negative correlations between time spent and AKQ score at 2 months and 4 months (r=-0.38, p=0.02; r=-0.33, p=0.11).

CONCLUSIONS: Older patients demonstrated decreased post-intervention asthma quality of life, diminished satisfaction with the intervention, and spent more time using the software program relative to younger participants. We will need to validate these findings on a larger scale, and determine how to adapt the program’s features for older patients.
652 Gamma Tocopherol (γT) Supplementation Reduces Endotoxin-Induced Sputum Neutrophilia in Healthy Volunteers and Asthmatics Regardless of BMI or glutathione-S-transferase M1 (GSTM1) Genotype

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RATIONALE: Through its unique antioxidant and anti-inflammatory properties, γT supplementation has shown benefit in reducing airway inflammation in preclinical and early-phase clinical studies. However, obesity increases systemic inflammation while the GSTM1 null genotype may alter host antioxidant defenses. This study, therefore, examines whether BMI and/or GSTM1 genotype modifies the response to inhaled endotoxin and the reduction of endotoxin-induced sputum neutrophilia following γT supplementation in healthy volunteers (HV) and asthmatics.

METHODS: Thirteen HV and 15 asthmatics underwent γT treatment followed by inhaled endotoxin challenge in two double-blind, placebo-controlled, cross-over studies. γT supplementation reduced post-challenge sputum neutrophilia compared to placebo in HV (p = 0.03) and asthmatics (p = 0.04). The effect of BMI and GSTM1 genotype on response to inhaled endotoxin and the reduction in endotoxin-induced sputum neutrophilia following γT treatment in each study was assessed using linear regression models and Wilcoxon Rank Sum Tests, respectively.

RESULTS: BMI and GSTM1 genotype had no effect on response to inhaled endotoxin, as measured by increase in sputum neutrophils, in HV (p = 0.17 and p = 0.90, respectively) or asthmatics (p = 0.81 and p = 0.52, respectively). GSTM1 genotype had no effect on the reduction in endotoxin-induced sputum neutrophilia following γT treatment in HV (p = 0.42) or asthmatics (p = 0.78). Higher BMI was associated with greater reduction in post-challenge sputum neutrophilia following γT treatment in HV (p = 0.03) but not in asthmatics (p = 0.14).

CONCLUSIONS: Response to inhaled endotoxin in HV and asthmatics is not affected by BMI or GSTM1 genotype. γT treatment reduces endotoxin-induced sputum neutrophilia regardless of BMI and GSTM1 genotype with enhanced responses seen in those with higher BMI.

653 Real-world Study Characterizing Patients Prior to Receiving Albuterol Multidose Dry Powder Inhaler or Short-acting β2-Agonist Via Pressurized Metered-Dose Inhalers for Asthma and COPD in the United States

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RATIONALE: Short-acting β2 agonists (SABA) are administered primarily using pressurized metered-dose inhalers (pMDIs). Albuterol multidose dry powder inhaler (MDPI; ProAir RespiClick®), a novel, breath-actuated device, eliminates hand-breath coordination required of pMDIs. A gap exists in understanding real-world differences in patients prior to receiving albuterol MDPI or SABA pMDI.

METHODS: This retrospective study used a large, nationally representative managed care database including asthma (aged ≥2 years) and chronic obstructive pulmonary disease (COPD; aged ≥40 years) patients receiving ≥1 albuterol MDPI or any SABA pMDI prescription between April 2015 and March 2016. Baseline patient demographics, provider specialty, disease severity (GINA step level or COPD severity score), comorbidities, and healthcare resource use (HCRU) were assessed over 6 months before first SABA fill date.

RESULTS: The study included 2140 albuterol MDPI (n = 1244 asthma; n = 896 COPD) and 230,822 SABA pMDI (n = 172,911 asthma; n = 57,911 COPD) patients. At baseline, albuterol MDPI patients were elderly, more likely to be female (asthma only), had higher baseline comorbidities, more respiratory specialty visits, and higher respiratory-related ambulatory visits (all P ≤ 0.05 vs SABA pMDI); no difference with inpatient or emergency HCRU was observed. Greater proportions of albuterol MDPI versus SABA pMDI users had more severe disease at baseline (asthma: 12.71% vs 8.13%; COPD: 28.57% vs 23.37%; P < 0.05), with more asthma exacerbations (7.64% vs 1.40%; P < 0.05) but similar COPD exacerbations (19.08% vs. 21.30%; P = 0.108).

CONCLUSIONS: More albuterol MDPI patients saw respiratory specialists and had severe disease at baseline versus SABA pMDI patients. Further research may elucidate how patient characteristics (eg, disease severity, comorbidities) influence SABA inhaler choice.

654 The effects of Spirulina (Arthrospira platensis) dietary supplement as an adjunct therapy for children aged 7-14 years old with asthma: A randomized – double blind placebo controlled clinical trial

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RATIONALE: This study aimed to determine the effects of Spirulina supplementation on asthma control and lung function among children aged 7-14 years old.

METHODS: This is a randomized, double-blind, placebo-controlled study wherein children 7 to 14 years old diagnosed with mild to moderate persistent asthma were randomly assigned to receive either Spirulina (1,000 mg to 2,000 mg daily) or placebo for three months. Asthma Control Test (ACT) and Composite Asthma Severity Index (CASI) were used for patient report-based measures. Forced expiratory volume at 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC and peak expiratory flow rate (PEFR) were determined through spirometry. Post-supplementation assessment for three months was done.

RESULTS: A total of 39 patients (Spirulina = 20, placebo = 19) were enrolled in this trial. During the supplementation phase, both the Spirulina and placebo groups showed significant improvement in ACT scores (Spirulina, P < 0.0001; placebo, P = 0.19) compared to baseline. There was no significant change in CASI scores in both groups. However, during post-supplementation phase, the Spirulina group showed significantly sustained improvement on both the ACT (P < 0.0001) and CASI scores (P < 0.0001) compared to placebo. The FEV1 (P = 0.014), FVC (P = 0.008), and PEFR (P = 0.0001) of the Spirulina group significantly improved by the end of supplementation. Overall, significant intergroup differences revealed only in FEV1 (P = 0.0002) and PEFR (P < 0.0001).

CONCLUSIONS: Daily supplementation with Spirulina significantly improved asthma control, FEV1 and PEFR compared to placebo.
Comparison Of Acute Bronchodilator Effects Of Inhaled Ipratropium Bromide And Salbutamol In Adults With Bronchial Asthma

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Rationale: A heterogeneous response to beta-agonists and muscarinic-antagonists is reported in asthmatics; only a few studies have looked for predictive factors of response to these two classes of drugs. We evaluated separately the bronchodilation after ipratropium bromide (IB) and after salbutamol and looked for possible association/correlation between the response to bronchodilators and markers of atopy, bronchial and systemic inflammation.

Methods: We recruited 53 asthmatics consecutively referred for investigation to our Allergy Department. Age range was from 18-75 years, with asthma severity mild to moderate. Patients underwent history taking, physical examination, skin prick tests (SPTs), total IgE levels, CBC, FENO measurement, spirometry and bronchodilation test (BDT) with IB and salbutamol separately.

Results: Forty-one patients showed a positive BDT: 11 to IB alone, 8 to salbutamol, 22 to both drugs. Forty-two patients were atopic (at least one positive SPT). In 5 patients FENO measurement was not successful due to poor compliance. FENO levels (ppb) were inversely correlated with the difference between FEV1 after IB and FEV1 after salbutamol (∆FEV1postBDs): Pearson’s r = -0.413, p < 0.005. After dichotomizing patients according to ∆FEV1postBDs, we found that the subgroup of patients (n=27) with a higher FEV1 after IB versus FEV1 after salbutamol showed lower FENO values with respect to the other subgroup (n=26): 32.6 ± 39.3 versus 50.7 ± 48 (Student t test: p < 0.05).

Conclusions: Our results suggest that in a population of asthmatics, mostly atopic, low FENO values are associated with a better response (higher FEV1 post BD) to ipratropium bromide versus salbutamol.

A Self-Regulation Intervention Can Decrease Asthma Exacerbations Among Older Adults

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Rationale: Older adults have high rates of asthma morbidity and mortality compared to younger age groups. The purpose of this study was to evaluate a self-management asthma intervention as a means to decrease asthma exacerbations.

Methods: Adults age 55 and above with persistent asthma were enrolled into blinded, randomized controlled trial of a 6-session asthma self-management intervention. This educational intervention was conducted in group sessions and through individual telephone calls. Outcomes including asthma exacerbations (defined as unscheduled office visits, emergency department visits, or hospitalizations for asthma), spirometric values, FeNO, asthma control, asthma quality of life, and asthma self-management were assessed at 3, 6, and 12 months.

Results: 189 subjects were enrolled, 172 were randomized and received at least one treatment dose, and 145 (84%) were analyzed at 12 months. On a modified intent to treat analysis, those in the intervention group were less likely to have an asthma exacerbation (26.9% vs 47.2%, p = 0.01), had a lower asthma exacerbation rate (0.8 vs 1.9, p = 0.02), had better asthma control (19.9 vs 18.6, p = 0.08) and had a higher asthma self-management score (8.9 vs 8.4, p = 0.04). After a mixed model analysis to control for potential confounding factors, a decrease in asthma exacerbations (p = 0.046) and a decreased asthma exacerbation rate (p = 0.016) remained statistically significant while asthma control and self-management did not. No other significant outcome differences were found.

Conclusions: A 6 session self-management intervention can successfully decrease asthma exacerbations among older adults.
Inhaled corticoids in asthmatic patients: effect on body mass index and spirometry

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RATIONALE: The key treatment for persistent asthma is inhaled corticosteroid (IC). Severe asthmatic patients usually require high doses of IC for long periods of time. High doses of IC may lead to suppression of adrenal and other adverse effects, as obesity

METHODS: This was a retrospective study based in electronic medical records of adult asthmatic outliers followed at a tertiary hospital. Asthmatic patients according to GINA were assessed for a period of six years. All of them were in IC treatment. Body mass index (BMI) and spirometry were assessed after a period of six years, as well as eventual change in IC dose during that period

RESULTS: Eighty-six patients were included in the study. The mean age was 58.1 years, and 81.4% of the patients were female. All of them initially, in 2010, used budesonide ≥ 800 mcg/day. After six years of follow-up, 20 patients (23.3%) decreased their IC dose to 600 mcg/day or under (mean dose of 390 mcg/day): 66 patients (76.6%) maintained or increased their IC dose (mean dose of 1152 mcg/day). There was no change in BMI and FEV1 during this period. FEV1 changed from 71.7% of predicted value to 68.6% at the end of evaluation.

CONCLUSIONS: Patients with severe asthma require high doses of IC to control the disease. This study observed that patients who maintained a high dose of IC for a period of 6 years showed no change in BMI and only a slight reduction of FEV1 was observed in this period

The Efficacy Of Fluticasone Propionate Versus Montelukast In Different Genotypes Of ASP299GLY TLR-4 Polymorphisms In Adult Asthmatics

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RATIONALE: The Asp299Gly polymorphism (rs4986790) of the TLR4 gene leads to a single nucleotide substitution of adenine (A) for guanine (G) at position of +896 exon 4. The AG genotype is associated with atopic asthma and AA genotype with non-atopic asthma.

METHODS: 39 adults with mild persistent asthma were studied, 21 with AA and 18 with AG genotypes. The study had 2 periods: a 2-week run-in period, when all patients received low dose (125 μg) fluticasone propionate (FP) once a day; a 24-week treatment period, when patients took either FP once daily or montelukast 10 mg daily. 11 patients with AA (AA-FP) and 9 with AG (AG-FP) took FP. 10 patients with AA (AA-M) and 9 with AG (AG-M) took montelukast. Single nucleotide polymorphism of A896G (rs4986790) was detected by PCR.

RESULTS: FP used in AA genotype patients for 24 weeks was more effective than montelukast, based on significant increase in FEV1 (AA-FP – 93.99 ± 5.52 vs AA-M – 87.25 ± 5.57 %, p=0.012), improvement in asthma control (ACQ: AA-FP – 0.93 ± 0.27 vs AA-M – 2.00 ± 0.75 points, p=0.001) and quality of life (AQLQ(S): AA-FP – 5.88 ± 0.31 vs AA-M – 5.41 ± 0.43 points, p=0.012). The clinical efficacy of montelukast in AG genotype patients was superior to FP (FEV1: AG-FP – 86.24 ± 5.82 vs AG-M – 92.41 ± 5.48 %, p=0.035; ACQ: AG-FP – 1.49 ± 0.51 vs AG-M – 1.03 ± 0.34 points, p=0.043; AQLQ(S): AG-FP – 4.72 ± 0.35 vs AG-M – 5.87 ± 0.29 points, p=0.001).

CONCLUSIONS: The effectiveness of inhaled corticosteroids and leukotriene modifiers may relate to polymorphisms of Asp299Gly-TLR-4 in adult asthmatics.
Inhaler technique among adults with uncontrolled asthma from low-income Philadelphia neighborhoods

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RATIONALE: Correct inhaler technique is essential for asthma control. We evaluated metered dose (MDI) and dry powder inhaler (DPI) technique in adults with uncontrolled asthma. We hypothesized that inhaler technique is suboptimal, and wanted to determine which steps of inhaler technique are most error-prone.

METHODS: 301 adults living in low-income Philadelphia neighborhoods were recruited. All had uncontrolled asthma, defined as requiring prednisone, an ED visit, or hospitalization for asthma in the past 12 months. At enrollment, subjects’ inhaler techniques were rated by community health workers. MDI technique was rated using inhaler guidelines from the NAEPP Expert Panel Report 3, and DPI technique by published and manufacturers’ instructions. MDI technique had 7 steps; DPI technique had 6 steps; each step was rated as ‘yes’ or ‘no’. Incorrect steps were corrected.

RESULTS: The mean age was 49 ± 13 years. 90% were female. 50% experienced hospitalizations and 83% had ED visits for asthma in the prior year. Among 203 patients with spirometry, mean FEV1 percent predicted was 69.5%. Of the 300 evaluable subjects, 281 were rated using MDIs; 81 were rated using DPIs. Among MDI users, 93 (33%) made at least one error. Common missed steps were exhaling before actuating the inhaler (23%), actuating only once per inhalation (19%), and breath hold for 6–10 seconds (16%). Of DPI users, 18 (22%) made at least one error. Common missed steps were inhaling deeply (11%), breath hold for 6 seconds (17%), and not blowing into the Diskus (12%).

CONCLUSIONS: MDI and DPI technique is suboptimal and should be reviewed regularly.

Efficacy of Once-Daily Tiotropium Respimat® on Lung Function and Asthma Control in Adults with Asthma at GINA Steps 2–5

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CONCLUSIONS: MDI and DPI technique is suboptimal and should be reviewed regularly.

Comparison of PEF vs. FEV1 Endpoints in Trials with Tiotropium in Adults and Adolescents with Moderate or Severe Symptomatic Asthma

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RATIONALE: In adults and adolescents FEV1 is generally viewed as the preferred lung function assessment in asthma clinical trials. PEF was assessed as an alternative endpoint.

METHODS: FEV1 and PEF outcomes from 7 trials with tiotropium Respimat® add-on to ICS ± additional controllers were compared. Change from baseline in peak FEV1(0–3h) trough FEV1 and PEF in adults with tiotropium 5 µg or 2.5 µg and placebo, delivered by Respimat® (2 puff(s) once daily), were analyzed from studies in patients with symptomatic asthma (adults: GraziaTinA-asthma®, PrimoTinA-asthma®, and MezzoTinA-asthma®; adolescents: PensieTinA-asthma® and RubaTinA-asthma®). Correlation of in-clinic and weekly mean home measurements (AM® Home Spirometer and eDiary) of FEV1 and PEF was also analyzed post hoc.

RESULTS: Improvements in both measures of lung function were seen in all studies with tiotropium Respimat®: FEV1(0–3h) 90–185mL and 111–223mL with 5 µg and 2.5 µg, respectively; and PEF(2–7 min) 15.8–25.6L/min and 9.7–26.3L/min with 5 µg and 2.5 µg, respectively. PEF appeared better able to identify tiotropium dose-response relationships. Measurements at home versus those in-clinic correlated better for PEF (intraclass correlation coefficient [ICC] 0.724–0.839) than for FEV1 (ICC 0.575–0.818), at Week 12 or 24, depending on the study, indicating that home assessed PEF as an endpoint may give additional information over and above FEV1.

CONCLUSIONS: FEV1 and PEF both improved with tiotropium added to ICS ± other controllers versus placebo in all studies. However, home PEF measurements may have certain advantages over home FEV1 measurements such as identification of dose ordering, ease of use and increasing convenience for the study subject.
CONCLUSIONS: Disparities in asthma control, as well as increases in asthma-related morbidity and mortality, have been identified among patient populations who lack access to ambulatory care; the purpose of this study is to determine whether a school-based health care delivery model improves asthma outcomes in at-risk pediatric populations.

METHODS: The study enrolled 41 patients, ages 6-12 years, from 6 elementary schools. Subjects were followed over a 3-month period; services were delivered by a board certified allergist and a pharmacist, who provided disease- and drug-specific education. Throughout the study, subjects and caregivers were assessed for visit compliance, medication compliance, and asthma treatment plan knowledge. Binomial distribution tests and Wilcoxon signed ranks tests were utilized to compare pre- and post-intervention knowledge.

RESULTS: A total of 38 study subjects (92.7%) achieved a visit compliance of 70% or greater. At the final visit, 19 subjects were assessed for controller medication compliance; 5 subjects (26.3%) achieved a medication compliance of 80% or greater. 60.6% (n = 33) of subjects attained full knowledge of their asthma treatment plan at final visit, in comparison to 6.9% (n = 39) of subjects at baseline (p < 0.001). 71.4% (n = 28) of caregivers attained full knowledge of their child’s asthma treatment plan at the final visit, in comparison to 30.6% (n = 36) at baseline (p = 0.006).

CONCLUSIONS: A school-based health care delivery model is a feasible approach to improve asthma treatment plan knowledge and compliance with visits in at-risk pediatric populations.

Health Care Practitioner Knowledge About Dosing And Side Effects Of Fluticasone Propionate Metered-Dose-Inhaler For Children With Asthma

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RATIONALE: A 6 year-old child developed Cushing’s Syndrome after 16 months of treatment with an FDA-unapproved dose (110mcg) of the inhaled corticosteroid (ICS) fluticasone propionate metered-dose-inhaler (FP-MDI) for asthma. The objective was to assess health care practitioner (HCP) knowledge about FP-MDI dosing and side effects.

METHODS: Anonymous and interactive polling was conducted using TurningPoint software and hand-held devices before and after PowerPoint presentation of the case during live meetings of HCPs across the United States. During the presentation, education about FDA-approved FP-MDI doses and side effects was provided.

RESULTS: Presentations (n = 40) were delivered to 790 HCPs, including asthma specialists. Before the presentation, only 26% of HCPs knew the dose of FP-MDI that is FDA-approved for children <12 years of age (44mcg only), and only 28% were confident in their ability to detect and diagnose growth and adrenal suppression secondary to ICS in a child with asthma. After the presentation, the respective values were 97% and 89% (p < 0.05). FP-MDI was the ICS with which 43% were most experienced, yet only 11% knew the Asthma Guideline-recommended medium dose of FP-MDI for 5-11 year old children (>176-352mcg daily). A high percentage (49%) indicated that between 21% and 80% of 5-11 year old children that they treat with FP-MDI receive the 110mcg dose.

CONCLUSIONS: HCPs are deficient in knowledge about FDA-approved FP-MDI doses and side effects and use FDA-unapproved doses, placing children at risk for developing serious systemic side effects. The reasons are unclear, but better methods to educate HCPs about ICS dosing and side effects are needed.
668 The Association Between Educational Levels Of Asthma Patients Using The ASTHMA-Educator Mobile Application And Emergency Department Visits

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RATIONALE: Although asthma self-management mobile apps are readily available, there is a lack of published literature regarding how a patient’s educational level may influence the response to these mobile interventions. This study correlates the educational levels of asthma patients using the ASTHMA-Educator mobile application with asthma emergency department (ED) visits.

METHODS: We developed the ASTHMA-Educator program to provide guideline-based asthma education for patients at our institution in the Bronx. 25 adult asthma patients received a tablet-based version of the program, and were included in this study. We collected baseline data for each subject including self-reported highest educational level. At baseline, 2 months, and 4 months, we queried patients regarding the number of asthma ED visits in the prior 2 months. We performed statistical analyses through the paired t-test.

RESULTS: Of the 25 subjects, 6 did not finish high school, 3 finished high school, 10 finished college, 3 completed a higher degree, and 3 reported ‘other’. Among patients that finished college, we observed a statistically significant decrease in mean asthma ED visits from baseline to 2 months and 4 months (p = 0.01 and p = 0.04, respectively). Among patients that did not finish high school, finished high school, or completed a higher degree, there was no significant reduction in asthma ED visits from baseline to follow-up.

CONCLUSIONS: The study showed that patients who finished college showed the most benefit from the ASTHMA-Educator. Larger sample sizes are needed to further validate these results and target the mobile software program to patients from other educational backgrounds.

669 Efficacy and Safety of Specific Immunotherapy for Allergic Asthma Patients with Mold Extracts

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RATIONALE: Specific Immunotherapy (SIT) is a significant treatment for allergic asthma, but were not sufficient clinical studies that support the effectiveness of SIT for mold allergies. We evaluated the efficacy and safety of SIT with mold extracts in a 5-year study of asthma patients who were allergic to mold.

METHODS: Asthma patients who were allergic to either Alternaria alternate or Cladosporium were given SIT with mold extracts during the past 5 years. The level of asthma control, Asthma control test (ACT), Asthma Control Questionnaire (ACQ), medication scores and FEV₆% were regularly assessed and compared for pre- and after SIT among the patients. Adverse reactions were also recorded.

RESULTS: Twenty-four patients completed the study. 62.50% asthma patients were well controlled after SIT for 1 year, and 80.00% for 2 years, statistic significantly higher than baseline (33.33%). ACT and ACQ scores were significantly improved than baseline after SIT for 1–4 years (P<0.01). The FEV₆% ([90.79±8.57]% at baseline was statistic significantly increased than before ([72.04±11.90]%), but there was no significant difference compared with FEV₆% after SIT (P>0.01). The medicine scores after 2-year SIT were significantly lower than baseline (P<0.01), and continued to decline gradually during immunotherapy. The incidence of local adverse reactions was 1.4% among 6203 injections of 24 patients, and mild systemic adverse reactions were observed in 5 cases.

CONCLUSIONS: Specific Immunotherapy with mold extracts led to reduced asthma symptoms, reduced medication use, and well maintained lung function. It is an effective and safety treatment for allergic asthma patients.

670 Clinical validation of Environmental Exposure Chamber in Strasbourg (ALYATEC®) with cat in asthmatic patients

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RATIONALE: As recommended by the Task Force on Environmental Exposure Chamber (EEC), allergenic and non-allergenic exposure must be better controlled in EEC.

AIM: To validate Strasbourg EEC by determining the concentration of Fel d1 inducing 50% of early asthmatic response (EAR) and/or late phase asthmatic response (LAR) in subjects sensitized to cat.

METHODS: It was a randomized, double blind, cross-over study including group A:20 asthmatic subjects allergic to cat and group B:10 asthmatic subjects allergic to another allergen. All subjects were first exposed to placebo. Group A was exposed to 2 Fel d1 concentrations. The number and size of particles were recorded online during the exposure. Group B was exposed to the concentration of Fel d1 which fulfills the objective of the study.

RESULTS: The mean age of subjects was 29 years (±8). For the 2 concentrations of Fel d1 we obtained more than 50% EAR and/or LAR. The mean time necessary to obtain an EAR was: 59.7 ±8 min and 138.6±90 min for the LAR. The mean fall in FEV1 during EAR and LAR was -29,22% and -17,64% respectively. We didn’t observe any severe reaction. No subjects in group B experienced any symptoms during exposure.

CONCLUSIONS: We have validated ALYATEC’s EEC in subjects with asthma sensitized to cat. We also demonstrated its specificity. That is of interest for future clinical studies with asthmatic treatments.

671 Managing Inner City Asthma with Sublingual Immunotherapy: A Retrospective Chart Review

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RATIONALE: A retrospective chart review has been conducted for 38 inner city asthmatics whose asthma and allergic rhinitis have been managed by sublingual immunotherapy (SLIT) and medication therapy for six months. Just as with traditional subcutaneous immunotherapy (SCIT), a three to five year course of treatment is recommended with SLIT to generate the most effective and lasting tolerance to allergens.

METHODS: The inner city asthmatic population is difficult to manage on traditional SCIT as there is a high attrition rate in therapy due to discontinuation/lapses of insurance coverage, lack of transportation, language barriers, lack of tolerance and noncompliance. By treating this population with SLIT, some of these factors are ameliorated as the patient has less frequent office visits and there is better tolerability than with traditional SCIT.

RESULTS: There was an average increase in FEV1 of 21% after six months of SLIT in 24 subjects. There was an average increase in ACT scores of 20% after six months of SLIT in 16 subjects. There was an average decrease in TSS of 28% after six months of SLIT in 36 subjects. 46% of patients had a decrease in asthma medication use after six months of SLIT in 38 subjects.

CONCLUSIONS: These results are encouraging and suggest that this modality of therapy should be seriously explored in the management of bronchial asthma in this population.
Evaluation Of The Device Mechanics And Inspiratory Flow Rate Required Of The Beclomethasone Dipropionate Breath-Actuated Inhaler

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RATIONALE: A new, breath-actuated inhaler (BAI, QVAR® RediHaler™) has been developed to deliver beclomethasone dipropionate hydrofluoroalkane (BDP HFA) solution. The BAI eliminates the need for hand-breath coordination, which remains a concern with poor inhalation technique. Device mechanics and the minimum reliable inspiratory flow rate required to trigger an actuation of the BAI were evaluated.

METHODS: Device development and optimization was completed through Drug Product Characterization studies. The inspiratory flow rate required was evaluated among 3 batches each of BDP BAI 40 and 80 mcg. Air was drawn through the devices at flow rates from 12 L/min to 20 L/min, in 2 L/min increments. The inhaler was weighed before and after each test to determine actuation (60 mg weight difference confirmed actuation).

RESULTS: Main components of the BAI includes: mouthpiece cover, to maintain cleanliness when not in use and prepare the device for the next metered dose when opened; canister, contains the pressurized inhalation solution; primeless valve, allows for primeless metering for the delivery of metered dose when opened; canister, contains the pressurized inhalation solution; primeless valve, allows for primeless metering for the delivery of metered doses and the Force Holding Unit, provides sufficient energy to actuate the canister during inhalation. Evaluation of the inspiratory flow rate required to actuate was conducted on ten inhalers in each of the 6 batches. Across the 40 mcg batches, 83.3% actuated at 16 L/min and all actuated at 18 and 20 L/min. Among the 80 mcg batches, 66.7% actuated at 18 L/min and all actuated at 20 L/min.

CONCLUSIONS: BDP BAI was designed for easier administration and is actuated with a minimum inspiratory flow rate of 20 L/min.

Improvement Of Lung Function As Early As Day 1 With Beclomethasone Dipropionate Breath-Actuated Inhaler In Patients With Persistent Asthma

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RATIONALE: Guidelines recommend inhaled corticosteroids as daily maintenance for patients with persistent asthma. Post-hoc analysis was conducted to evaluate improvement of lung function with beclomethasone dipropionate (BDP) via a new, breath-actuated inhaler (BAI, QVAR® RediHaler™).

METHODS: Phase 3, 6-week, double-blind, placebo-controlled trial (NCT02513160) evaluated efficacy of BDP BAI in patients ≥12 years with persistent asthma. Following a 14- to 30-day single-blind run-in period (asthma medication discontinued), patients were randomized to BDP BAI (320 mcg/day, 640 mcg/day), BDP metered dose inhaler (MDI) 320 mcg/day or placebo. Daily trough morning forced expiratory volume in 1 second (FEV1) and peak expiratory flow (PEF) were evaluated pre-dose by handheld spirometry at home. Safety was monitored.

RESULTS: Primary and secondary endpoints were statistically significant with active treatments versus placebo. Change from baseline in weekly average of daily trough morning FEV1 was significant for active treatments versus placebo over 6-weeks (p<0.001). Weekly average of daily trough morning PEF also demonstrated significant changes from baseline versus placebo over 6-weeks (p<0.001). Post-hoc analysis evaluated 425 patients. Differences from placebo were revealed for FEV1 and PEF with active treatments starting day 1 (BAI 320 mcg/day: 129 mL, 14.3 L/min; BAI 640 mcg/day: 71.9 mL, 14.9 L/min; MDI 320 mcg/day: 89.4 mL, 9.5 L/min, respectively) and maintained throughout the treatment period. Sustained onset of action (significant change in FEV1 over two consecutive days versus placebo) was observed starting day 2. No new safety signals.

CONCLUSIONS: Treatment effect of BDP BAI was evident as early as day 1 and maintained for the 6-week treatment period.
675 Long-term follow-up of patients with aspirin-exacerbated respiratory disease status post-desensitization

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RATIONALE: Aspirin desensitization and continuous daily aspirin is the gold standard treatment for aspirin-exacerbated respiratory disease (AERD). We compared the long-term effects of different maintenance doses of aspirin and assessed the success of bridging AERD subjects for surgery with ibuprofen to prevent losing desensitization.

METHODS: We retrospectively assessed 34 subjects with AERD who successfully underwent aspirin desensitization from 2011-2017. We performed comprehensive medical record reviews and subsequent phone interviews with standardized questionnaire.

RESULTS: Of 34 subjects, 65% were female, with average age of 52.8 years, and average of 3.2 years since desensitization. Subjects reported decrease in frequency of nasal symptoms (p<0.001), asthma (p=0.016), and sinus infections (p<0.001) post-desensitization. Improvements were reported in sense of smell, taste, quality of sleep, and quality of life (p<0.001). Difference in benefits was not observed between subjects on 325 mg compared to 650 mg of daily aspirin. Ten subjects required bridging of aspirin for 15 surgeries, but only 8 of 15 (53%) were bridged. Subjects were bridged with ibuprofen on average 5.5 days before surgery, restarted aspirin on average 1.9 days after surgery, with no incidence of adverse events or loss of desensitization.

CONCLUSIONS: No difference in benefits was observed between 325 mg compared to 650 mg of daily aspirin doses. Bridging AERD patients who require surgery with ibuprofen is safe and effective in maintaining aspirin desensitization.

676 Effects Of Exposure To New Car Interiors On Patients With Asthma And Allergic Rhinitis

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RATIONALE: Volatile organic compounds, particulate matter, odors and pollutants in the interior of new vehicles have been postulated to exacerbate asthma and allergic rhinitis. This study evaluated the subjective and objective physiologic and clinical effects of exposing subjects with concomitant asthma and allergic rhinitis to new 2017 Mercedes vehicles during 90-minute rides.

METHODS: After signing informed consent, ten adult asthmatics with allergic rhinitis were assessed at baseline and 45 and 90 minutes into a ride in a 2017 Mercedes Benz S-Class sedan and GLE-Class SUV on two separate days. Assessments included spirometry, fractional exhaled nitric oxide (FeNO), peak nasal inspiratory flow (PNIF), asthma symptom scores, and physical examinations.

RESULTS: Of the 10 subjects, 6 were female, mean age was 32, and 6 and 4 were using chronic asthma controllers or intranasal corticosteroids, respectively. None of the subjects had worsening of asthma or rhinitis symptoms during the rides. There were no statistically significant changes from baseline in FEV1, FEV1/FVC, FEF 25-75, FeNO, or PNIF at 45 or 90 minutes into the rides with either Mercedes vehicle (all p-values > 0.1 using generalized linear mixed model). No changes were noted on physical examination and no adverse events were reported.

CONCLUSIONS: The interior environment of the tested Mercedes vehicles did not cause changes in subjective or objective measures of asthma and allergic rhinitis. We suggest that this model can be used to determine whether other new vehicle types provide safe environments for patients with asthma and allergic rhinitis.

677 Asthma remission in North America: from childhood to adulthood

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RATIONALE: Few data exist on the longitudinal history of childhood asthma and predictors of asthma remission in adulthood in North America. This study aimed to define the prevalence and predictors of asthma remission from childhood to adulthood in an ethnically diverse population of mild-to-moderate persistent asthmatics.

METHODS: Adult asthma remission was measured using two remission definitions, a loose and a strict definition. Both included normal percent predicted lung function and the absence of symptoms, exacerbations, and medication use. The strict definition also included normal airway responsiveness. Predictors of remission were identified from 23 baseline measures using multinomial logistic regression.

RESULTS: Of 879 participants, mean baseline age was 8.8 years (SD ± 2.1), 59.4% were males, and 68.7% were Caucasian. In adulthood, 229 (26.0%) of 879 participants were in loose remission and 111 (15.0%) of 741 participants were in strict remission. Both definitions were associated with decreased baseline airway obstruction (loose remission OR 4.62, 95% CI 3.35-6.50; strict remission OR 5.71, 95% CI 3.58-9.45) and airway hyperresponsiveness (loose remission OR 1.23, 95% CI 1.09-1.39; strict remission OR 1.52, 95% CI 1.26-1.84). Females with less airway obstruction had higher odds of loose remission than males (females OR 8.03, 95% CI 4.60-14.93; males OR 3.88, 95% CI 2.62-5.92). Strict remission was inversely associated with serum IgE level (OR 0.88, 95% CI 0.78-1.00) and positive aeroallergen skin testing (OR 0.48, 95% CI 0.24-0.97).

CONCLUSIONS: A large minority of persistent childhood asthmatics will undergo disease remission. Predictors of asthma remission at adulthood can be seen from an early age.
Chicago Public School Nurse Opinions About School Asthma Care Coordination

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RATIONALE: Asthma disparities are well documented in Chicago. Chicago Public Schools (CPS) is the 4th largest school district in the country and serves predominately minority children.

METHODS: Coordinated Healthcare for Complex Kids (CHECK) is a large health care demonstration project funded by a Centers for Medicare and Medicaid Services Health Care Innovation Award. A collaborative partnership was formed between medical directors in CHECK and CPS nurse administration to address asthma disparities. With CHECK support, CPS administered a survey in December 2016 to 160 school nurses in order to understand the asthma problems nurses perceived and their interest in intervention options. Data included Likert scale questions and open-ended queries. Analyses were conducted using SAS 9.4.

RESULTS: Seventy-five percent of nurses completed the survey. While asthma was a top diagnosis managed by 95% of respondents, 72% felt gaps existed in their understanding of asthma. Appropriate communication between school nurses and providers was reported 33% of the time; 18% of nurses believed that they receive the support needed to follow-up on deficient paperwork. In open-ended responses, the most common barriers mentioned were lack of medications (73%), time (67%), and communication (61%). When asked their opinions on a variety of interventions, 78% of nurses supported a web-based application, 66% supported community health workers, 66% supported stock albuterol policy for schools, and 61% supported directly observed therapy.

CONCLUSIONS: The greatest barriers for CPS school nurses with asthma management are time and communication. Potential interventions such as web-based communication applications and community health workers involvement in schools were well received.

Asthma and Anaphylaxis Preparedness in K-12 Schools

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RATIONALE: Asthma accounts for more than 10 million days of missed school every year, and more than 15% of children with food allergy have a reaction at school. Despite the broad reach of these diseases, many K-12 schools lack the clinician-to-classroom bridge to help improve care for these children. That bridge begins with assessing the state of asthma and allergy management in the schools.

METHODS: Two school systems (34 schools) were invited to complete an assessment on asthma and food allergy management in their schools. The assessment was completed in the first school system via Excel spreadsheet, then the assessment was refined and adapted into Qualtrics software for the second school system. The questions were completed by school nurses; information had been provided to school nurses through collaboration on education, beginning to bridge the clinic to the classroom.

CONCLUSIONS: Schools would benefit from physician support in preparing for asthma and allergy emergencies. Physicians can provide support to schools through collaboration on education, beginning to bridge the clinic to the classroom.

CHRONIC RHINITIS AND THE RISK OF EARLY ASTHMA READMISSION - A RETROSPECTIVE COHORT STUDY

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RATIONALE: Early hospital readmission (i.e., within 30-days of index admission) concerns most healthcare stakeholders. Comorbid conditions increase the risk of such readmissions. The characteristics of 30-day asthma-related readmission rate (30d-AR-RR) and the comorbidities significantly influencing the risk were investigated in this study. Objectives were to examine the hypothesis that allergic/non-allergic rhinitis (AR/NAR) among other comorbidities can influence 30d-AR-RR.

METHODS: A retrospective hospital-based database study was performed using the University of Cincinnati Hospital (UCH) data from all-payer hospital inpatient stays of patients aged 3-99, hospitalized for asthma exacerbation between mid-2012-mid-2017. Initially, all asthma-related admissions were extracted from the database. Those patients readmitted ≤30-days at UCH and their comorbidities were identified. Primary outcome was 30d-AR-RR between AR/NAR vs. non-rhinitis patients. Chi-square test and multivariate logistic regression were used to examine associations between 30d-AR-RR and patient demographics or comorbidities.

RESULTS: Between 2012-2017 there were 10,111 asthma-related hospital encounters. Of these, 1,670 (16.52%) were readmissions within 30-days. Specifically, the odds of 30d-AR-RR were significantly higher in patients with AR/NAR [vs. non-rhinitis patients; OR = 4.3 (AR), 4.9 (NAR) p<0.0001] after adjustment for significant other comorbidities (i.e., tobacco smoking). The average number of 30d-readmissions for AR/NAR were ~5.4/5.8 (vs. 1.7/1.9 for non-rhinitis). The cumulative risk of 30d-AR-RR also was significantly higher for AR/NAR patients.

CONCLUSIONS: Asthma is a high-priority health and economic burden in the US. Early readmissions worsen this burden. Comorbid chronic rhinitis had a significant effect on the 30-d-AR-RR suggesting that further investigation is warranted to determine if its proper diagnosis and treatment reduces related healthcare costs.
681 Highest Level of Household Education is Associated with Asthma Action Plan Receipt in an Urban School-Based Cohort

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RATIONALE: Previous studies have identified that most asthmatic children do not have written asthma action plans (AAPs), which serve as a self-directed tool of asthma management/communication between physicians and school nurses. We evaluated the predictors of AAPs in urban school-age asthmatic children.

METHODS: School Inner-City Asthma Study is a NIH/NIAID prospective cohort evaluating school/classroom-specific environmental factors and asthma morbidity of urban asthmatic children 4-13 years. Baseline surveys were conducted of 351 enrolled students evaluating demographics, clinical symptoms and health care utilization. Logistic regression was used to determine the clinical and socioeconomic predictors of AAPs.

RESULTS: Among 351 enrolled asthmatic students, 37% denied AAP receipt. Compared to students with AAPs, students without AAPs had significantly higher proportion of: household educational level attained (72.8% vs 85.5% with at least GED/HS diploma, p = 0.005); being on ICS (38.4% vs 65.2%, p = 0.0001). Students without AAPs also had significantly higher proportion of: no routine asthma follow-up care (15.5% vs 3.5%, p = 0.001). A significantly higher proportion of students with AAPs reported seeing a specialist that prescribed their asthma medicines (% vs 2.6%, p = 0.005). In the final multivariate logistic regression model, highest household educational level (OR 1.27, CI 1.04-1.55); being on ICS (OR 1.9, CI 1.07-3.38); and place of routine asthma care (OR 0.3, CI 0.09-0.94) were significant predictors of AAP receipt.

CONCLUSIONS: Highest household educational level attained, being on ICS and place of routine asthma care were significant predictors of AAP receipt, suggesting that sociodemographics and access to care are integral to outcomes in this inner-city school-based cohort.

682 Title: Association between Obstructive Sleep Apnea and Allergen Sensitization in Pediatric Asthmatic Patients

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RATIONALE: Whether obstructive sleep apnea (OSA) is associated with presence of allergic disease is not fully known. Research has shown that allergic rhinitis is a risk factor for snoring in children and allergic rhinitis might worsen OSA in adults. However there have been no studies on the association between OSA and allergen sensitization in the pediatric age group.

METHODS: This is a retrospective case-control study (2010-2013) of pediatric asthmatic patients (1-21 years) treated in a university-based pediatric asthma clinic. OSA was diagnosed in 48 out of 78 patients who were referred for a sleep study with apnea hypopnea index (AHI) >1.5. Specific IgE for aeroallergen sensitization (ImmunoCAP®) was measured. Data were analyzed using t-tests and Chi-square tests.

RESULTS: 75% of children had a positive ImmunoCAP® test indicating sensitivity to allergens in our cohort. Patients with positive ImmunoCAP® tests had significantly higher hypopnea index (p = 0.03) but not AHI. There were no significant differences in allergen sensitization, total IgE, absolute eosinophil count, eosinophil percentage, asthma severity or BMI in OSA group compared to non-OSA group. The most common sensitized allergens were dust mite and cockroaches in the OSA group and dust mite and mouse in non-OSA patients. There was higher prevalence in perennial allergen sensitization (dust mites and animal dander) in the non-OSA group compared to OSA group (60.7% vs 35.4% respectively, P = 0.15).

CONCLUSIONS: Allergen sensitization complicates sleep disordered breathing with hypopneas but is not a significant risk factor for OSA in our cohort. A higher prevalence in perennial allergen sensitization was noted in non-OSA patients.

683 Comparison of epidemiological characteristics and medical utilization of asthma-predominant ACO(Asthma COPD Overlap) and COPD

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RATIONALE: Asthma-COPD overlap (ACO) is a disorder in which features of asthma and COPD are mixed, and the definition, characteristics and the socio-economic burden of the disease are still controversial. Thus we sought to compare the epidemiological characteristics and medical utilization of asthma-predominant ACO (A-ACO) and COPD.

METHODS: In the Korean National Health and Nutrition Examination Survey (KNHANES) conducted between 2007-2012, subjects who have FEV1/FVC < 0.7, FEV1 ≥ 50% over 40 years were included. Wheezing was indicated as presence (W+) or absence (W-), and smoking history was defined as S+ if subject was a smoker >10 pack-years and S- if subject was a never or ex-smoker <10 pack-years. The subjects were divided into 4 groups of W-S-, W-S+, W+S-, W+S+; W+S+ and W+S+ were regarded as an A-ACO and COPD, respectively. KNHANES and linked National Health Insurance data was analyzed.

RESULTS: Subjects aged 50 to 70s were more frequent in W+S+ group. Socioeconomic status (SES) was the lowest in the W+S+ group. Regarding the health-related quality of life (QOL), it was the poorest in the W+S+ group. Almost fundamental nutrients intake were decreased in the W+S+ group. Otherwise, costs and number of outpatient visits and total medical used days were the highest in the W+S+ group.

CONCLUSIONS: A-ACO group seems to suffer from poorer SES, malnutrition, and lower QOL than COPD groups. In addition, access to medical care is also lower than that of COPD patients. It seems that A-ACOS patients need more social and medical support and attention of government.
684 Influence of anxiety and depression in asthma control in Ecuador

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RATIONALE: Proper understandings of local factors related with poor asthma control are fundamental to care givers in order to develop health strategies. Recent literature says that anxiety and depression are common among patients with poor control asthma. It is imperative to acknowledge that cultural differences from country to country may impact in this association.

METHODS: It is an Observational, descriptive, anonymous cross-sectional survey study, conducted in the outpatient Respirology department of private hospitals in Ecuador. Patients with physician based diagnosis of asthma that agree to participate, filled the Spanish versions of the Hospital Anxiety and Depression Scale (HADS) and Asthma Control Test (ACT) questionnaires, previous or during his Respirology consult. Descriptive statistic was used to asses’ demographical data, and chi-square test was use to asses any association between emotional disorders and asthma control.

RESULTS: 73 patients finished both HADS and ACT questionnaire: mean age of patients with asthma was 55 years. 75.3% of the patients were female. Almost 70% of the patients had a high school degree or an elementary one. 13.7% of the patients smoked cigarettes’, with a mean of cigarettes smoked per day of 15.

Regarding to asthma control, 65.8% had a poor control. We found only a 2.7% of patients with anxiety and a 1.4% with depression. After doing the chi-square analysis we didn’t find any association among these variables in our population.

CONCLUSIONS: There are a high percentage of patients with poor asthma control but depression and anxiety does not seem to be associated with this phenomenon in our country.

685 Prevalence of Long Term Opioid Use in Patients with Asthma and Allergic Rhinitis

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RATIONALE: Opioids are known to increase histamine release from mast cells involved in asthma and allergic rhinitis. Opioids stimulate T cell responses via immune system polarization toward IgE promoting TH2 cytokine pathway.

METHODS: We conducted a retrospective chart review of patients (age 18-80) from inpatient, emergency room and ambulatory surgery settings at Kings County Hospital in Brooklyn, NY from 2013 through 2017. ICD coding for opioid abuse/dependence, chronic pain conditions (chronic pain syndrome, osteoarthritis, joint disorder, fibromyalgia), asthma, and allergic rhinitis were obtained. We determined the percent of these patients having asthma/allergic rhinitis as well as chronic opioid use, which was determined by the presence of opioid prescription.

RESULTS: In patients with opioid abuse/dependence (n=1977), 18% had asthma. There were more males than females in patients with opioid abuse/dependence without asthma (73% vs. 27%) and with opioid abuse/dependence with asthma (56% vs. 44%) [Chi square analysis, p<0.001]. In patients with chronic pain conditions (n=3259), 7% had asthma, and less than 1% had allergic rhinitis. There were more females than males in patients with chronic pain conditions without asthma (64% vs 36%) and with asthma (75% vs 26%) [Chi square analysis, p<0.05]. In patients with chronic pain conditions and asthma/allergic rhinitis, 51% had opioid prescriptions. 68% with opioid prescriptions were female.

CONCLUSIONS: We showed that the prevalence of asthma in patients with opioid abuse/dependence was higher than the national prevalence of asthma. The prevalence of opioid abuse/dependence is known to be higher in males, so females are more likely to use prescribed opioid for non-cancer pain.

686 Characterization of the impact of Stress Exposure on Asthma in African American Children

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RATIONALE: African-American children are almost twice as likely to be diagnosed with asthma as non-Hispanic white children and mortality rates are 7.6 times higher. Studies revealed that Adverse Childhood Experiences (ACEs) have long term effects in children, including increased odds of asthma diagnosis. We aimed to determine if there is an association between chronic stress and asthma control in African-American children.

METHODS: We conducted a cross-sectional pilot study among parent/guardians of African-American children age 1-6 years with an asthma diagnosis who attend an urban Head Start program to determine the association between parental chronic stress and child asthma control. Chronic stress domains were assessed by parental report via questionnaires regarding the following: parental City/Urban related stressors, Depression, Racial Discrimination, and ACEs; and child/family Housing and Food Security. Correlation coefficients were used to assess associations between questionnaire scores and the Test for Respiratory and Asthma Control in Kids (TRACK) scores.

RESULTS: Sixteen child and parent/guardians completed TRACK and stress questionnaires, with mean±SD TRACK scores 66±20; 47% previously required hospitalization of which 30% required intensive care. Fifty-five percent of parents had experienced >4 ACEs. An inverse relationship existed between TRACK score and ACE, food insecurity, and lifetime racial discrimination scores (r = -0.61; r = -0.50; r = -0.74 respectively, unadjusted ps = .012, .046, .001).

CONCLUSIONS: ACEs, food insecurity, and racial discrimination may be important contributors to the morbidity experienced by African American children with asthma. Interventions to address these factors in children and their families may improve asthma outcomes in this population.
687 Patient Needs Assessment in an Inner-City Pediatric Asthma Disease Management System

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RATIONALE: Unanticipated patient needs may be the reason inner city children do not attain asthma control. We hypothesize existence of significant unmet patient needs in a focused asthma disease management program.

METHODS: As part of quality improvement project a 30 question English and Spanish survey instrument assessing needs of asthmatic patients were administered to caretakers of asthmatic pediatric patients from 10/16 to 02/17 followed at an asthma disease management program in the greater Los Angeles area. Needs assessment was scored on a scale of 1–10. A secondary assessment of patient satisfaction was also included to assess patient satisfaction with providers, nursing and pharmacy care also on a scale of 1-10.

RESULTS: 843 surveys were given out and 580 returned (44% return rate). Needs identified (those with a significantly low mean score) were: Ability to afford medication co-pays, ability to obtain medical equipment (spacer and nebulizers), ability to make same day urgent appointments and ability to find parking at provider sites. Only pharmacy care received a low patient satisfaction score (significantly low mean score).

CONCLUSIONS: Results show that external factors unrelated to the quality of medical care may significantly impact ability of inner city asthmatic children to achieve asthma control. Patients were very satisfied with the interactions with the care team and medical care/education they received. Strategies aimed at improving unmet patient needs such as such as availability of parking, paying for medication, and acquiring medical devices may result in improved asthma control among inner city asthmatic children.

688 Asthma Control, Viral Infections, and Severity of Asthma Exacerbation Symptoms in Children Seen in the Emergency Department

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RATIONALE: While rhinovirus (RV) infection is shown to be associated with asthma exacerbations, prior research has not identified reliable predictors of acute symptom severity in virus-related asthma exacerbations. We enrolled 97 subjects with asthma exacerbations in the emergency department (ED) to evaluate the effect of pre-existing asthma control on the severity of current illness.

METHODS: We prospectively enrolled children with physician diagnosed asthma and current wheezing who presented to Arkansas Children’s Hospital ED. The Asthma Control Test (ACT) was used to stratify well (ACT≥19) and poorly-controlled (ACT<19) asthma, while Pediatric Respiratory Symptoms Score (PRSS) and Modified Jackson Criteria (MIC) were used to assess current symptoms. Nasopharyngeal swab samples were obtained for viral PCR and genome sequencing.

RESULTS: There were 28 well-controlled and 69 poorly-controlled asthmatics. Sixty-seven percent tested positive for a viral infection, RV most commonly (39.2%). Of those with poor control, 71.4% were infected vs. 60.7% of those with good control. In virally infected subjects, those who were poorly-controlled demonstrated more acute symptoms as compared to those who were well-controlled as measured with PRSS and MIC (p<0.05). The PRSS detected more acute symptoms in the poorly-controlled asthmatics with viral infection than those poorly-controlled asthmatics without infection. Subjects with well-controlled asthma and RV-induced exacerbations had higher viral loads than those with poor control (p<0.05).

CONCLUSIONS: Virally infected poorly-controlled asthmatics demonstrate more symptoms during exacerbations by PRSS and MIC, even when compared to uninfected poorly-controlled asthmatics. With RV infection, those with well-controlled asthma have higher viral loads than those with poorly-controlled, suggesting intact immune responses.

689 Morbidities Associated with Chronic Oral Glucocorticoid Exposure in Children with Asthma: A Real-World Analysis of Medical and Pharmacy Claims

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RATIONALE: Although a mainstay of asthma therapy, oral glucocorticoids (OG) may increase risk of morbidities in children. We aimed to assess the possible adverse events (PAE) of chronic OG (C-OG) exposure in a large claims dataset of children with asthma.

METHODS: We identified continuously-enrolled privately-insured children (6-17 y.o.) with asthma (ICD-9-CM: 493.xx) who did or did not initiate C-OG (>15-day continuous use) during 2009-2014. We excluded subjects with C-OG or chronic PAE 12 months before initiating C-OG. We used Cox proportional hazard model to estimate PAE relative risk, adjusted for: cumulative-dose ICS, other prescription glucocorticoids (topical, inhaled, IV), number of ICD-9 diagnoses, number of national drug codes, demographics, and treatment year.

RESULTS: Among 2,376 C-OG initiators (mean age: 10.5 years; 62.0% male), the mean cumulative prednisone-equivalent exposure (PEqE) totaled 1,125.5 mg/year; 21.8% used high-dose ICS. Among 7,584 children without C-OG (mean age: 10.5 years; 61.6% male), mean PEqE comprised 178.6 mg/year (OCS bursts); 12.2% used high-dose ICS.

The following PAE’s were associated with C-OG exposure (adjusted relative risk): adrenal insufficiency, 12.13 (p<0.0001), recurrent pneumonia, 1.97 (p<0.0001), gastrointestinal disorders, 1.68 (p<0.0001), persistent cough, 1.67 (p<0.0001), behavioral problems, 1.37 (p=0.0002), sleep disorders, 1.45 (p=0.0156), sinusitis, 1.17 (p=0.0068). Other PAE were studied, but did not demonstrate statistical significance: bone related events (fracture, osteoporosis, osteopenia), fracture, hypertension, short stature, obesity, oropharyngitis.

CONCLUSIONS: Children with asthma treated with chronic oral glucocorticoids experience significant morbidities, including adrenal suppression, recurrent pneumonia, and behavioral problems. In appropriate patients with uncontrolled asthma, clinicians should consider effective alternative treatments to avoid these potential complications.

All abstracts are strictly embargoed until the date of presentation at the 2018 AAAAI/WAO Joint Congress.
690 Does Level of Allergen Sensitization Impact Asthma Related Outcomes Differently in Adult and Pediatric Asthma Patients?

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Rationale: Studies have shown that environmental allergen sensitivity is an asthma risk factor. However, studies in severe asthma suggest the presence of specific IgE responses may be “protective” in relevant asthma outcomes. It is unknown whether there are differences in adults versus children.

Methods: 101 asthmatics [77 adults, 24 pediatric] were enrolled in the Severe Asthma Research Program at the Pittsburgh site. We analyzed the relationship between number of positive environmental allergens based on serum specific IgE testing in adult and pediatric asthmatics, comparing those with and without a history of an ED visit or hospitalization in the previous year.

Results: Pediatric asthmatics had a greater number of total allergens vs. adult asthmatics (median 7 vs. 3, p=0.007). In adult asthmatics, patients with no ED visits had more positive environmental allergen tests than those who had visited the ED (median 3 vs. 1, p=0.044) versus no difference in the pediatric asthmatics (p=0.79). Similarly, adults who had been hospitalized in the previous year had fewer positive environmental allergen specific IgE tests than those who had not been hospitalized (median 3 vs. 1, p=0.027), while there were no differences in number of allergens in children with or without a history of a hospitalization, (p=0.25).

Conclusions: In adult asthma, sensitization to a greater number of environmental allergens does not increase the risk of asthma exacerbations, and may be protective. However, in children, the number of positive tests does not seem to influence the risk for exacerbations. This suggests differences in asthma pathobiology in adults and children.

691 The Impact of Patient Autonomy on Older Adults with Asthma

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Rationale: Understanding patient preferences and desire for involvement is crucial in managing medical conditions. Previous studies have utilized the Autonomy Preference Index (API) in younger patients with asthma to evaluate and recognize their preferences. The purpose of this study was to assess whether the API score can impact asthma related outcomes among older adults with asthma.

Methods: 189 older adults (>55) with persistent asthma were included. Preferences for autonomy were assessed using the API, with a higher score indicating a higher desire for autonomy. Scores were separated into the two domains of ‘information seeking’ preferences and ‘decision making’ preferences. The separated scores were correlated with asthma specific outcomes and demographic variables. To further control for confounding variables, a linear regression analysis was performed.

Results: Higher decision making preference scores were correlated with male gender (p=0.007), higher spirometry values (p=0.07), higher asthma quality of life questionnaire (AQLQ) scores (p=0.01), and lower depression scores (p=0.04). On linear regression analysis, only the AQLQ score remained significantly associated with the decision making preference score (p=0.02). There was no association with ACT score, spirometry values, and healthcare utilization. There was no correlation with information seeking preference scores and other variables.

Conclusions: A higher decision making preference score of the API is associated with a higher quality of life in older adults with persistent asthma. Further longitudinal studies may help establish a potential causal relationship.

692 Atopic Sensitization and Inflammation in Depressed versus Non-depressed Asthmatic Children

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Rationale: Asthma is the most prevalent chronic disease of childhood. While most child asthmatics are atopic, a small subset are non-allergic. Depression is seen more frequently in asthmatics compared to the general population and is associated with unfavorable asthma outcomes, including medication nonadherence, increased emergency room visits, hospitalizations, and even asthma-related death. Comorbid depression may be associated with decreased response of asthma to bronchodilators or corticosteroids. We assessed atopic sensitization and inflammation in depressed vs non-depressed asthmatics to investigate whether children with depression have evidence of distinct underlying asthma pathology.

Methods: Eighteen children with asthma ages 7 to 17 years were evaluated for depressive symptoms using the Children’s Depression Inventory (CDI). Markers of inflammation including exhaled nitric oxide (FeNO) and peripheral blood eosinophils (PBE) were compared in depressed vs non-depressed groups. Atopic status and allergic sensitization were evaluated by total serum IgE (TSE) and skin prick testing (SPT) to environmental allergens.

Results: There was no significant association between depressive symptom score and in the degree of inflammation measured by FeNO or PBE. TSE and number of SPT was not significantly different in depressed versus non-depressed child asthmatics in our study population.

Conclusions: Evidence exists that depression worsens asthma outcomes and predicts non-responsive to typical asthma therapies. Children with high CDI scores, suggestive of depression, have similar markers of inflammation and atopic sensitization as children without evidence of depression on the CDI. However, larger sample sizes will be needed to truly differentiate whether the inflammation in depressed asthmatics is distinct from that in non-depressed asthmatics.
**693 Asthma Does Not Explain A Decline In Post Bronchodilator Lung Function In Early Adult Life**

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**RATIONALITY:** Using the Isle of Wight Birth Cohort (IOWBC), we investigated lung function deficits in young adults with asthma to identify whether airways obstruction in that group accounted for a decline in post-bronchodilator lung function within the overall population seen by 26 years.

**METHODS:** The IOWBC is a population based cohort (n=1456), recruited in 1989-90 and assessed at birth, 1, 2, 4, 10, 18 and 26 years for asthma, allergic diseases and environmental exposures. Spirometric lung function tests were carried out using standardized methodology at 18 (n=839) and 26 years (n=555) before and after inhaled bronchodilator (salbutamol 400mcg). Forced vital capacity (FVC), forced expiratory volume in one second (FEV\(_1\)), FEV\(_1\)/FVC ratio and mid-expiratory flows (FEF\(_{25,75}\)) at 26 years plus changes in these indices between 18 and 26 were assessed. Asthma was defined as physician diagnosis plus current wheeze and/or treatment.

**RESULTS:** Pre-bronchodilator FEV\(_1\), FEV\(_1\)/FVC, and FEF\(_{25,75}\) were all significantly reduced (P<0.001) in those with asthma (3.52L, 0.73 and 3.11L) compared to those without asthma (3.90L, 0.73, and 3.89L). However, there was no significant difference in post-bronchodilator FEV\(_1\), FEV\(_1\)/FVC, and FEF\(_{25,75}\) between the two groups.

**CONCLUSIONS:** Airways obstruction at 26 years of age is usually fully reversible in most people with asthma. An observed decline in post-bronchodilator FEV\(_1\), FEV\(_1\)/FVC, and FEF\(_{25,75}\) from 18 to 26 years in this cohort therefore does not appear to be accounted for by the influence of asthma.

**694 Oral Habits and Association with Lower Rate of Asthma and Seasonal Allergies**

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**RATIONALITY:** Environmental exposures play a role in the development of allergic disease and oral route of exposure generally induces tolerance. Children with oral habits such as thumb-sucking, chewing on objects or nail-bitng introduce antigens into the gastrointestinal tract orally. Previous studies have shown that some of these behaviors are associated with less atopic sensitization, however, the relationship between oral habits and food allergy has not been examined. We hypothesize that children with oral habits would have lower risk of food allergy and atopic disease in general.

**METHODS:** Patients at a university-based pediatric allergy clinic with a history of eczema that were 10 years old or younger were eligible for the study. Parents filled out a questionnaire during the clinic visit. The questionnaire included information about the parents’ and children’s oral habits, environmental exposures, and allergic disease history.

**RESULTS:** So far 84 questionnaires have been collected and analyzed. Children who had a habit of chewing on objects had significantly lower rates of asthma (p=0.002) and seasonal allergies (p=0.025). There was no significant difference in the rate of food allergy between groups with and without oral habits.

**CONCLUSIONS:** The habit of chewing on objects as a child is associated with a lower risk of asthma and seasonal allergies. Data collection continues to increase our sample size.

**695 Comparative Cost Analysis of Monitoring Exhaled Nitric Oxide (FeNO) in Asthma Management**

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**RATIONALITY:** Asthma guidelines recommend periodic assessment and management of symptoms to prevent exacerbations, which can lead to hospitalization, increased healthcare utilization and cost. According to recent Cochrane meta-analysis data, FeNO monitoring is associated with a 40-50% reduction in the risk of exacerbations. Cost modelling of these data indicated the potential for significant cost savings with FeNO use. Therefore we attempted to verify this potential for cost savings within a real-world database of Medicare recipients.

**METHODS:** This retrospective observational study investigated asthma-related claims from a Medicare database. Patients were included that had 2 years of records following an asthma-related inpatient hospitalization (IP) or emergency department (ED) claim and had a history of an asthma-related event in the prior year. A case-crossover analysis was completed of asthma-related IP/ED events before and after FeNO use during the two-year study period.

**RESULTS:** 63 patients of the 2,828 asthma patients who met the inclusion criteria within the database had a FeNO test during the two-year study period. During the period before FeNO use, 61/63 (97%) patients had an asthma-related IP/ED event compared to 30/63 (48%) during the FeNO period. Asthma-related IP/ED claims and charges per patient per day during the period before FeNO were 0.026 and $12,368 compared to 0.003 and $1,340 during the FeNO period (p<0.018/0.0043, respectively).

**CONCLUSIONS:** FeNO monitoring in patients with a history of exacerbations was associated with a substantial reduction in asthma-related IP/ED claims and charges. These data support cost modelling estimates and demonstrates FeNO use in asthma management is cost-effective.
Development of Adherence Questionnaire for Children and Adolescents with Asthma

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METHODS: A 53-item working questionnaire was developed based on concepts obtained by semi-structured interview with children with inhaled corticosteroids (ICS)-treated asthma. The questionnaire was administered to 445 patients (9-15 years old) with asthma on ICS. Adherence was separately evaluated by "confidential" questions to ask frequency of "forgetting to take medicine" by non-medical study staff. Then, 6 questions for assessing adherence were selected from the 53 questions by stepwise logistic regression methods. We named that set of questions the Pediatric Asthma Adherence Questionnaire (PAAQ). Validation of PAAQ was performed using answers to the questions from a separate group of 276 ICS-treated asthma patients of same age.

RESULTS: The 6 questions asked about recognition and awareness of medication and treatment, habitual behavior in taking medicine, fear for exacerbation, negative feeling to taking medicine, self-confidence in taking medicine and attention-deficit behavior. The 6-item logistic model showed good statistical fit and well discriminated poor adherence with a good predictive power. A 53-item working questionnaire was developed based on concepts obtained by semi-structured interview with children with inhaled corticosteroids (ICS)-treated asthma. The questionnaire was administered to 445 patients (9-15 years old) with asthma on ICS. Adherence was separately evaluated by "confidential" questions to ask frequency of "forgetting to take medicine" by non-medical study staff. Then, 6 questions for assessing adherence were selected from the 53 questions by stepwise logistic regression methods. We named that set of questions the Pediatric Asthma Adherence Questionnaire (PAAQ). Validation of PAAQ was performed using answers to the questions from a separate group of 276 ICS-treated asthma patients of same age.

CONCLUSIONS: PAAQ may be a useful tool to evaluate adherence in children and adolescents with ICS-treated asthma.

Using Predictive Analytics to Identify Risk of Clinical Asthma Exacerbations

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METHODS: Analysis cohorts were defined via cloud-based, de-identified, longitudinal data of over 1.6 million patients diagnosed with asthma (IBM® Explorys Platform). Gradient boosting trees were used to model CAE risk and assess the predictive power of reduced sets out of thousands of demographic and clinical features. Baseline and history-limited models were developed to predict the risk of future CAEs based on retrospective records of all available data (unlimited timing), and the last 365 days, respectively. A short-term model was used to estimate CAE risk in the following 30 days, considering records from the previous 180 days.

RESULTS: The final cross-validated models – which incorporated 269, 166 and 116 CAE predictors for baseline, history-limited and short-term models, respectively – exceeded benchmarks reported in the literature from studies utilizing comparable settings. They demonstrated performance (measured by area under the curve) of 0.83, 0.83 and 0.74 for CAE predictors for the three models. Many of the risk factors included in our models were consistent with previously published findings, further supporting the validity of our results.

CONCLUSIONS: Combining predictive analytics and real-world data may be effective in developing clinically useful models to identify risk of future asthma exacerbations, allowing healthcare systems to design preventive interventions for at-risk patients.
699 Epidemiology and Risk Factors of Allergic Diseases in Adolescents

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RATIONALE: ISAAC (International Study of Asthma and Allergies in Childhood), assessed epidemiological data on allergic diseases was not addressed to allergic conjunctivitis.

METHODS: ISAAC questionnaire was filled by 4,520 adolescents 13-14/y/o from Curitiba, Brazil. Specific allergic conjunctivitis questions were added to the questionnaire. Four hundred and seventy-two students were submitted to allergic skin testing (AST) and answered a supplementary questionnaire on family history, immunization status, infectious diseases, environmental conditions and diet.

RESULTS: The prevalence of asthma was 17.5%, medical diagnosis of asthma 13.2%, rhinitis 34.7%, rhinoconjunctivitis 20.1%, medical diagnosis of rhinitis 51.1%, atopic eczema 5.9% and medical diagnosis of eczema 13.2%, allergic conjunctivitis 15.5%. There was an association between asthma, rhinoconjunctivitis, atopic eczema and allergic conjunctivitis in 1.3% of adolescents. Risk factors were father with asthma, (OR = 3.18; CI95% 1.24-7.95), mother with asthma (OR = 2.92; CI95% 1.36-6.09), symptoms of eczema (OR = 2.38; CI95% 1.28-4.35) and allergic conjunctivitis (OR = 3.12; CI95% 1.67-5.88), AST positive for Blomia tropicalis (OR = 2.66; CI95% 1.49-4.92) and presence of humidity at home (OR = 1.85; CI95% 1.07-3.19). Among the 85 students with asthma, 82.3% had positive AST, being 11.7% monosensitized and 70.5% polysensitized. Among the 387 participants without asthma, 64.3% had positive AST, 11.9% monosensitized and 52.4% polysensitized.

CONCLUSIONS: Prevalence of asthma is high in Curitiba. Risk factors were atopy in family, symptoms of eczema and allergic conjunctivitis, positive AST for Blomia tropicalis and presence of humidity at home. Sensitization rate in both groups was high.

700 The economic impact of uncontrolled asthma among treated, adherent patients with persistent asthma

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RATIONALE: Research on the economic burden of treated, adherent asthma is lacking. This study compared economic outcomes between controlled versus uncontrolled treated, adherent patients with persistent asthma.

METHODS: Controlled (N=242) and uncontrolled (N=645) treated, adherent patients with persistent asthma were identified from the 2015 and 2016 US National Health and Wellness Survey. Adherence was assessed with the Morisky Medication Adherence Scale (MMAS-8 ©); patients with medium/high adherence were considered “adherent”. The Asthma Control Test (ACT; uncontrolled: scores ≤19; controlled: scores 20-25) assessed control. Economic outcomes included the Work Productivity and Activity Impairment-General Health Scale (WPAI-GH), health resource utilization (HRU), annual indirect and direct costs. Main analyses utilized generalized linear models.

RESULTS: Sample mean age was 49 years; 66.7% female. Uncontrolled vs. controlled patients experienced 1.4 times greater work productivity loss (adjusted means = 34.96% vs. 25.21%, p=.036) resulting in 1.5 times higher annual indirect costs (adjusted means = $11,537 vs. $7,630, p=.016). Uncontrolled vs. controlled patients incurred twice as many annual hospitalizations (adjusted means = 0.26 vs. 0.12, p<.001) and significantly more medical visits (emergency room: adjusted means = 0.53 vs. 0.31, p=.003; healthcare provider: adjusted means = 7.83 vs. 6.14, p=.011); incurring 1.5 times higher annual direct costs (adjusted means = $31,793 vs. $21,240, p=.001).

CONCLUSIONS: Uncontrolled asthma in treated, apparently adherent patients was associated with higher work impairment, HRU, and costs compared with controlled asthma. Significant unmet need in asthma management, independent of adherence or asthma severity, was demonstrated. Better understanding of patients’ treatment needs could aid in achieving improved asthma control and reducing the economic burden associated with uncontrolled asthma.

701 Effect of pregnancy on lengths of stay of admitted asthmatic patients in an urban inner city tertiary hospital

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RATIONALE: 8% to 9% of pregnant women report current asthma, which worsens in one-third, is stable in one-third, and improves in one-third. We investigated the effect of pregnancy on lengths of stay of admitted asthma patients in an urban inner city tertiary hospital, which serves a large inner city population which is at increased risk for asthma morbidity and mortality.

METHODS: A retrospective review of adult asthma inpatient discharge data from 2013-2015 was done for patients treated at Kings County Hospital Center. 315 pregnant asthmatics were matched with female asthmatic patients of similar age with no significant comorbidities managed on the medicine floor. The severity of asthma and details of treatment were unknown from the dataset.

Length of stay between the two groups was analyzed using a 2 tailed Mann-Whitney test.

RESULTS: Pregnant asthmatics admitted with exacerbation had reduced length of stay compared to matched controls on the medicine floor (3.5 days vs 4 days, p=0.002).

CONCLUSIONS: The large majority women who are pregnant receive prenatal care, which addresses their health concerns and promotes adherence to medications. This increased health care may improve asthma severity and decrease asthma length of stay for pregnant women compared to those who are not pregnant.
702 Caregiver report of child asthma control predicts future acute visits in a mouse-sensitized population, independent of guideline-based measures of asthma control

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RATIONALE: Parent-reported asthma control, which is not included in many rubrics for assessing asthma control, may be an indicator of future risk.

METHODS: 350 mouse sensitized and exposed children (5-17y) from Baltimore and Boston with persistent asthma enrolled in a randomized clinical trial were studied. Questionnaires were administered at baseline, 3, 6, 9, and 12 months, spirometry was performed at baseline, 6 and 12 months, and allergy skin testing at baseline. Controlled, uncontrolled, and poorly controlled asthma were defined using National Asthma Education and Prevention Program (NAEPP) guidelines (symptom days, activity limitation, albuterol use, nighttime awakenings in the past two weeks, FEV1/FVC and acute visits in the past 3 months). Relationships between caregiver-reported control and acute visits in the subsequent 3 months were examined using logistic regression and generalized estimating equations.

RESULTS: 38% were female, 79% African American and 88% had public insurance. 47% of participants were categorized as not well controlled, and 44% as poorly controlled. 25% of parents reported that their child’s asthma was not well controlled. Participants whose caregivers reported uncontrolled asthma had a 1.7-fold greater odds of having an acute visit in the subsequent 3 months than those whose caregivers reported that their child’s asthma was controlled (95% CI 1.2 – 2.3). The odds ratio remained similar after adjusting for guideline-based control, age, sex, race, controller medication, insurance type, and atopy (OR 1.7; 95% CI 1.2 – 2.4).

CONCLUSIONS: In this population, caregiver-reported asthma control is a predictor of future acute asthma visits, independent of guideline-based asthma control measures.


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RATIONALE: Little is known about the prevalence of asthma among US migrant and seasonal farmworkers nationally. We examined the association between occupational exposures and lifetime and current prevalence of asthma in this unique population.

METHODS: We used the 2001-2014 public access data from the National Agricultural Workers Survey, which is a nationally representative employment-based random sample survey of US migrant and seasonal cropworkers, using face-to-face interviews. In bivariate and logistic regression analysis, we examined cross-sectional associations between demographic factors, occupational exposures (type of crop, number of years farmworking, and pesticide use) and self-reported physician-diagnosed lifetime and currently treated asthma.

RESULTS: Our analysis included data from 31,493 seasonal and migrant farmworkers. Self-reported lifetime prevalence of physician-diagnosed asthma was 3.0% [95% CI 2.6, 3.4] and self-reported prevalence of currently treated asthma was 1.7% [95% CI 1.4, 2.1]. After adjustment, significant predictors for lifetime asthma were female gender (OR 1.9, p<0.001), speaking English partially (OR 1.9, p<0.001) or well (OR 2.4, p<0.01), citizenship status (OR 3.0, p<0.001), and pesticide use in the last 12 months (OR 1.4, p<0.05). After adjustment, significant predictors for currently treated asthma were female gender (OR 2.6, p<0.001), speaking English partially (OR 2.1, p<0.001) or well (OR 3.0, p<0.01), and citizenship status (OR 3.6, p<0.01). Type of crop exposure and number of years farmworking were not significant predictors for lifetime or currently treated asthma.

CONCLUSIONS: US farmworkers had low asthma prevalence. Women, US citizens, and those with better English proficiency and pesticide exposure were more likely to report lifetime prevalence of physician-diagnosed asthma.

704 Insomnia among Hispanics/Latinos with Asthma

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RATIONALE: Asthma disproportionately impacts the Hispanic/Latino population. Poor sleep quality frequently coexists with asthma. We used the Hispanic Community Health Study of Latinos (SOL), a large-scale multicenter study, to examine the relationship between asthma and insomnia in Hispanics/Latinos.

METHODS: We performed an exploratory survey analysis of the relationship between self-reported asthma and insomnia, measured by the Epworth Sleepiness Scale (ESS, >10 for insomnia) and the Women’s Health Initiative Insomnia Rating Scale (WHIIRS, >9 for insomnia). Multiple survey logistic regression with backward model selection adjusted for demographic, behavioral, and other clinical factors found significant in exploratory and bivariate analyses was performed.

RESULTS: In bivariate analyses, asthma was associated with insomnia by ESS (Odds Ratio (OR): 1.34, 95% Confidence Interval (CI): 1.07-1.68) and by WHIIRS (OR: 1.41, 95% CI: 1.16-1.71). Age, higher body mass index (BMI), tobacco use, greater physical activity, higher income, antidepressant use, and Central American, Mexican, Puerto Rican, and South American heritage (Reference: Multiple/Other/Unknown heritage) were independently associated with insomnia by either ESS or WHIIRS. In multivariate models, asthma remained associated with insomnia by ESS (Adjusted OR (AOR): 1.31, 95% CI: 1.03-1.67) after adjusting for BMI, tobacco use, physical activity, antidepressant use, and Hispanic heritage and by WHIIRS (AOR: 1.27, 95% CI: 1.03-1.56) after adjusting for age, tobacco use, income, antidepressant use, and Hispanic heritage.

CONCLUSIONS: Insomnia is associated with asthma in a large Hispanic/Latino asthmatic population with multivariate modeling. Future studies should consider the contribution of insomnia to asthma morbidity in the Hispanic/Latino population.
Effect of Rescue Inhaler Dose Counters on ER Utilization, Asthma Admissions and Health Care Claims Costs in a Population of Children in Medicaid Managed Care

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Rationale: The effect of dose counter on rescue inhalers has not been studied in Medicaid children

Methods: Claims data for Medicaid HMO children were analyzed for effect of dose counters on ER utilization, hospital admissions and health care costs. Outcomes included hospital admissions/1000, ER visits/1000, health care costs. The potential cost savings from having a dose counter were calculated.

Results: ER visits without dose counter were 149.36 per 1000 and 101.44 per thousand with. Admissions per 1000 without dose counter were 7.91 per 1000 and with 4.36. Admissions were 81.6% higher without dose counter and ER Visits 47.2% higher without dose counter. ER cost per visit without dose counter averaged $792.85 per visit compared to $545.53 with. Cost per hospital admission without was $8788.59 compared to $6854.28 with. ER cost per visit and cost per admission were 45.3% and 28.1% higher. Excess costs associated with absence of a dose counter were $84,670 excess admission costs due to higher cost admissions, $10,882 ER cost for higher cost visits, $216,903 due to a higher number of admissions and $181,667 due to a higher number of ER visits.

Conclusions: Absence of dose counters in children covered by Medicaid is associated with higher ER visits and hospital admission, higher cost per admission and ER visit and higher overall health care costs due to ER visits and hospital admissions. Absence of a dose counter represents a risk to the life and safety of Medicaid children with asthma as well as wasted health care costs.

Eosinophilic Digestive Diseases attending the Gastroenterology Department of the National Institute Of Pediatrics in Mexico City

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Rationale: Eosinophilic digestive diseases (EDD) are rare disorders characterized by gastrointestinal eosinophil infiltrates without underlying primary etiology. Its pathogenesis remains unclear, but is suspected to be related to an hypersensitivity reaction given its relation with other allergic disorders and clinical response to steroid therapy. The objective of this study was to describe the clinical and paraclinical profile of pediatric patients with EDD.

Methods: We conducted a retrospective, observational, transversal and descriptive study, in which we reviewed every histopathological report of patients who underwent endoscopy and/or colonoscopy in the Gastroenterology department of the National Institute of Pediatrics in Mexico city from 2014 to 2016. EGE was defined by biopsies showing eosinophilic infiltration of at least 20 eosinophils per high power field, according to Talley criteria. Socio-demographic, clinical and treatment data were searched in the clinical files and registered.

Results: EDD was diagnosed in 27 patients, average age was 5±4.6. 72% of patients had evidence of food sensitization (14% IgE mediated and 86% non IgE-mediated): 81% cows’ milk allergy, 19% egg allergy and 11% to others. Most frequent symptoms were: pain (50%); regurgitation, vomit and diarrhea (30%); dyschezia, constipation and bleeding (25%). Eosinophilic duodenitis was the most common EDD (59%), followed by eosinophilic esophagitis (26%) and eosinophilic colitis (18.5%); 22% had combined forms of EDD.

Conclusions: EDD are poor studied entities that may be more frequent that thougt. In our study two thirds of patients had evidence of food allergy. More studies should be adressed in order to better understand this entity.

X chromosomal linkage to eosinophilic esophagitis susceptibility

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Rationale: Eosinophilic esophagitis (EoE) is a chronic allergic disease with a marked difference in sex distribution; ~65% of patients are male. Prior genome-wide association studies (GWAS) have identified replicated EoE-risk loci but these analyses did not assess non-autosomal genomic loci.

Methods: We assessed 14,481 subjects with esophageal eosinophilia living in 48 contiguous states and found a male predominance regardless of region (61.4%-66.4%), population density (63.6%-64.8%), or age (59.2%-67.4%) collectively emphasizing consistent sex differences. We performed an association study of the X and Y chromosomes, including the pseudoautosomal region, data in 732 cases and 9288 controls from two independent cohorts. High-depth RNA sequencing and the eosinophil diagnostic panel were used to measure gene expression of 20 biopsies from well-matched male and female children with and without EoE.

Results: We identified a new EoE risk locus at Xq28 associated with increased EoE risk in both males and females and encoding the genes VMA21 and GPR50 (ORcombined =2.11x10^-10). Odds Ratio (ORAcombined =1.31; P_allele =2.4x10^-9, ORmak =1.30 and P_allele =0.002, ORema =1.35). Sex-specific analyses of common variants did not reveal non-autosomal genetic variation sufficient to explain the observed male-predominated disease. Gene expression from esophageal biopsies was largely similar across sex with non-statistically significant trends towards sex-dependent expression of some members of the EoE-transcriptome. A subset of 20 genes expressed from the X and Y chromosomes were expressed in a sex-dependent manner (fold-change>2; Pcorrected<0.05).

Conclusions: Altogether, our work establishes a new EoE risk locus at Xq28 and was unable to identify evidence that male predominance is dictated by non-autosomal genetic variants.
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**The Anti-protease SPINK7 is a Checkpoint Regulator of Esophageal Epithelial Inflammatory Responses**

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**RATIONALE:** The serine peptidase inhibitor kazal-type (SPINK)7 is down-regulated in eosinophilic esophagitis (EEoE), a type-2 immune disease of the esophagus. Loss of SPINK7 in esophageal epithelial cells unleashes a pro-inflammatory response and loss of barrier function. Herein, we investigated the mechanism by which SPINK7 mediates its function.

**METHODS:** We performed SPINK7 silencing and genetic depletion of SPINK7 in human esophageal epithelial cells that were cultured at the air-liquid interface. Protease activity of SPINK7 deficient epithelial cells and human esophageal tissue was measured, and receptor expression of esophageal epithelium was measured, and receptor expression of esophageal tissue-derived eosinophils was quantified. We assessed whether genetic variants in atopic genes were associated with EEoE susceptibility. In vitro assays using recombinant proteins were conducted to identify direct targets of SPINK7. Last, we used murine EEoE model to identify the role of SPINK7 target protease; Kallikrein (KLK)5.

**RESULTS:** Epithelial deficiency of SPINK7 promoted increased uronate plasmogen activator (uPA) and trypsin-like activities (1.8-fold and 3-fold; \(p=0.013, p=0.004\) respectively). uPA activity was increased by 10-fold in the esophagus of EEoE patients as compared to control individuals (\(p=0.043\)). uPA had the capacity to promote eosinophil activation. Genetic studies revealed a strong epistasis between genetic variants in PLAU (gene product, uPA) and the atopy risk variant in TSLP gene. Furthermore, we revealed KLKS as SPINK7 target (K injection 5393±372 ng/mL vs. 6727±427 ng/mL, \(p=0.034\)) and was higher compared to children without exposure to passive smoking (\(p=0.039\)). Children sensitized to HDM allergens yielded higher concentration of E-cadherin before and after the surgery compared to non-sensitized (before AT: 7248±599 vs. 5302±387 ng/mL, \(p=0.028\); after AT: 6446±513 vs. 5722±419 ng/mL, \(p=0.045\)). Children allergic to Alternaria had higher E-cadherin after AT (7294±906 vs. 5607±336 ng/mL, \(p=0.049\)).

**CONCLUSIONS:** Passive smoking and sensitization to perennial allergens damage and modify the immunological functions of airways epithelium and could contribute to the development of adenoid hypertrophy.

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**E-cadherin, Passive Smoking and Allergen Sensitization in Children with Adenoid Hypertrophy**

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**RATIONALE:** Adenoid hypertrophy (AH) represents a common problem in children associated with many complications. It was suggested, that allergic sensitization and immune dysregulation could contribute to AH development.

**METHODS:** In a group of 97 children undergoing adenoidectomy (AT), we analyzed the contribution of allergic sensitization and passive smoking to the development of AH and to the changes of mucosal microbiome. We evaluated the concentration of E-cadherin (measured by standard human ELISA E-cadherin kit), a mediator of immunological functions of airway epithelium, in relationship to the surgery and allergic background (evaluated by skin prick tests).

**RESULTS:** Atopy was confirmed in 83% of children and the most prevalent allergens were house dust mites (HDM) and animal dander. Passive smoking was detected in 37% of children assessed by the questionnaires. In the whole group, no changes in E-cadherin levels before and after the surgery were detected. However, in children exposed to passive smoking, E-cadherin significantly increased after the AT (5393±372 ng/mL vs. 6727±427 ng/mL, \(p=0.034\)) and was higher compared to children without exposure to passive smoking (\(p=0.039\)). Children sensitized to HDM allergens yielded higher concentration of E-cadherin before and after the surgery compared to non-sensitized (before AT: 7248±599 vs. 5302±387 ng/mL, \(p=0.028\); after AT: 6446±513 vs. 5722±419 ng/mL, \(p=0.045\)). Children allergic to Alternaria had higher E-cadherin after AT (7294±906 vs. 5607±336 ng/mL, \(p=0.049\)).

**CONCLUSIONS:** Passive smoking and sensitization to perennial allergens modify and damage the immunological functions of airways epithelium and could contribute to the development of adenoid hypertrophy.

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**Maternal Exposure to Antibiotics Increases the Severity of Asthma in Offspring Mice**

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**RATIONALE:** The prevalence of allergic asthma has been increasing steadily in recent decades, a time frame too short to be due to genetics alone, suggesting that environmental changes may be responsible. As many environmental exposures also alter microbial colonization, we sought to determine if early life changes in microbial colonization would influence asthma development in a murine model of asthma.

**METHODS:** On day 15 of gestation, the water of dams was supplemented with sucrose, or an antibiotic cocktail until birth, when regular drinking water was supplied. At 6 – 7 weeks of age, offspring of control, and antibiotics (ABX)-exposed mothers were given PBS, or sensitized with HDM i.p. (experimental days 0, 7) and i.i. (experimental days 14, 21), 72 hours after the last HDM treatment, mice were sacrificed and airway hyperresponsiveness (AHR) was measured. Flow cytometric analysis of lung cell populations was performed, and allergen-stimulated cytokine production was assessed in lung cell cultures.

**RESULTS:** Compared to offspring of control mothers, offspring of ABX-exposed mothers demonstrated significantly elevated AHR. More severe AHR was associated not with altered Th2, Th17 or ILC2 recruitment, but excessive ILC3 recruitment, and production of IL-17A and IL-22.

**CONCLUSIONS:** Consistent with epidemiological data, we find that early life microbial dysregulation is associated with altered asthma development. Moreover, we identify a potential link between microbial dysbiosis, long term alterations in ILC3 recruitment and activity, and elevated production of IL-17A/IL-22. Dissecting the mechanisms whereby ILC3 recruitment is altered may suggest ways of mitigating the risk of early life microbial dysregulation on asthma development.
Increased TREM-2 Expression on Dendritic Cell Subsets and Th2 and Th17 Immune Response in Allergic Airway Inflammation

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**RATIONALE:** We have previously shown that allergen exposure increases TREM-2 and CCR7 expression on mature DCs in the lungs and lymph nodes. Here, we further examined the phenotype of DC subsets and determined the T-helper cell responses associated with increased TREM-2 expression in the lungs and lymph nodes of allergen-sensitized and -challenged mice.

**METHODS:** Female Balb/c mice were sensitized and challenged with ovalbumin (OVA) for a total of 20 days. PBS was used in the control group. Whole lungs and lymph nodes were collected, prepared for FACS analysis and quantification of mRNA transcripts of CD4\(^+\) cell cytokines.

**RESULTS:** In the lungs and lymph nodes of OVA-sensitized and challenged mice, TREM-2\(^+\) DCs from all three populations (CD11b\(^+\), CD103\(^+\), and CD11b/CD103\(^+\)) had higher expression of CD86 and CCR7 compared to their TREM-2-negative counterparts. Cells expressing CD103 had overall high CCR-7 expression whereas CD86 was high on the CD11b\(^+\)subset. In the FACS analyses, we observed increased expression of GATA-3 and ROR\(\gamma\)T, increased mRNA transcripts of IL-4, IL-6, and IL-17 (p <0.01) and a decreased expression of T-bet and FoxP3 in both lungs and lymph nodes of OVA-sensitized and challenged mice.

**CONCLUSIONS:** These results suggest that increased TREM-2 expression on DCs in the lungs and lymph nodes is associated with Th2 and Th17 responses. Increased expression of CD86 and CCR7 on these cells highlights a potential role of TREM-2 in driving migration and/or maturation of DC subsets. Thus, TREM-2 could be an effective target for therapeutic intervention.

Nitric Oxide Production by PBMC from IgE+ Allergic Adults Varies with Time of Day and Correlates with Total Serum IgE and Exhaled Breath NO

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**RATIONALE:** We previously showed that low levels of melatonin increase nitric oxide (NO) production by PBMC from IgE+ adults. As allergy/asthma symptom severity varies with time of day (AM high; PM low), we investigated NO responses of PBMC isolated in AM and PM and their correlation with exhaled NO (FeNO) levels and serum IgE.

**METHODS:** Blood was collected from IgE+ (>100 IU/ml) (n=12), and IgE- (<100 IU/ml) (n=8) adults at 9-10 AM and 3-4 PM; FeNO and serum IgE were determined (Niox Vero; fluoroenzymimmunoassay). PBMC were incubated for 5 days with bradykinin (100 nmol/ml), IL-15 (1 ng/ml), IL-18 (1 ng/ml), IFN\(\gamma\) (10 ng/ml) and Vitamin D3 (20 pmol/ml) (CYT+D3). Recombinant human melanotin (1 pmol/ml) was added for the last 4 hrs of culture, and NO production measured (Griess reaction). Data analysis used Spearman - Pearson coefficients and t-test.

**RESULTS:** PBMC from IgE+ subjects made significantly more NO than IgE- adults when obtained either AM (10.14 ±5.96 μM vs. 3.65 ±0.99 μM, p<0.01) or PM (11.09 ±6.03 μM vs. 3.19 ±1.1 μM, p<0.01). Inclusion of CYT+D3 increased NO production by PBMC obtained PM (from 4.71±4.16 μM to 8.62±6.23 μM (p=0.05) but not AM (p=0.23). NO production correlated with IgE levels in AM and PM (p=0.04, 0.02, respectively), but correlated with FeNO only in PM (p=0.09, 0.02, respectively).

**CONCLUSIONS:** NO production by PBMC corresponds to circadian rhythm shown by daily changes in melatonin secretion from pineal gland in the brain. NO production by PBMC may be a useful biomarker in IgE+ adults.

Biological effect of IL-33R/ST2 in atopic asthmatic children; serum IL-33 changes by administration of omalizumab

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**RATIONALE:** To analyze serum ST2 changes in severe atopic asthma in children by administration of omalizumab. And also find a correlation between the serum ST2 concentration and respiratory function measured by forced oscillation technique.

**METHODS:** We performed a retrospective study of patients with atopic asthma in children over 6 years old. The subjects of the present study are 9 patients who received omalizumab as a treatment for bronchial asthma in our department in 2016-2017. There were aged from 7-13 years (median 9 years 6 months). The patients were administered in doses of omalizumab determined from body weight and serum IgE levels. We investigated blood examinations and respiratory function, compared with before administration. Blood examination also contains of their serum levels of antigen-specific IgE, IL-33, ST2.

**RESULTS:** We confirmed that ST2 levels did not change, but a significantly lower concentration of IL-33 level was detected in after-administration group, suggesting the improvement of allergic reaction in bronchial epithelial cells. We are currently measuring the concentration of soluble ST2 in some samples.

**CONCLUSIONS:** It has already reported that IL-33 plays important roles in inflammation in atopic asthma. It can be inferred from previous reports so far that ST2 was an isolated receptor that was considered to the context of inflammatory and allergic disease. On the other hand, it remains possible that soluble ST2 as decoy receptor selectively inhibited the expressions of membrane bound type ST2. The mechanism is still unknown, but we speculate that ST2, especially soluble ST2, is an important factor in atopic asthma in children.
714 Premedication For Oral Desensitization To Anaphylactoid Reactions At OPD

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RATIONALE: There are some situations that oral desensitization to a strong allergen has to be unavoidably done at OPD. Premedication before triggering immune reaction can weaken the adverse reactions and reduce the dose of immune suppressive agents. To prevent anaphylactoid reaction during oral desensitization at OPD and to reduce the dose of corticosteroids, premedication protocol is necessary.

METHODS: Children over 5 years of age with symptomatic IgE-mediated allergy to hen’s egg underwent a 17-day oral tolerance induction regimen and were subsequently maintained on the daily intake of a whole boiled egg for 12 weeks. Oral antihistamines and cimetidine were daily taken from day0 for 6 months. Dexamethasone was intramuscularly injected from day3 times a week for 3 weeks. Oral challenge of boiled egg white was done from day7 in escalating doses of 8 steps for 17 days. Human Chorionic Gonadotropin (hCG) was intramuscularly injected from day21 3 times a week for 2 weeks and then 2 times a week for 2 weeks. Oral dexamethasone was daily given from day21 for 6 weeks.

RESULTS: Three patients between 5 and 6 years of age entered the protocol. All patients were successfully desensitized to hen’s egg. All patients showed allergic reactions but the reactions in general were mild. The allergic reactions were subsided by additional dexamethasone injection. During follow-up between 1 and 5 years, egg was well tolerated by all patients.

CONCLUSIONS: This premedication protocol is useful and safe for inducing desensitization to anaphylactoid reaction by strong allergen, egg at OPD.

715 Fibrinolytic Pathways In Interleukin-17A-induced Lung Injury

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RATIONALE: Accumulation of inflammatory cells and elevated interleukin-17A levels contributes to chronic inflammation, which results in the narrowing of small airways and alveolar wall destruction. Interleukin-17A is produced by T-lymphocytes, macrophages and mast cells, and augments lung inflammation. We hypothesized that interleukin-17A-mediated induction of plasminogen activator inhibitor-1 (PAI-1) expression leads to abnormal fibrin turnover and death of airway and alveolar epithelial cells (AECs) during lung injury.

METHODS: Wild-type and interleukin-17A-deficient mice were exposed to 20 weeks of environmental tobacco smoke (ETS) to induce lung injury. We analyzed lung tissues of patients with severe (stage III and IV) COPD and mice exposed to 20 weeks of ETS for elaboration of interleukin-17A, inflammatory cytokines and chemokines, PAI-1 and AEC apoptosis to test the hypothesis. This was further confirmed using primary human and mouse AECs treated with interleukin-17A in vitro, and lung tissues and AECs isolated from wild-type and PAI-1-deficient mice exposed to interleukin-17A in vivo.

RESULTS: We found elevated levels of T-lymphocytes, macrophages and neutrophils, and interleukin-17A in the lungs of patients with COPD and in wild-type mice exposed to ETS for 20 weeks. ETS and interleukin-17A exposure caused significant increase in PAI-1 and lung injury in wild-type mice. Mice deficient in interleukin-17A expression resisted ETS-induced lung injury, while those lacking PAI-1 expression resisted both ETS and interleukin-17A-induced lung injury.

CONCLUSIONS: Induction of PAI-1 expression due to increased interleukin-17A is associated with lung inflammation, AEC apoptosis and worsening of lung injury. Inhibition of this feedforward induction mitigates AEC apoptosis, inflammation and severity of lung injury.

716 Novel Basophil Activation and Degranulation Markers for the Basophil Activation Test

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RATIONALE: The Basophil activation test (BAT) is used for the diagnostics of IgE-mediated allergy. Currently only 2 markers of basophil activation are used: CD63 and CD203c. Screening for basophil activation markers is important for the improvement of the assay results.

METHODS: Blood samples from 10 healthy donors were used. Basophils were gated as CD123hiHLA-DRneg cells. Expression of CD11b, CD13, CD69, CD107a, CD164 and CD300a on anti-IgE stimulated basophils was assessed.

RESULTS: To estimate the increase of expression of miscellaneous CD-markers by basophils the activation index (AI) was used, as the ratio of molecule expression in the negative control to the expression in the positive control. The AI was calculated for the percent marker expression (AIm) and for mean fluorescence intensity (AIMFI) only was measured for the following molecules: CD11b (1.7; range 1.3 to 2.1), CD13 (1.9; range 1.3 to 2.1) and CD300a (1.7; range 1.7 to 1.9).

CONCLUSIONS: The most effective basophil activation and degranulation markers were CD63, CD107a and CD164 due to highest AI. CD11b, CD13, CD69 and CD300a markers may also be used to improve BAT results.
Ferritin Particles Accumulate in Human Mast Cell Secretory Granules and Are Released upon FcεRI-Mediated Activation

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RATIONALE: Transcriptome analyses revealed that mast cell (MC) gene expression correlates better with macrophages than other granulocytes. Macrophages produce ferritin in inflammatory conditions like hemophagocytic lymphohistiocytosis. We hypothesized that MCs could be an alternate source of extracellular ferritin during inflammation.

METHODS: Primary human skin MCs were isolated and cultured from discarded surgical specimens. MC gene expression was evaluated by RNA expression array. Cellular ferritin light and heavy chains were assayed by Western blot. Ferritin content in culture supernatants was measured by ELISA after treating MCs with various stimuli. MC degranulation after stimulation was measured by β-hexosaminidase release. Ferritin localization within MCs was confirmed by superresolution microscopy.

RESULTS: MCs express ferritin light and heavy chain mRNA at similar levels to tryptase, among the genes with the highest expression in these cells. MCs do not release ferritin upon stimulation with pro-inflammatory cytokines, but release copious amounts after anti-FcεRI antibody treatment. Ferritin is detected within minutes of activation, suggesting it is released during degranulation. Western blots suggest ferritin particle releases released by MCs within minutes of activation may be released by degranulation. Ferritin localization within MCs was confirmed by superresolution microscopy.

CONCLUSIONS: Human skin MCs generate and store ferritin within secretory granules, and ferritin particle releases are released quickly upon FcεRI-mediated activation, similar to other mediators like tryptase, histamine, and TNFα. Ferritin is known to have direct modulatory activity on T cells as well as accumulation within tryptase-containing granules.

Low Density Lipoprotein enhances the in vitro production of IL-18 from peripheral blood mononuclear Cells

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RATIONALE: We wanted to study the effects of in vitro hyperlipidemia (high Low Density Lipoprotein (LDL) or Bad Cholesterol) on one aspect of the immune function as of level of cytokine production of IL-18 (related to hyperlipidemia). Ferritin is known to have direct modulatory activity on T cells and APCs, and ferritin particles released by MCs during degranulation may help to moderate inflammation at local sites within tissues.

RESULTS: MCs express ferritin light and heavy chain mRNA at similar levels to tryptase, among the genes with the highest expression in these cells. MCs do not release ferritin upon stimulation with pro-inflammatory cytokines, but release copious amounts after anti-FcεRI antibody treatment. Ferritin is detected within minutes of activation, suggesting it is released during degranulation. Western blots suggest ferritin particle releases released by MCs within minutes of activation may be released by degranulation. Ferritin localization within MCs was confirmed by superresolution microscopy.

CONCLUSIONS: Human skin MCs generate and store ferritin within secretory granules, and ferritin particle releases are released quickly upon FcεRI-mediated activation, similar to other mediators like tryptase, histamine, and TNFα. Ferritin is known to have direct modulatory activity on T cells as well as accumulation within tryptase-containing granules.

Remote Respiratory Allergen Challenge Increases the Frequency of Small Intestinal Eosinophils in Allergen-Sensitized Mice

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RATIONALE: Accumulated data suggest that allergen sensitization predisposes susceptible individuals for the development of eosinophilic GI diseases: GI allergic manifestations are observed in asthmatic, allergic rhinitis, and atopic patients; EoE patients exhibit higher rates of aeroallergen sensitization than the general population; and several clinical studies directly implicate aeroallergens in the pathogenesis of EoE. These findings suggest susceptibility to intestinal allergic inflammation may be enhanced by allergen exposure of the skin or respiratory mucosa. However, the interplay between allergen exposure to the skin or respiratory tract and remote eosinophilic GI inflammation remains enigmatic.

METHODS: Endotracheal administration of allergen to naïve or allergen-sensitized mice was used to provide allergen exposure to the respiratory mucosa while avoiding direct allergen exposure of the GI tract inherent in standard models of airway allergen challenges (i.e. intranasal inhalation or aerosolization). Eosinophilic inflammation was assessed in allergen-challenged mice through complementary approaches, including researcher-blinded counts of histological sections and flow cytometry analyses of disaggregated intestinal tissues.

RESULTS: Remote allergen challenge increased the frequencies of eosinophils associated with both lamina propria and intraepithelial compartments of the small intestines of allergen-sensitized mice. In contrast, percentages of intestinal CD4+, CD8+, and CD11c+SiglecF- (dendritic) cells remained static following remote (pulmonary) allergen challenge.

CONCLUSIONS: Remote respiratory allergen exposure increases the frequency of small intestinal eosinophils in systemically allergen-sensitized mice. These data may shed light on the relationship between aeroallergens and eosinophilic gastrointestinal inflammation.
720 Safety And Efficacy Of Dupilumab In Adult Patients With A History Of Eczema Herpeticum

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RATIONALE: Eczema herpeticum is not uncommon in patients with severe eczema. Prior studies have showed an increase rate of some herpes simplex exacerbation (oral ulcers) in retrospective analysis of patients treated with dupilumab versus placebo but no increase in eczema herpeticum. Efficacy and side effects of dupilumab, recently FDA approved for severe eczema, have not been reported in patients with a prior history of eczema

METHODS: We retrospectively analyzed three adult patients (denoted A, B, C) with a history of eczema herpeticum on antiviral prophylaxis (valcyclovir) who initiated Dupilumab therapy. We calculated an Eczema Area and Severity Index (EASI) score for each patient before and after Dupilumab therapy and analyzed reported side effects in the first month of therapy.

RESULTS: None of the patients had exacerbations of eczema herpeticum, herpes simplex or any herpes related symptoms in the first month of treatment. Patient A had no change in EASI and discontinued dupilumab due to increased intraocular pressure and headaches. Patient B had some improvement in EASI and has continued therapy but reports arthralgia. Patient C had no change in EASI score and discontinued dupilumab due to fatigue, headaches and arthralgia.

CONCLUSIONS: Dupilumab therapy in patients with a history eczema herpeticum did not result in eczema herpeticum in the first month of therapy but was discontinued in 2 of 3 patients because of other possible medication related symptoms. We suggest prospective studies of safety and efficacy of dupilumab in patients with a history of eczema herpeticum are indicated.

721 B Antigen Protects Against the Development of α-Gal-mediated Red Meat Allergy

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RATIONALE: Red meat allergy (RMA) is a recently recognized disease characterized by delayed-onset anaphylaxis, angioedema, and/or urticaria occurring approximately 3-6 hours after ingesting mammalian meats containing the antigen galactose-α-1,3-galactose (α-Gal). The molecular structure of α-Gal is similar to that of the B antigen, a self-antigen in patients with blood types B or AB. This provokes the hypothesis that patients who harbor the B antigen are less likely to undergo allergic sensitization to α-Gal and develop RMA.

METHODS: To test this, we employed a cohort of n=92 RMA patients and n=188 controls, all with known ABO types. We compared expected and observed frequencies of blood types O, A and AB in the two groups, and we performed logistic regression to determine the odds ratios (OR) and 95% confidence intervals (95%CI) of having RMA according to blood type.

RESULTS: Among those with RMA, the observed frequency of the B antigen (types B or AB) was markedly lower than expected (expected 20.3%, observed 4.35%, P=0.005). Patients expressing the B antigen were less likely than those without the B antigen (blood types O or A) to produce α-Gal-specific IgE (OR 0.19, 95%CI 0.04-0.80, P=0.023) or beef-specific IgE (OR 0.29, 95%CI 0.11-0.80, P=0.016) and were 5-times less likely to have been diagnosed with red meat allergy (OR 0.20, 95%CI 0.07-0.62, P=0.004).

CONCLUSIONS: Patients whose red blood cells express the B antigen are protected from developing red meat allergy and are less likely to produce anti-α-Gal IgE. These findings suggest that ABO blood type affects one’s susceptibility to RMA.

722 Peculiarities of phenotyping of lymphocytes in patients with pollen allergy against the backdrop of active herpesvirus infection type 4, 5 and 6

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RATIONALE: Study the peculiarities of the phenotypic characteristics of lymphocytes and their activation markers in patients with pollen allergy against herpesvirus infections.

METHODS: 162 persons were examined with clinical and laboratory manifestations of pollen allergy, age 32.6 ± 2.4 years, 53.1% - women, 46.9% - men. SPT Diater, Spain, total and specific IgE, ELISA. EBV, CMV, HHV6 by the polymerase chain reaction using Rotor Geen 6000. Phenotyping of lymphocytes - a flow cytometer "Bekton Dickenson" (USA).

RESULTS: Based on specific allergic studies, pollen allergy was confirmed in 158 (97.5%) patients, in 112 (70.8%) of whom polysensitization was detected, and in 46 (29.2%) monosensitization was confirmed. According to the data of molecular genetic studies, in 128 (81.0%) cases activated herpesvirus infection was detected: in 48 (37.5%) cases - monoinfection, in 80 (62.5%) - combined infection and in most 47 (58.7%) cases EBV + HHV6. Patients were divided into 3 groups: the first one - people with pollen allergy without viral activity; the second one - people with pollen allergy + viral activity. Third group - 50 healthy people. In patients in the second group showed an increase in CDHLA-DR + cells and B-lymphocytes and decreased NK-cells (p<0.05). In 75.0% of these patients, increases of levels of total IgE, that was 1.1 times more than in patients in the first group.

CONCLUSIONS: In patients with pollen allergy against the backdrop of active herpesvirus infection, there was an increase in the cell-dependent inflammatory process with the creation of conditions for the formation of hyper-IgE syndrome.
**Abstracts AB231**

**723** Epicutaneous immunotherapy with peanut directly targets Langerhans cells in human skin

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**RATIONALE:** Allergen applied on intact skin during epicutaneous immunotherapy is mainly taken-up by Langerhans cells (LCs) and transported to regional lymph nodes, explaining in part the induction of tolerance in allergen-sensitized mice. This study aimed to characterize allergen uptake after epicutaneous administration in an *ex vivo* human intact skin model.

**METHODS:** NativeSkin models consist of *ex vivo* human skin collected after plastic surgery, which maintain viability for 7 days. Patches loaded with fluorescein-tagged peanut protein extract or PBS were applied to freshly harvested skin inserts from 2 donors for 12 and 24 hrs. Co-localization of PPE-AF647 and LCs (stained with anti-CD207 and anti-CD1a) was evaluated on skin cross-sections by classical fluorescent microscopy and *in situ* on epidermal sheet layers by confocal microscopy.

**RESULTS:** Peanut protein loaded on epicutaneous patches solubilized within 12 hrs due to transepidermal water loss and reached the epidermis. After 24 hrs, a significant increase of PPE-AF647 was co-localized with LCs. For donor#1, 8% of the LCs were co-localized with PPE-AF647, while for Donor#2, 22% of cells were positive. Observation of LCs in contact with PPE-AF647 suggest that there are 2 phases in the process: at 12 hrs, the allergen associates with the surface membrane and at 24 hrs it is internalized in LCs. Other analyses are under investigations (i.e. mRNA expression of cytokines in the tissue).

**CONCLUSIONS:** The role of LCs in the antigen uptake and processing following epicutaneous application was confirmed on *ex vivo* human skin model.

**724** Fel d1 and Fel d4 Fur, Urine and Saliva Levels in Domestic Cats

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**RATIONALE:** Sensitization to cat dander is associated with increased risk of asthma and rhinitis. Cat allergic patients mainly have IgE to Fel d1 but recent reports indicate that some react to Fel d4. There is little information about Fel d4 levels in cats. The purpose of this study was to evaluate and compare Fel d4 in fur, saliva and urine of house cats.

**METHODS:** Cats having general surgical procedures at a local animal hospital were recruited for this study. Owners volunteered their cats and signed an informed consent prior to sample collection. Fur, urine and saliva samples were obtained from male and female cats of various breeds and ages. Commercially available ELISA kits were used to measure Fel d1 and Fel d4.

**RESULTS:** The study included 26 cats. 13 male, 13 female, age 5.6 ± 4.3 years (mean ± SD). Fur was obtained from all cats; urine and saliva from 20 and 17 cats, respectively. Urine Fel d1 (0.02, 0.065-0.071 ug/ml, median, 25-75 percentile) and Fel d4 (<0.4 ug/ml, limit of detection) levels were low. In fur, Fel d4 (0.1, 0.03-0.19 ug/g) was lower than Fel d1 (12.2, 5.0-25.0 ug/g), (p<0.001). Conversely, Fel d4 was higher than Fel d1 in saliva (7.6, 1.3-18.5 vs. 2.5, 0.75-5.7 ug/ml, respectively, p=0.039). Allergen levels were not dependent on age, gender or breed.

**CONCLUSIONS:** This study demonstrates that saliva is the main source of Fel d4 while fur is the main source for Fel d1 in cats. It is possible that levels of Fel d4 in fur arise from saliva deposited when grooming rather than from secretion from the sebaceous glands.

**725** Milk-specific IgE and IgG4 responses are lower in Amish than Hutterite children

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**RATIONALE:** Despite the emergence of food allergy as a significant health care burden, the mechanisms that lead to sensitization are not well understood. The Amish of Indiana and Hutterites of South Dakota represent two genetically and culturally similar farming populations in the United States that nonetheless have significant differences in the prevalence of aeroallergen sensitization and asthma. Recent work highlights a difference in endotoxin exposure related to traditional versus modern farming as one explanation, though other lifestyle differences, such as consumption of raw versus processed milk, could also be important. Here we compared specific IgE and IgG4 responses to common food in children from these two groups.

**METHODS:** We assessed specific-IgE to milk, wheat and peanut as well as specific-IgG4 to milk proteins (alpha-lactalbumin, beta-lactoglobulin, bovine serum albumin, caseins), egg, wheat and peanut in sera from 26 Amish and 26 Hutterite children.

**RESULTS:** The number of sera with detectable IgE to milk (p<0.05) and levels of IgG4 to alpha-lactalbumin >1ug/mL (p<0.01) were lower in Amish than Hutterite children. There was a similar trend for IgG4 responses to beta-lactoglobulin, bovine serum albumin, caseins and egg, but not for wheat or peanut.

**CONCLUSIONS:** Despite many shared genetic and lifestyle features, milk IgE and IgG4 responses are significantly lower in Amish than Hutterite children. This finding is in keeping with an inverse relationship between levels of endotoxin exposure in early childhood and aeroallergen sensitization. The fact that the difference is evident for milk, but not wheat or peanut, suggests that dietary differences may also be relevant.
726 Additive effect between prenatal depression and transepidermal water loss on atopic dermatitis via Th2 immune responses: COCOA study

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RATIONALE: Stress during pregnancy and a defect in skin barrier function may influence childhood allergic diseases, potentially through effects on immune development.

METHODS: Study subjects consisted of 1,716 mother-baby pairs from the longitudinal Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA) birth cohort study. Prenatal stress scales were evaluated using self-reported questionnaires by Center for Epidemiologic Studies Depression (CESD) on 36th weeks of pregnancy. AD in children was diagnosed by pediatric allergists at 1 year. Serum IgE and transepidermal water loss (TEWL) at 1 year and cord blood cytokine assay were measured.

RESULTS: Prenatal maternal depression was not associated with the risk of TEWL and AD at 1 year. High TEWL increased the risk of AD at 1 year (aOR 1.896, 95% CI 1.034-3.479). When divided into four groups using CESD and TEWL, high CESD and high TEWL showed a significant positive association with AD (aOR 5.487, 95% CI 1.572-19.148). Infants with high CESD and high TEWL had the highest ratio of IL-13/IFN-γ in cord blood and serum IgE at 1 year among 4 groups.

CONCLUSIONS: This study showed an additive effect of CESD and skin barrier dysfunction for increasing risk for the development of AD through Th2 immune response in early life.

727 Gut Streptococcus species affect persistence and severity of atopic dermatitis during infancy

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RATIONALE: Perturbations of gut microbiota in early life can disrupt the development of immune system and directly associated with the risk of atopic dermatitis (AD). This study evaluated the association between persistence and severity of AD and the composition of gut microbiota at 6 months of age.

METHODS: The composition of gut microbiota was analyzed in fecal samples from 116 infants (6-month-old) by pyrosequencing, including 58 healthy infants and 58 infants with AD from Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA). AD in infants was diagnosed by a pediatric allergists at 6 months and 1 year of age, and severity of physical symptoms assessed by the SCORAD (Scoring Atopic Dermatitis) index at 6 months. Persistence was defined as AD symptom up to 12 months.

RESULTS: The OTUs (P = 0.027) and Simpson index (P = 0.006) of diversity in gut microbiota were lower in healthy infants than those in persistent AD infants. The composition of Streptococcus was enriched in persistence AD infants than healthy infants (P = 0.001). The composition of Streptococcus pseudopneumoniae, Streptococcus mitis and Streptococcus salivarius were enriched in infants with persistent AD, compared to healthy infants. The relative abundance of S. pseudopneumoniae was increased in persistence AD infants compared with non-persistence AD. The relative abundance of gut S. mitis and S. pseudopneumoniae were positively correlated with serum IgE in infants with AD. S. pseudopneumoniae was positively correlated with SCORAD.

CONCLUSIONS: Gut Streptococcus may affect persistence and severity of AD via IgE mediated allergic inflammation.

728 Phenotypic changes and IOD over-expression in splenic dendritic cells after epicutaneous immunotherapy

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RATIONALE: Epicutaneous immunotherapy (EPIT) was shown to induce Tregs expressing a variety of homing receptors, which are able to migrate and inhibit allergic responses by antigen-presenting cells locally. This study aimed to characterize the effect of EPIT on splenic dendritic cells at the conclusion of immunotherapy and determine whether those changes are sustained.

METHODS: BALB/c mice were orally sensitized to peanut and treated with EPIT for 8 weeks or left untreated (Sham). Splenic dendritic cell subsets were characterized and activation of expression markers were analyzed by flow cytometry [MFI (median of fluorescence) for IOD, CD68, CD80 and MHC-II] immediately following treatment and 8 weeks after the end of the treatment.

RESULTS: Total splenic dendritic cells (CD11c+MHC-II+) exhibited higher MFI for IOD, MHC-II and CD80 following EPIT treatment compared to Sham (respectively 4632 vs 3565, 12978 vs 9447 (p<0.05), 2365 vs 212 (p<0.01)). More specifically, only the resident CD11c+MHC-II+CD11b-CD8- subset demonstrated over-expression of those molecules compared to Sham (IOD: 4548 vs 3543, CD80: 370.5 vs 353, MHC-II: 13881 vs 9624 (p<0.05)). Increases in IOD and MHC-II expressions (p<0.01) was sustained 8 weeks after the end of treatment in CD11c+MHC-II+ and CD11c+MHC-II+CD11b+CD8- subsets (IOD MFI p<0.01).

CONCLUSIONS: EPIT upregulated expression of IOD, CD80 and MHC-II in total splenic dendritic cells and resident CD11b+CD8- IOD over-expression being sustained for 8 weeks after treatment in both populations. EPIT seems to specifically modify the CD11b+CD8- subset, which might inhibit CD4+ proliferation by co-expression of IOD and MHC-II, and promote a tolerogenic environment.

All abstracts are strictly embargoed until the date of presentation at the 2018 AAAAI/WAO Joint Congress.
**Type-1 Regulatory T Cell Frequencies Fluctuate in the First 6 months of Peanut Oral Immunotherapy**

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**Rationale:** Type-1 regulatory T-cells (Tr1) are antigen induced immunosuppressive T-cells that differ from classic CD4+Foxp3+ T-reg cells which are thymic derived. Peanut oral immunotherapy (POIT) has provided desensitization to peanut allergic individuals. Delineation of immunological evaluation exists during the first 6 months of POIT. Here early immunologic changes contributing to the development of peanut allergy are described.

**Methods:** Allergic rhinitis patients which were positive to house dust mite (n=8) were challenged with inhaled Der p1. Peripherial blood were collected and ST2+mDCs were determined using flow cytometry at 0, 0.5 h, 2 h and 4 h after the allergen challenge. Moreover, mDCs were induced from CD14+ monocyte cells, and the levels of ST2+mDCs were investigated under the stimulation of IL-33 and IL-2 by flow cytometry.

**Results:** Inhaled Der p1 significantly increased ST2*mDC levels in the PBMCs of AR patients at 0.5 h and 2 h after challenge, and the ST2*mDC reached the peak at the time point of 0.5 h. Moreover, the percentage of ST2*mDC was up-regulated after the stimulation of IL-33 and IL-2 in vitro.

**Conclusions:** ST2 expression is up-regulated on blood mDCs after allergen inhalation in AR patients. IL-33 stimulation upregulated ST2 expression on mDCs. It suggests that the ST2*mDCs may play important roles in the pathologies of allergic diseases.

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**The Expression of ST2*mDC in Allergic Rhinitis after Inhaled Allergen Challenge**

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**Rationale:** Myeloid dendritic cells (mDCs) are professional antigen-presenting cells. Allergic inflammation increases the number of peripheral blood mDCs and the release of epithelial derived cytokines, such as IL-33 in allergic rhinitis patients. The effects of IL-33 have been implicated in the pathogenesis of allergic disease, which are IL-33 receptor (ST2) depended. However, the effects of inhaled allergens on the levels of ST2*mDCs, and the effects of ST2*mDCs in the pathogenesis of allergic rhinitis are unknown.

**Method:** Allergic rhinitis patients which were positive to house dust mite (n=8) were challenged with inhaled Der p1. Peripherial blood were collected and ST2*mDCs were determined using flow cytometry at 0, 0.5 h, 2 h and 4 h after the allergen challenge. Moreover, mDCs were induced from CD14+ monocyte cells, and the levels of ST2*mDCs were investigated under the stimulation of IL-33 and IL-2 by flow cytometry.

**Results:** Inhaled Der p1 significantly increased ST2*mDC levels in the PBMCs of AR patients at 0.5 h and 2 h after challenge, and the ST2*mDC reached the peak at the time point of 0.5 h. Moreover, the percentage of ST2*mDC was up-regulated after the stimulation of IL-33 and IL-2 in vitro.

**Conclusions:** ST2 expression is up-regulated on blood mDCs after allergen inhalation in AR patients. IL-33 stimulation upregulated ST2 expression on mDCs. It suggests that the ST2*mDCs may play important roles in the pathologies of allergic diseases.

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**Sensitization to House Dust Mites in Patients with Irritable Bowel Syndrome**

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**Rationale:** House dust mites (HDM) may enter the digestive tract in significant quantities, inducing allergic inflammation of gastrointestinal mucosa.

**Methods:** The incidence of sensitization to HDM in Irritable Bowel Syndrome versus healthy individuals was assessed in 90 patients with IBS diagnosed based on the Roman criteria 4 and 60 healthy subjects of comparable gender and age. All patients responded to an initial questionnaire and a detailed allergy medical history. An enzyme-linked immunosorbent assay for specific IgE in serum was done for D.pteronisimus and D. farinae.

**Results:** 58 patients with IBS (64.4%) and 18 patients (30%) in the control group (p<0.01) had moderate and high level of sensitization to D. pteronisimus and 42 patients with IBS (46.6%) and 17 (28.3%) patients in the control group had similar sensitization to D. Farinae. Simultaneous sensitization to both mites was detected in 35 patients with IBS (38.8%) and only in 6 (10%) patients in the control group (p<0.005). Very high sensitization to these allergens was detected in 2 patients with IBS and none in the control group.

**Conclusions:** Sensitization to HDM occurs in patients with IBS significantly more often than in healthy people. HDM is a possible new environmental trigger that contributes to the pathogenic mechanism of IBS in susceptible patients.

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**Sensitization to House Dust Mites in Patients with Irritable Bowel Syndrome**

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**Rationale:** Despite the wide application of HAART, the number of HIV-positive patients continues to grow steadily. This shows an urgent need for a directed search for new antiviral drugs against HIV. The purpose of this study was to investigate the anti-HIV activity of huminic substances.

**Methods:** The corresponding HS samples were huminic (HA), fulvic (FA), and humatomelanic (HMA) acids. The evaluation of anti-HIV efficacy of HA was performed using laboratory adapted HIV strains and different cell targets. The level of virus replication was detected by p24 HIV1 antigen ELISA. Cytotoxicity was determined using the MTT assay.

**Results:** The results showed that the HA and HMA fractions exhibited a distinct antiviral activity within the concentration range from 0.78 µg/mL to 100 µg/mL with respect to HIV1, while fulvic acids showed much less activity. Time of addition assay show that HS have antiviral activity at the stage of HIV fusion, and at the stage of reverse transcription of DNA to RNA, and at the stage of integration of viral DNA into the genome of the host cell. The results of HIV1cell attachment assay show that all HS blocked cellular HIV1 attachment reducing an amount of the GFP-spots per cell.

**Conclusions:** The low cytotoxicity and high anti-HIV activity of HS indicate that these substances hold significant promise as a safe and efficacious antiviral drugs. The ability of HS to interfere with multiple stages of the HIV replication cycle of is viewed as an added benefit suggesting potential for further development as antiviral drugs.
733 Serum periostin levels associates to secondhand tobacco smoke exposure and exercise in children

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RATIONALE: Recent studies have suggested an important role for periostin in the pathogenesis of allergic disease. However, serum periostin levels are limited by lack of reference range values and influencing factors in children.

METHODS: This cross-sectional study examined 1,265 children from the general pediatric population who were first grade to sixth grade attended 6 elementary schools in Korea between June and July 2016. Of the 1,265 children, 249 children from first grade of elementary school were included randomly for the analysis.

RESULTS: The mean levels of periostin and eosinophil were 106.0 (interquartile range [IQR], 92.0 - 124.0) ng/mL and 3.2 (IQR 2.1 - 5.0) %, respectively. Serum periostin level did not show significant difference in gender, body mass index status, eosinophil level, and 25-(OH)D3 status. After univariate linear regression, secondhand tobacco smoke (SHS) exposure in pregnancy was associated with a statistically significant increased risk of serum periostin level (aOR 1.890, 95% CI 1.047 – 3.410, P = 0.035), but no SHS exposure in afterbirth 1 year. Serum periostin level was not associated with current smoking dose and time of weaning. The frequency of exercise ≥2days/week was associated with a statistically significant increased risk of serum periostin level (aOR 2.134, 95% CI 1.211 – 3.761, P = 0.009).

CONCLUSIONS: Serum periostin levels may correlate with SHS exposure during pregnancy and frequency of exercise in children.

734 Comparison of Serum Eosinophil-Derived Neurotoxin Levels between Wheezing and Non-wheezing Groups in Children with Respiratory Tract Infections

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RATIONALE: Eosinophil-derived neurotoxin (EDN) is associated with recurrent wheezing episodes after bronchiolitis, childhood asthma, and allergic rhinitis. We investigated if there is a measurable difference between serum EDN levels in children with wheezing and non-wheezing respiratory infections.

METHODS: 171 children who visited a University Hospital with respiratory infections were enrolled in the study. We divided the children into two groups, which were wheezing (n=46) and non-wheezing (n=125), and compared the levels of serum EDN in these two groups.

RESULTS: The level of serum EDN in the wheezing group was significantly higher than the level of serum EDN in the non-wheezing group (P<0.001). We divided the non-wheezing group into three subgroups: pneumonia, common cold, and tonsillitis. The level of serum EDN in the wheezing group was significantly higher than the level of serum EDN in the pneumonia, the common cold, and the tonsillitis groups (P<0.001). There was no significant difference in the levels of serum EDN among the pneumonia, common cold, and tonsillitis groups.

CONCLUSIONS: These findings suggest that elevated serum EDN levels could be one of the distinctive features of respiratory infections with wheezing.

735 Relationship between Vitamin D status and atopic measures in patients with Strongyloidiasis

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RATIONALE: We previously associated vitamin D deficiency with increased allergic sensitization. Through another project, we diagnosed Strongyloidiasis in a large number of patients presenting with allergic symptoms. This study evaluates whether baseline vitamin D status correlates with atopy in our cohort of patients with Strongyloidiasis.

METHODS: We analyzed the charts of 58 patients with positive Strongyloides serumology seen in our institution’s Allergy/Immunology clinics between 2011 and 2014. We included patients with available data regarding baseline serum 25-hydroxyvitamin D levels, baseline absolute eosinophil counts (AEC), baseline serum total IgE, and number of positive environmental skin prick tests (SPT) from a battery of 18 northeastern allergens. We stratified all patients into Vitamin D sufficient (>30 ng/mL) and Vitamin D deficient (<30 ng/mL) subgroups.

RESULTS: Among 58 patients, 9 were vitamin D sufficient and 49 were deficient (mean levels of 54.3 and 18.3 ng/mL, p<0.0001). In vitamin D sufficient patients, mean AEC was 0.76 K/uL, mean serum total IgE was 664 KU/L, and mean number of positive SPT was 8. In vitamin D deficient patients, mean AEC was 0.38 K/uL, mean serum total IgE was 638.9 KU/L, and mean number of positive SPT was 4.35. The 2-sample t-test revealed that the mean values of AEC, total IgE, and numbers of positive SPT were similar between the vitamin D sufficient and deficient patients (p>0.05).

CONCLUSIONS: We observed no association between Vitamin D deficiency and increased atopy in this patient cohort. Larger studies are necessary to evaluate how vitamin D status correlates with atopic measures in patients with Strongyloidiasis.

736 Combination anti-IgE and anti-IL5 therapies in patients with severe persistent asthma and allergic bronchopulmonary aspergillosis (ABPA)

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RATIONALE: Many patients with severe persistent asthma have evidence of both Th2 and eosinophilic inflammation. This is often seen in ABPA with IgE levels >1000 U/mL and peripheral eosinophil counts >500 cells/mL, however, can also be seen without aspergillus sensitization. The optimal approach to steroid-sparing biologic therapy in such patients is unclear, and many continue to have active disease after a single biologic therapy is initiated.

METHODS: We performed a retrospective review of severe asthma patients treated with both anti-IgE and anti-IL5 therapies simultaneously after failing single monoclonal therapy. Three met diagnostic criteria for ABPA. The average pre-treatment IgE was 997 U/mL, (range 134-1730), eosinophil count 725 cells/mL (range 360-1080), and FEV1 52% (range 26-72% predicted). All patients were initially treated with omalizumab and had a partial response defined as decrease in systemic corticosteroids and improvement in pulmonary function or symptoms; however, none could completely discontinue systemic corticosteroids. Sequential addition of anti-IL5 therapy allowed cessation of systemic corticosteroids in all patients. There have been no adverse events related to dual therapy.

CONCLUSIONS: Combination anti-IgE and anti-IL5 therapy should be considered in patients with severe persistent asthma or ABPA who continue to require systemic steroids or have frequent exacerbations despite single biologic therapy. Blocking Th2 and eosinophilic inflammation may be synergistic resulting in significant clinical improvement in these patients.
**737** Differences in the proliferative capacities of 2014 Epidemic and Fermon EV-D68 Strains

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**RATIONALE:** Enterovirus D68 (EV-D68), first isolated in 1962, caused an epidemic of pediatric respiratory disease in 2014. Genomic analysis of EV-D68 strains from this epidemic revealed point mutations not present in the fermon (1962) strain. Such mutations are thought to facilitate EV-D68 replication due to the proximity of these polymorphisms to viral protease cleavage sites. We sought to assess whether the 2014 EV-D68 strain possesses an increased proliferative capacity when compared to the 1962 fermon strain.

**METHODS:** Using an established rhabdomyosarcoma based model of EV-D68 infection we directly compared proliferative capacity of ATCC VR-1826 EV-D68 (fermon) virus to that of VR-1823 (epidemic) EV-D68. RT-PCR utilizing EV-D68 specific primers and probes was used to compare delta Ct values of the two EV-D68 strains at different time points following inoculation. Indirect immunofluorescence was employed to compare the time course of VP2 protein appearance on rhabdomyosarcoma cells following infection. Graphpad Prism software was utilized to perform student t-test on PCR data and assess statistical significance between groups with significance set at p<0.05

**RESULTS:** EV-D68 virus derived from the 2014 epidemic was able to proliferate with a 1.6 fold increase in genome copy number over 24 hours compared to an increase of 1.09 in the fermon strain by RT-PCR (p<0.001). VP2 protein of EV-D68 was first detected at 7 hours post-infection compared with 10 hours for the fermon strain.

**CONCLUSIONS:** The 2014 epidemic EV-D68 strain displays an increased proliferative capacity when compared to the 1962 fermon strain, probably attributed to the previously described point mutations.

**738** Sensitization pattern in a group of patients with allergic disease through a molecular diagnostic study using microassay-based multiplex technology (ISAC)

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**RATIONALE:** Knowledge of which allergens are sensitized in children aged 1-18 years with allergy symptoms in a group of patients who were given multiplex platforms (ISAC®).

**METHODS:** This study has a transversal, observational, descriptive and retrospective design. All clinical records of patients with ISAC study were reviewed during the period from January 2016 to December 2016

**RESULTS:** Allergic diseases reported in order of frequency were: allergic rhinitis (60%), asthma (26%), and other allergic diseases were atopic dermatitis, urticaria and allergic conjunctivitis, and food allergy. In general, the most frequent sensitizations of seasonal aeroallergens were grasses (Phl d 1, Phl d 5, Phl d 11, Cyn d 1), and in less frequencies Ole e 1, Cup a 1, Sal 1 and Che a 1, perennial allergens, Der f 2 and Der p 2 in more than 50% of patients, Lipocalins (Can f 1, Feld 4), a high frequency of sensitization was found in Bet v1 (PR-10) in 90% of patients, a pattern of Sensitization in 30% of respiratory nSPTs with positive nSPT from food without clinical relevance. Among the most frequent food allergens were Bos d8 (Casein), Gal d2 (ovalbumin), with 20% of sensitization in pocalincis (Bet v4, Phil 7).

**CONCLUSIONS:** The diagnosis of allergic components (natural or recombinant) is a great qualitative leap that allows a significant improvement in the diagnosis and treatment of allergic patients, it is of great importance to know the pattern of sensitization in each population.

**739** Belief, Knowledge, and Practice on Electronic Cigarettes among Allergists, Pulmonologists and General Practitioners

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**RATIONALE:** There has been a striking recent increase in electronic cigarette (e-cig) use in the U.S. The beliefs and practices towards e-cigs among physicians across specialties are unknown.

**METHODS:** An anonymous survey on personal use, knowledge and beliefs of e-cigs was sent to general practitioners (GPs), allergists, and pulmonologists at the University of Michigan. Statistical analysis was performed using T-tests, ANOVA, and logistic regression.

**RESULTS:** A total of 264 physicians completed the survey (222 GPs, 33 pulmonologists, and 9 allergists). All physicians report asking about cigarette use more frequently than e-cig use in the office (p<0.001). Respondents were more likely to attribute use of cigarettes to malignancies, heart, lung and allergic diseases compared to the use of e-cigs (P<0.001). Compared to pulmonologists and GPs, more allergists believe that e-cigs have some advantages over traditional cigarettes (p<0.05). Allergists’ performance on e-cig knowledge questions was significantly lower than pulmonologists but not GPs. Compared to pulmonologists and GPs, allergists did not feel as comfortable at providing e-cig cessation counseling (p<0.001), and fewer allergists agree with banning e-cig sales and advertisement (p<0.05). Age, gender, and faculty status were not significant predictors of e-cig cessation comfort level.

**CONCLUSIONS:** Physicians across specialties lack knowledge and confidence in providing education and cessation counseling for e-cig users. As allergists see an increasing number of patients who use e-cigs, there is an urgent need to incorporate e-cig education into medical teaching and research agendas.

**740** Withdrawn
741 Are smoker asthmatics different than non-smokers in terms of symptoms, risk factors and comorbidities?

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RATIONALE: Smoking is one of the most significant triggers for asthma patients. The aim of this study was to evaluate the differences between smoker asthma (S) patients with non-smoker (NS) and ex-smoking (ES) patients in terms of symptoms, risk factors and comorbidities.

METHODS: A web-based data entry of 500 patients living in the urban area of Istanbul/Turkey who were followed for at least one year after asthma diagnosis was made via Microsoft Access 2013. The registered respiratory symptoms, habits, risk factors, comorbidities of NS, ES, and S patients were compared statistically.

RESULTS: Number and percentage of the NS, ES and S groups and their mean age were respectively 353 (70.6%) 39.9 ± 15.4; 88 (17.6) 44.8 ± 12.7; and 59 (11.8%) 38.0 ± 15.4. No group difference was found between cough, wheeze, chest tightness and dyspnea symptoms; asthma ratios in parents; body mass index; non-steroid anti-inflammatory hypersensitivity; pollen, mite, mold, pet sensitivity; heating methods in both home and workplace; allergic conjunctivitis, rhinitis and or sinusitis comorbidities (p>0.05). Percentage of allergic dermatitis and hypertension was lower in NS group (3.4%; 3.4% respectively) compared to ES and S groups (12.7% 12.7%; and 59 (11.8%) 38.0 15.4). No group difference was found between patients in terms of symptoms, risk factors and comorbidities.

CONCLUSIONS: Smoker and ex-smoker asthma patients of the urban area had similar asthma symptoms and risk factors but they had higher allergic dermatitis and hypertension than non-smoker asthma patients.

742 The Invasiveness of the Genus Sylvilagus in Massachusetts and the Resulting Increase in Human Allergen Sensitization to Rabbits

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RATIONALE: There has been a marked increase in the incidence of Eastern Cottontail rabbits (Sylvilagus floridanus) in Massachusetts. Patients in a community allergist’s office who were seen for rhinosinusitis symptoms had positive skin prick tests (SPT) to rabbit epithelia. Many reported encountering rabbits in their community without actual physical contact. We hypothesized that airborne exposure from rabbit proteins in close-quarters was likely causing sensitization. Rabbit species are difficult to control due to their high reproductive potential. In New England, due to their vigor and adaptability, S. floridanus has displaced S. transitionalis. Conservation measures are likely being applied (wrongly) to the invasive S. floridanus due their physical similarity with S. transitionalis. Identification and controlling the rabbit populations are necessary to curtail further spread of such diseases.

METHODS: We reviewed 250 patient charts with positive SPT to rabbit epithelia. Nearly all patients with positive rabbit skin test had noticed rabbits in their vicinity but denied physical contact.

RESULTS: The invasive S. floridanus outnumbers the native S. transitionalis. There is an increased incidence of positive SPT in children and adults. Cross-reactivity of rabbit epithelia to cats was considered and discarded as not all patients had SPT reactivity to cats, dogs, or rodents.

CONCLUSIONS: We hypothesize that the increasing level of positive SPT results is from airborne exposure to rabbit proteins from increasing S. floridanus population. Besides allergic rhinosinusitis symptoms, rabbits are also known to spread other vector-borne diseases such as the tularemia outbreak in Martha’s Vineyard in 2000. Identifying and controlling the rabbit populations are necessary to curtail further spread of such diseases.

743 Comparison of symptoms during a conjunctival provocation test (CPT) and a controlled exposure to birch pollen in the Strasbourg Environmental Exposure Chamber (EEC) (ALYATEC)

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RATIONALE: As recommended by the task force (Pfaar O et al. Allergy 2017) we compared the results obtained during allergen exposure in EEC with the reference conjunctival provocation test.

AIM: To compare clinical scores obtained during the CPT and in the EEC.

METHODS: 16 patients with an allergic conjunctivitis to birch pollen were selected. They had a positive CPT to birch pollen. They were exposed on 2 consecutive days to nebulized birch pollen in the EEC. Abelson score were performed before and every ten minutes during the 240 minutes of exposure. Challenges were considered positive when Abelson score ≥5.

RESULTS: Among 16 positive CPT, 12 subjects had a positive challenge in the EEC. The mean Abelson score was 6.2 with CPT and 5.8 on day 1 and 5.5 on day 2. A positive response was faster obtained with the CPT (36 ±15min) compared to EEC (92±15min) (p=0.0001). The mean cumulative amount of Bet v1 inducing a positive CPT was 8759.5 ng ±7000 vs 0.2 ng ±0.12 in the EEC (p=0.0001).

CONCLUSIONS: 75% of positive CPT was also positive in EEC. There was a difference in amount of Bet v1 responsible of positive response in CPT and in EEC. The amount in the EEC is closer to the natural exposure (20 to 60 pollen grains) than the individual CPT. ALYATEC’s EEC is a good tool to assess anti-conjunctival drugs.
**744 Specific IgE for Staphylococcus Aureus In Patients With Allergic Rhinitis**

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**RESULTS:** Improved the diagnostic performance of the single components. Moreover, AUC (0.706). A combination of Gly m 8 and Nomenclature Subcommittee, Gly m 8 (2S albumin) showed the highest characteristic (ROC) curves (AUC).

**METHODS:** Oral food challenge (OFC) testing. Specific IgE antibodies to each recombinant allergen component were analyzed.

**CONCLUSIONS:** Specific IgE antibody levels to the fusion protein of allergen components had a higher accuracy for diagnosing soybean allergy than any single allergen component.

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**745 Gly m 5/Gly m 8 fusion component for diagnosing soybean allergy**

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**RESULTS:** Of the 42 analyzed samples, 20 corresponded to AR patients (65% male, and 35% female) and 22 controls (55% female and 45% male). For the AR group, the specific IgE for S. aureus toxins by ImmunoCap. In controls, negative allergy was corroborated by clinical history and aeroallergen skin prick test.

**CONCLUSIONS:** Our data suggest that AR patients have higher levels of specific IgE for S. aureus. Therefore it is necessary to identify in patients who present with frequent exacerbations.

**746 Impact of Cross-reactivity between Major Peanut Allergens Ara h 2 and Ara h 6 on Specific IgE Measurements**

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**METHODS:** Ara h 2 and Ara h 6 were produced in E. coli in order to ensure absence of cross-contamination. Cross-reactivity between allergens was then evaluated with 26 sera from peanut-allergic patients by measuring the residual IgE binding to one 2S-albumin after depletion of IgE antibodies specific to the other 2S-albumin.

**CONCLUSIONS:** Although the profile of IgE specificity was highly variable among the different sera, IgE responses to 2S-albumins were mainly due to antibodies specific to Ara h 2 or to Ara h 6, with only 17% of IgE binding due to cross-reactive IgE antibodies. Moreover, relevance of this cross-reactivity depends on the affinity of the IgE binding, as illustrated by two sera displaying comparable IgE responses to Ara h 6 but related to different capacities of Ara h 6 to induce mast cell degranulation.

**CONCLUSIONS:** Despite high structural homologies between Ara h 2 and Ara h 6, IgE responses to 2S-albumins do not result predominantly from cross-reactive antibodies. However, as direct binding to coated allergens reveals indistinctly low and high-affinity binding, the clinical relevance of this cross-reactivity needs to be further investigated.
747 IgE-reactive 11S globulin from chickpea with homology to Ara h 3

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RATIONALE: Sensitivity to legumes is a prevalent food allergy in the Mediterranean area, with lentil and chickpea being the most frequent causes of allergic reactions. Most of the legume allergens identified are seed storage proteins, profilins, or pathogenesis-related proteins. However, allergenic proteins from chickpea have not been well characterized. This study presents the purification of an allergenic 11S globulin from chickpea.

METHODS: Proteins were extracted from chickpea flour through a series of precipitation and centrifugation steps. Globulin fractions, containing 7S vicilins and 11S legumins, were further purified using ion exchange- and gel-filtration chromatography. The protein was analyzed by SDS-PAGE and LC-MS/MS. Sera from patients with known peanut, chickpea and/or lentil allergies were used to test for IgE reactivity using a chimeric IgE ELISA. Sequence homology was analyzed using BLASTp.

RESULTS: Chickpea 11S globulin consists of multiple polypeptides, which present as 20kD, 37kD, and 54kD bands on SDS-PAGE. All three polypeptides were identified as 11S seed storage protein by LC-MS/MS. Eight out of thirty-six sera from patients allergic to peanut and/or lentils showed IgE reactivity against the purified globulin. The chickpea legumin amino acid sequence shares 53% identity and 72% homology with the major peanut allergen Ara h 3.

CONCLUSIONS: The purified chickpea allergen was confirmed to be an 11S globulin. Presence of multiple polypeptides indicates proteolytic processing characteristic for 11S plant storage proteins. Detection of IgE reactivity to chickpea legumin in sera from peanut and lentil allergic patients suggests that 11S globulins may be cross-reactive allergens of the legume family.

748 Epitope Mapping of 2S albums and Comparison of Ara h 2, Ara h 6 and Ara h 7 from Peanut

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RATIONALE: Peanut allergy is increasing worldwide. Of all the peanut allergens identified, Ara h 2 has been shown to be most correlated with and diagnostic of peanut allergy. In this work, we probed peptide microarrays with peanut allergic sera to identify and compare the linear epitopes of the peanut conglutinins, Ara h 2, Ara h 6 and Ara h 7, and other potentially cross-reactive tree nut 2S albums.

METHODS: 15-mer peptides that were offset by 5 amino acids were printed on glass slides. Patient sera were incubated with the slides. IgE and IgG4 binding was detected with a combination of fluorescently-labelled antibodies. The linear epitopes were mapped to molecular models of the 3-dimensional structures of the allergens.

RESULTS: The majority of the epitopes mapped to the surface of the proteins. In addition, while Ara h 6 and Ara h 7 share 77% and 60% homology with Ara h 2, respectively, not all epitopes identified in these conglutinins were shared among the three allergens. Common epitopes of cross-reactive 2S albums in tree nuts were identified.

CONCLUSIONS: These results not only identify important epitopes for 2S albums as well as Ara h 6 and 7, they demonstrate that while the peanut conglutinins share some epitopes, they also have their own unique IgE and IgG4 epitopes and may not necessarily be diagnostically or immunologically equivalent to Ara h 2.

749 Comparative Analysis Of Specific Allergen Levels In Baked Milk Products

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RATIONALE: Oral food challenges are considered the ‘gold standard’ to determine allergic reactions to food. The recent death of a 3-year-old boy during a routine oral food challenge raises questions about whether this could be related to residual allergen in the baked milk challenge material. The aim was to compare the levels of major milk allergens in uncooked and baked milk containing foods, including recipes used for making oral food challenge materials.

METHODS: Uncooked and baked muffin mix were compared using two-site monoclonal antibody ELISA for beta-lactoglobulin (Bos d 5) and for beta-casein (Bos d 11). The lower limit of detection (LLOD) of these assays were 0.19ng/ml and 31.25ng/ml respectively.

RESULTS: Bos d 5 (beta-lactoglobulin) was reduced from 1200µg/g in uncooked muffin mix to 2µg/g in baked muffin, representing a 99% decrease after baking. Conversely the level of Bos d 11 (beta-casein) decreased from 1000µg/g in uncooked muffin mix to 800µg/g. Representing only a ~20% decrease in allergen after baking.

CONCLUSIONS: The level of major milk allergen Bos d 11 remained high within the baked foods, including those used as oral food challenge material. These findings highlight the differences between specific milk allergen molecules and demonstrates the need to assess each potential allergen individually. These measurements could improve safety of food products in clinical practices for oral food challenges.
Long Term outcome of Peanut Oral Immunotherapy (OIT) in Patients Unable to Reach Maintenance Goal

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RATIONALE: Desensitization of peanut allergic patients by Oral-Immunotherapy (OIT) up to 3000mg peanut protein (PP) enables unlimited peanuts consumption. Some patients, however, have difficulties reaching this maintenance dosing. Knowledge regarding the long-term therapeutic efficacy of patients on lower maintenance doses is limited.

METHODS: The peanut-OIT treatment protocol consisted of an in-hospital initial induction-desensitization phase, in which a maximal individualized tolerated dose was determined and then consumed daily at home. Doses were gradually increased on a monthly basis in a day-hospital care setting. Patients with technical difficulties ingesting the maintenance dose or limited due to allergic reactions were placed on lower daily maintenance doses and instructed to avoid ingesting amounts of PP above it.

RESULTS: Eleven patients ranging from 6-19 years, with starting doses of 12.5 (3-150) mg PP, reached maintenance doses of 1200 (600-1500) mg (median (range), respectively). Duration of OIT-treatment was 5 (3-13) months (median (range), respectively). All patients reacted during induction and 5/11 (45%) experienced reactions during home treatment, including one requiring Epi-Pen. In long-term follow-up after 14 (6-68) months (median (range), respectively), the average SPT-wheat size was reduced from 8.9 to 3.6 millimeter and only 4 subjective reactions were reported. Oral food challenges up to 3000 mg PP were successful in 10/11 patients. One patient whose maintenance dose was 600mg reacted to 2100mg PP. Full compliance to daily dose consumption was reported by 8/11 patients while 3/11 occasionally stopped for greater than a week.

CONCLUSIONS: Prolonged consumption of lower maintenance doses may facilitate complete desensitization in patients experiencing difficulties during peanut-OIT.

Epitope Mapping for the Non-Specific Lipid Transfer Proteins (nsLTP) Among Peanut Allergic Patients

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RATIONALE: Plant food allergy in many European countries, especially in the Mediterranean, are often caused by nsLTP. Studies focused on nsLTP reactivity in patients from the United States are lacking. Our aim was to identify IgE and IgG4 epitopes for the 7 known nsLTP allergens, including the peanut allergen Ara h 9 and 6 homologous allergens from other plants, recognized by peanut-allergic patients from the United States.

METHODS: Synthetic overlapping 15-mer peptides offset by 5 amino acids of the 7 nsLTP allergens from peanut (Ara h 9), walnut (Jug r 3), peach (Pru p 3), kiwi (Act d 10), almond (Pru du 3), and tomato (Lyc e 3.0101 and Lyc e LTP3MAC) were spotted onto microarrays slides. Sera from 15 peanut allergic patients from the US enrolled in a Phase II Oral Immunotherapy trials were applied to the slides to test for IgE and IgG4 binding to the peptides using immunofluorescence. The pre-trial sera of patients in Phase II trial has been examined.

RESULTS: IgE and IgG4 epitope maps for multiple nsLTP allergens were developed. Of the 7 allergens analyzed, the ones from peanuts, walnuts, peaches, and tomatoes had a higher number of peptides recognized by US patients with confirmed peanut allergies.

CONCLUSIONS: Certain regions of the proteins are recognized more often indicating that they represent a conserved and possible cross-reactive region.

Nanoallergens: A Nanoparticle Based Platform for Assessment of Immunogenic Peanut Epitopes in a Clinical Population

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RATIONALE: Currently, the only way to reliably diagnose the severity of a patient’s allergic condition is through a food challenge, which is inherently dangerous to the patient. In our laboratory, we have developed a novel technique called nanoallergens which can predict the severity of a patient’s allergy.

METHODS: Nanoallergens were designed to effectively display individual allergen epitopes from the major peanut proteins Ara h2 and Ara h 6 on their surfaces. As we demonstrate in our experiments, the detailed engineering of these nanoallergens make them very efficient in triggering degranulation in an in vitro degranulation assay with RBL cells primed with peanut allergy patient serum (purchased from a commercial source (N=4)). We also proved their efficiency in degranulation assays using blood samples obtained from children between the ages of 2-15 with clinical history of peanut allergies (N=6). Lastly, nanoallergens were used in a basophil activation test (BAT) triggered by individual Ara h 2 and Ara h 6 epitopes to determine the extent of immunogenicity of these peanut protein epitopes. Identified immunogenic epitopes were then compared to clinical histories.

RESULTS: In vitro analysis from initial RBL cell studies revealed a group of 10 IgE binding epitopes that were then used in the ex vivo BAT analysis. BAT testing demonstrated a group of epitopes common to patients with a history of urticarial reactions but no anaphylaxis reactions.

CONCLUSIONS: This preliminary study demonstrated that nanoallergens can be used with BAT to efficiently determine the immunogenic epitopes for a particular patient and potentially predict clinical reactions to allergens.
Changes in quality of life of food-allergic children from initiation of oral immunotherapy, through updosing, upon reaching maintenance and after 6 months of follow-up

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RATIONAL: Data on changes in quality of life (QOL) of food-allergic children throughout the process of oral immunotherapy (OIT) is limited.

METHODS: Patients of children aged 4–12 years undergoing OIT for food allergy completed the FAQLQ-Parental Form (FAQLQ-PF) at OIT initiation and upon reaching maintenance (n = 158). A subgroup (n = 83) completed the questionnaire also in mid up-dosing phase, and another subgroup (n = 44) 6 months after reaching maintenance. Parents of age- and gender-matched food-allergic children not undergoing OIT, filled the FAQLQ-PF twice, with an interval of several months apart, and served as controls.

RESULTS: Patients who reached maintenance phase (peanut, n = 62; milk, n = 56; tree-nuts, n = 19; egg, n = 12; sesame, n = 9) had significantly improved (lower) FAQLQ-PF scores compared to OIT initiation (Total score: 3.607 vs. 3.133, p < 0.001). Emotional Impact (EI); 3.597 to 3.27
t < 0.001, Food Anxiety (FA); 3.803 to 3.24, p < 0.001, Social and Dietary Limitation (SDL); 3.415 to 2.815, p < 0.001) while no change was noted in the control group between the two time points. Among patients examined in mid up-dosing, those with diminished FAQLQ-PF scores improved significantly upon reaching maintenance, while those with improved scores in mid up-dosing, improved further. Patients who filled the FAQLQ-PF six months after reaching maintenance showed additional significant improvement as well. Emotional Impact (EI); 3.37 to 2.593, p = 0.004, Social and Dietary Limitation (SDL); 2.815 to 2.405, p = 0.007.

CONCLUSIONS: QOL of food-allergic children improves significantly upon reaching OIT maintenance, with additional improvement 6 months later. The detrimental effect of OIT on some patients’ QOL during up-dosing is reversed upon reaching maintenance.

Usefulness of Component-resolved diagnostics (CRD) in predicting hazelnut allergy in Japanese children

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RATIONAL: There have been no report of hazelnut allergy in Japan, while allergy to tree nuts are relatively common. Cor a 9 and Cor a 14 may be responsible for systemic reactions to hazelnut in Europe. We hypothesized that component-resolved diagnostics (CRD) would predict the result of hazelnut oral food challenge (OFC) in Japanese children.

METHODS: We recruited 71 subjects (median age: 7.8 years) who were sensitized to hazelnut and performed a hazelnut OFC at Sagamihara National Hospital from 2007 to 2017. OFCs were performed using roasted hazelnut. The sIgE levels (hazelnut/Cor a 1/Cor a 8/Cor a 9/Cor a 14/alder pollen) were measured using ImmunoCAP. We investigated the predictive factors of a positive hazelnut OFC.

RESULTS: Seven subjects (10%) had a positive OFC, and 3 had systemic reactions. The sIgE to hazelnut/Cor a 1/Cor a 8/Cor a 9/Cor a 14/alder pollen were 9.3/13.9/4.63/0.05/0.84/0.10 (median, U/mL). Hazelnut sIgE was strongly correlated with both Cor a 1 and alder pollen (r = 0.76/0.74).

The sIgE to Cor a 1/alder pollen in OFC positive subjects were significantly lower than those in OFC negative subjects (1.61 vs. 14.8, p = 0.028, 0.05 vs. 6.07, p = 0.029). The area under the receiver operating characteristics curve for hazelnut/Cor a 1/Cor a 8/Cor a 9/Cor a 14/alder pollen was 0.690/0.56/0.59/0.60/0.75 (p = 0.09/0.03/0.60/0.41/0.09/0.03).

CONCLUSIONS: Additional evaluation of sIgE to Cor a 1 or alder pollen seems to improve accuracy in diagnosis of hazelnut allergy in Japanese children sensitized to hazelnut.

Effects of Pressure and Thermal Processing on Pistachio and Cashew in vivo Allergic Reactivity

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RATIONAL: Tree nuts are primarily responsible for fatal allergic reactions. Thermal and non-thermal treatments are mainly carried out in industry to improve food quality. Food processing can modify the structure and function of food proteins and may alter their allergenic properties. We hypothesized that pressure and thermal treatment, could modify pistachio and cashew in vivo allergenicity.

METHODS: An ambispective study was carried out, including patients evaluated between 2006 and 2016, with clinical allergy to pistachio or cashew, confirmed on the basis of either a convincing history of anaphylaxis with positive skin prick test and/or specific serum IgE levels to pistachio or cashew by the fluorescent enzyme immunoassay, or a positive double-blind placebo-controlled food challenge. The SPT were performed with the untreated and treated pistachio and cashew extracts (boiling 30 and 60 minutes, and heat/pressure treatment at 121°C and 138°Celsius during 15 and 30 minutes).

RESULTS: 10 patients were included. 6 patients were allergic to pistachio (66.7% woman, median age 26.5 years), 4 patients were allergic to cashew (50% woman, median age 26.5 years). The SPT median with untreated extract was 9.5mm for pistachio and 12mm for cashew. A consistent decrease in the SPT results after boiling and heat/pressure treatments was observed, becoming negative in all the patients.

CONCLUSIONS: The results of our study indicate that pressure and thermal treatments were able to significantly reduce the size of SPT in patients allergic to pistachio and cashew. It did not seem that any of these treatments increased neither pistachio nor cashew in vivo allergenicity.
Impact of Irradiation on the Protein Content and Microbial Levels of Sesame Seed Flour for use in Oral Immunotherapy

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RATIONALE: Sesame seed flour used in oral immunotherapy studies has to meet specific criteria for allergen content and bioburden according to FDA guidelines for orally administered drugs. Thermal processing of sesame flour failed to decrease the microbial content and increase its shelf life. We studied the effect of gamma irradiation (a type of cold sterilization) on the protein content and bioburden of sesame flour allergens (Ses i 3 and Ses i 2).

METHODS: SDS-PAGE analysis coupled with densitometric scanning was conducted on sesame seed flour exposed to gamma irradiation (Minimum/Maximum Dose of 5.0kGy – 30.0kGy) to determine the effect of irradiation on protein content. Irradiated and non-irradiated sesame flour was tested for the presence of Escherichia coli, Salmonella, aerobic bacteria, mold and yeast levels.

RESULTS: Irradiating sesame flour resulted in <10% variance in the content of Ses i 3 and Ses i 2 proteins as revealed by SDS-PAGE and densitometry analysis. Bioburden testing revealed a significant decrease in aerobic plate count (>2500cfu/g in non-irradiated to <10cfug/g in irradiated) and Escherichia coli levels (Positive/10g in non-irradiated to Negative/10g in irradiated). Importantly, the levels of all microbes after irradiation met criteria established by FDA for an orally delivered drug product.

CONCLUSIONS: Irradiation of sesame seed flour leads to a significant decrease of bioburden levels without significantly altering the protein content. Future studies will determine the effect of irradiation on the allergenicity of sesame seed proteins using Western blotting, ELISA and basophil activation testing.

Nut Oral Immunotherapy (NOIT) for Allergy to One Nut Desensitizes to the Cross Reactive Nut

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RATIONALE: Nut oral immunotherapy (NOIT) has gained increasing popularity over the past ten years but remains a burdensome therapy. There is significant cross-reactivity between cashew and pistachio nuts and between pecan and walnuts. Patients were treated with NOIT to one of the cross-reactive nut pairs and then challenged to the other member of the dyad.

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

RESULTS: Patients were treated with cashew (13), pecan (4) and walnut (4) NOIT. 11/13 cashew, 4/4 pecan, and 4/4 walnut treated patients passed ~6,000mg nut protein challenges to pistachio, walnut and pecan protein, respectively. The two failing cashew treated patients tolerated 500mg and 1000mg of pistachio protein.

CONCLUSIONS: Most NOIT treated patients tolerated the other cross-reactive nut in the dyad. The two cashew treated patients who failed pistachio challenges were partially desensitized because they failed challenges at a relatively high dose of nut protein and would be able to complete pistachio NOIT relatively quickly. Patients allergic to cashew and pistachio or pecan and walnut may be treated with only one nut in the cross-reactive pair decreasing the number of nuts required for NOIT.

Urinary Prostaglandin D2 metabolite is an useful index of oral desensitization against food antigen in mice

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RATIONALE: The development of food allergy largely depends on the intestinal mast cell number and its activation. Previously, we demonstrated that the urinary tetranor-PGDM (te-PGDM), a metabolite of prostaglandin D2, positively correlated with the number and activation of intestinal mast cells. In this study, we examined how the urinary level of te-PGDM change in oral desensitization against food antigen using murine model.

METHODS: Increasing dose of ovalbumin (OVA, 1 – 50 mg) was orally administrated to the OVA-sensitized BALB/c mice. The number of intestinal mast cell and its degranulation were determined in chloroacacetate esterase stained sections. The urinary levels of te-PGDM were measured by using liquid chromatography-tandem mass spectrometry.

RESULTS: Urinary te-PGDM can be an objective and non-invasive biomarker reflecting manifestations. It may be useful to monitor oral immunotherapy.
Clinical characteristics of oral allergy syndrome in children with birch sensitization and atopic dermatitis

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Rationale: This study focused on the clinical characteristics of oral allergy syndrome (OAS) in children with birch sensitization and atopic dermatitis.

Methods: Total 186 patients (aged 2 to 18 old) with birch sensitization and atopic dermatitis between January 2016 and February 2017 were enrolled. The levels of serum total IgE (tIgE), birch and ragweed-specific IgE (sIgE) were measured by ImmunoCAP. The information of causative foods and symptoms were obtained by interview.

Results: Eighty one out of 186 (43.5%) children with atopic dermatitis who were sensitized to birch pollen were diagnosed as having OAS. Prevalence of OAS in children under age 7 years was 36.6%. There was a statistically significant correlation between the level of sIgE to birch pollen and prevalence of OAS. Kiwi was the most common cause in younger age group (under 7 years old) and apple was the most common cause in older age group (7 years older).

Conclusions: These findings provide that the levels of birch-sIgE were the important predictor. The prevalence of OAS in younger age was not a few in this study, therefore the clinicians should raise concerns about OAS even in young age.

Effects of Pressure and Thermal Processing on Chestnut in vivo Allergic Reactivity

Natalia M. Gimenez Licitra, Cinthia A. De La Cruz Martinez, Ruth Barranco, MD, Jesus F. Fernandez Crespo, Ph.D, and Ma Carmen Dieguez, MD; Hospital Universitario 12 de Octubre, Madrid, Spain.

Rationale: Tree nuts are primarily responsible for fatal allergic reactions. Thermal and non-thermal treatments are mainly carried out in industry to improve food quality. Food processing can modify the structure and function of food proteins and may alter their allergenic properties. We hypothesized that pressure and thermal treatment, could modify chestnut in vivo allergenicity.

Methods: An ambispective study was carried out, including patients evaluated between 2006 and 2016, with clinical allergy to chestnut, confirmed on the basis of either a convincing history of anaphylaxis with positive skin prick test and/or specific serum IgE levels to chestnut by the fluorescent enzyme immunoassay, or a positive double-blind placebo-controlled food challenge. The SPT were performed with the untreated and treated chestnut extracts (boiling 30 and 60 minutes, and heat/pressure treatment at 121° and 138° Celsius during 15 and 30 minutes).

Results: 16 patients were included. 68.7% were woman, median age was 42-years and 75% had an allergic respiratory disease. 31.2% were allergic to latex. 50% had allergies to other nuts (nut 75%, hazelnut 50% and almond 37,5%), showing sensitization to LTP (70%) and profilin (40%). The SPT median with untreated chestnut extract was 6.5mm. A consistent decrease in the SPT results size after boiling and heat/pressure treatments was observed. SPT results with heat and pressure treated chestnut extracts became negative.

Conclusions: The results of our study indicate that pressure and thermal treatments were able to significantly reduce the size of SPT in patients allergic to chestnut. It did not seem that any of these treatments increased chestnut allergenicity.

Analysis of Hazelnut Molecular Component Testing Reactivity

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Rationale: Hazelnut allergy, like other food allergies, can come in multiple forms ranging from local to system anaphylactic reactions. Molecular component testing allows risk stratification of patients.

Methods: A retrospective review of national reference laboratory data was performed over an eighteen month period for IgE to rCor a 1, 8, 9, and 14 (Phadia), utilizing data with de-identified patient health information. Data was compiled into risk groups based on current research utilizing a cutoff of 0.1 kU/L as a positive test.

Results: In the overall data set, 56% of samples were positive for either rCor a 9 or rCor a 14, which carries the highest risk for anaphylaxis. Only nine percent of samples were negative for all four of the hazelnut components. Samples that carried a low risk of reactions with only rCor a 1 positive represented 33 percent of the results. The remaining two percent had a variable risk of a serious reaction with only rCor a 8 being positive.

Conclusions: Molecular component allergy testing represents a major step forward in diagnosing and assessing risk for hazelnut allergic individuals. A significant rate of high risk identification indicates the importance of this information for patients and their families.

Long-Term Effect of Combined Therapy of Oral Immunotherapy and Japanese Traditional Medicine Kakkonto on Food Allergy Mice

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Rationale: Kakkonto (KKT), a traditional Japanese herbal medicine, enhances the therapeutic effect of oral immunotherapy (OIT) in a murine food allergy model, which is attributed to the induction of colonic regulatory T cells. This combined therapy (OIT+KKT) is currently undergoing clinical trial. We demonstrated the long-term effect of OIT+KKT that persists after completing the therapy to further clarify the utility of this therapy for clinical use.

Methods: An experimental OIT treatment for FA mice with already established OVA-induced allergic diarrhea was performed with an oral administration of increasing doses of heated OVA for 8 days. KKT was orally administrated 1 h before each oral heated OVA treatment for a combined therapy with OIT. After the completion of the therapies, mice were followed-up for 3 weeks and rechallenged to assess the sustained effect of the therapy. Plasma OVA-specific IgE and IgG1 levels were measured during the discontinuation phase.

Results: The occurrence of allergic diarrhea still remained lower in OIT+KKT-treated mice than OIT- treated mice even after completing the therapies. After discontinuation for 3 weeks, all of vehicle-treated mice and OIT-treated mice exhibited allergic diarrhea, whereas the occurrence of diarrhea was suppressed to 63% in OIT+KKT-treated mice (P<0.01, n=8). In the OIT+KKT treated mice, plasma OVA-specific IgG1 levels were increased compare to non-treated FA mice.

Conclusions: OIT+KKT induces sustained suppression of food allergic symptoms. OIT+KKT-included colonic regulatory T cells may be involved in the sustained effect. These findings suggest that the combined therapy with OIT+KKT is a useful therapy for FA.

Molecular component allergy testing represents a major step forward in diagnosing and assessing risk for hazelnut allergic individuals. A significant rate of high risk identification indicates the importance of this information for patients and their families.
764 Cluster analysis of food-allergy patient data reveals patterns of co-sensitization

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RATIONALE: Patients can be allergic to multiple substances due to IgE-mediated recognition of similar epitopes on proteins from different sources. We applied cluster-detection techniques to food-allergic patient data to detect groups of cross-reactive allergens. Such groupings will be useful for patient-classification, diagnosis, treatment and discovery.

METHODS: Skin prick test (SPT) results were obtained for confirmed food-allergic patients, for allergens common to Mediterranean areas. Patients/allergens with much missing data were excluded. Cluster analysis was performed using R/Cytoscape. Similarity was calculated using binary distance metrics. Patient self-reporting data was also obtained.

RESULTS: Following exclusion, 525 participants and 45 agents were analysed. The allergens giving rise to the most positive SPT results were olive pollen, peach, tree-nuts/peanuts, grasses and house-dust mites. Cluster analysis found that similar allergen-sources tended to group together, including fruits, nits, nuts, dander, trees, weeds and grasses. Comparison with self-reported previous reactions showed high overlap, albeit with notable exceptions including lentils and sesame seeds. The choice of distance metric and clustering method influenced cluster-building.

CONCLUSIONS: SPT analysis reveals patterns of co-reactivity between allergens. This information can aid diagnosis and suggest which allergen-sources to avoid. It can also guide studies of panallergens and epitope mapping. However, the choice of metric to calculate similarity is important: given the predominance of negative data, asymetric metrics are advised. Future work will investigate other geographical areas and patient IgE levels.

765 Effects of Pressure and Thermal Processing on Cashew and Pistachio in vitro Allergic Reactivity

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RATIONALE: Tree nuts are primarily responsible for fatal allergic reactions. Food processing can modify the structure and function of food proteins and may alter their allergenic properties. We hypothesized that pressure and thermal treatment, could modify cashew and pistachio in vitro allergenicity.

METHODS: An ambispective study was carried out, including sera from patients, evaluated between 2006 and 2016, with clinical allergy to cashew or pistachio, confirmed on the basis of either a convincing history of anaphylaxis with positive skin prick test and/or specific serum IgE levels by the fluorescent enzyme immunoassay, or a positive double-blind placebo-controlled food challenge. Immuno blotting was performed in the untreated and treated cashew and pistachio extracts (boiling 30 and 60 minutes, and heat/pressure treatment at 121ºC and 138ºC Celsius during 15 and 30 minutes), and determined the effects of those treatments over the IgE binding capacity of each allergen, quantifying them by ELISA.

RESULTS: Sera from 10 patients were analyzed (6 allergic to pistachio, 4 to cashew). The results showed IgE-binding proteins from 13-33 KD in the pistachio extracts and bands from 19-50 KD in the cashew extracts. A consistent IgE-reactivity decrease after boiling and heat/pressure treatments was observed in IgE-ELISA. The IgE reactive bands disappeared completely in many cases.

CONCLUSIONS: The results of our study indicate that pressure and thermal treatments were able to decrease the IgE-binding properties of pistachio and cashew protein extracts evaluated in IgE-ELISA and IgE-western blot. It did not seem that any of these treatments increased neither pistachio nor cashew allergenicity.

766 Association of quinoa and apple sensitization

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RATIONALE: Quinoa (Chenopodium quinoa) is a plant used for centuries in South America, but is more recently gaining popularity in North America. Quinoa is technically considered a fruit, although many use its seeds as a grain supplement. We tested the hypothesis that sensitization to quinoa is associated with increased apple sensitization.

METHODS: We reviewed the patient research database at Children’s Mercy Hospital, which included patients who were deemed by allergist to need IgE testing (performed by the ImmunoCAP method). We found 212 patients were tested for IgE of quinoa, apple, wheat, and soy. We queried for allergen specific serum IgE of apples, and used wheat and soy as comparisons. Spearman correlation (p) was determined for each variable. Sensitization was defined as an IgE level of 0.35 KU/L or higher.

RESULTS: Of the 212 tested, 64(30.1%) were positive for quinoa with a mean(SD) of 4.32(1.29), 71 were positive for apple sensitization(33.5%) with a mean(SD) of 6.09(1.83). We found that 54 patients(25.4%) were positive for all 4 variables. Apple had a correlation of 0.656 with quinoa(p-value<0.0001), Wheat and quinoa had a correlation of 0.646(p-value<0.0001), and quinoa and soybean had a correlation of 0.713(p-value<0.0001). These associations were consistent with chi-square testing completed. Pairwise comparison of test results showed highest percentages in double negative test results; however, double positive results were also strong at ~30% of sample for all comparisons.

CONCLUSIONS: These findings demonstrate that in this group of patients sensitization to quinoa is associated with sensitization to apple. This association has not been demonstrated in previous literature.

767 Identification of a relevant allergen in the induction of rhinoconjunctivitis in subjects sensitized to peach pollen

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RATIONALE: Peach pollen has been shown to be relevant in the induction of sensitisation in areas of rosaceous fruit agriculture. We have identified a protein of 15 kD as Pru P X that is recognized by patients who are sensitized to peach pollen. Our aim was to prove that in cases with skin test positive to peach pollen and Pru p X, symptoms were induced after nasal challenge with this new allergen.

METHODS: We evaluated subjects who referred nasal/conjunctival symptoms during the exposure to peach tree pollen. Criteria for inclusion were skin prick test positive to peach pollen extract as well as to Pru p X. A nasal provocation tests was made with whole pollen peach extract (5 mg/ml) and if positive further provocation with Pru p X (20 mcg/ml) was made. The response was measured by acoustic rhinometry and symptoms score.

RESULTS: Out of 8 cases evaluated with the selection criteria mentioned above, 5 cases we showed a positive nasal response to both whole pollen extract and Pru p X. In all of them there was a decrease in acoustic rhinometry greater than the 20% of nasal volume plus the appearance of symptoms within the first 30 minutes after challenge and persisted for several hours.

CONCLUSIONS: Pru p X is a relevant allergen present in peach pollen that induces symptoms after pollen exposure and challenge with the purified Pru p 3. Futher work in progress to ass the clinical relevance.
AB244 Abstracts

**768 The Efficacy of Hazelnut IgE Component Testing in Determining Hazelnut Sensitivity**
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**RATIONALE:** Prior studies indicate that hazelnut component testing (HCT) may serve as a better indicator for clinical reactivity than skin prick (SPT) and hazelnut-specific IgE testing (hIGE) in patients with birch pollen allergy. The efficacy of HCT in determining clinical reactivity represents a potential gap in clinical management.

**METHODS:** A retrospective chart review was performed on six patients who underwent HCT to Cor a 1, 8, 9, and 14. None of the patients ate products containing hazelnut (PCH) at the time of HCT due to prior positive allergy testing with hIGE testing (one patient had positive SPT). Four of the patients reported tolerating PCH prior to allergy testing, one had no exposures, and one developed throat itching upon ingestion. The charts were reviewed for demographic data, birch specific IgE (bIgE), hIGE levels, SPT test results, hazelnut Cor a 1, 8, 9, and 14 levels, and trial of PCH.

**RESULTS:** Average total IgE = 411.11 (SD: 529.07; N: 6), hIGE = 15.95 (SD = 17.36; N = 6), bIgE = 9.57 (SD = 15.06; N = 6), Cor a 1 = 29.85 (SD = 40.16; N = 6), Cor a 9 = 0.06; N = 6, Cor a 14 = 0.27 (SD = 0.37; N = 6), and Cor a 14 = 0.27 (SD = 0.37; N = 6). Five of six patients introduced PCH into their diet. Their average Cor a 1 = 15.80 (SD = 41.84; N = 5) and Cor a 9 = 0.12 (SD = 0.06; N = 5) versus the one patient who did not introduce PCH (Cor a 1 = 0.1 and Cor a 9 = 1.43).

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

**769 Characterizing the IgE Reactivity in Oral Allergy Syndrome to Celery and Carrots**
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**RATIONALE:** Few studies have been performed in the U.S. to characterize the IgE reactivity of patients with oral allergy syndrome (OAS) to carrot and celery, which we report here.

**METHODS:** IgE reactivity to raw carrot, celery and almond prepared commercially or in-house in a twenty-seven year old woman with a clinical history of oral allergy syndrome was extensively characterized by a variety of immunological assays including prick to prick testing, denaturing and non-denaturing SDS-PAGE, spot blot and peptide microarray analysis of Bet v 1-like and other allergic proteins.

**RESULTS:** IgE binding to raw celery and carrot protein was significantly increased on spot blot and non-denaturing SDS-PAGE in comparison to denaturing SDS-PAGE. Meanwhile, commercial extracts showed very little to no IgE reactivity in prick to prick or other assays. Microarray analysis of patient’s sera had weak or no IgE binding to linear peptides of Bet v 1-like proteins (Vig r 6, Gly m 4, Pru av 1, Cor a 1 Mal d 1 & Api g 1) but showed strong binding to Lipid Transfer Proteins (Ara h 9, Jug r 3, Pru p 3, Act d 10, lyc e 3, Pru da3) and some 2S albumins.

**CONCLUSIONS:** While linear IgE epitopes are primarily cross-reactive with LTP proteins, conformational epitopes are more important in IgE binding to celery and carrots. Commercially prepared celery and carrot extracts should be re-evaluated for potency and effectiveness in skin prick tests.

**770 Safety of a Two-visit Cluster Schedule with Venom Immunotherapy**
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**RATIONALE:** Venom immunotherapy (VIT) is an effective treatment for subjects with hymenoptera allergy, but systemic reactions may occur in 5% to 15% of patients, especially in the build-up phase. The standard protocol for the build-up phase lasts 8-15 weeks to reach the maintenance dose. During this time, the patient does not have protection and remains at risk for a reaction. However, cluster schedules reduced number of visits. We present the safety of a cluster schedule comprising 5 doses of VIT over 2 weeks/2 visits.

**METHODS:** Thirteen patients with a new diagnosis of bee venom allergy were included. All of them have indication for VIT, (12 males and 1 female, mean age 41.3 years, range 8-67 years). We used Apis mellifera venom depot extract (Hal Allergy: Venomenhal) in 2-day, 5 doses induction cluster schedule: On day 0: 10µg, 20µg, 20µg, and on day 7: 50µg, 50µg were administered subcutaneously at 30-minutes intervals. This was followed by a monthly administration of 100µg. Pretreatment with antihistamines were given, and local cold were applied on arms immediately after the injections.

**RESULTS:** No systemic reactions were observed. Delayed local reactions were seen in 4 patients in the build-up phase and disappeared in 2-4 days with oral antihistamines. Four patients tolerated spontaneous bee sting at countryside.

**CONCLUSIONS:** Two day cluster program with VIT is safe and appropriate for patients at high risk of anaphylactic reactions to spontaneous stings, in our population.

**771 Survey on the proper use of anadrenaline auto-injectorin 551 Japanese outdoor workers after hymenopteran sting**
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**RATIONALE:** Only 23%-57% of Japanese outdoor workers (OWs) with a history of a systemic reaction (SR) to a Hymenoptera venom had been prescribed adrenaline auto-injectors(AAI). Nonetheless, no survey has investigated the proper use of AAI by affected workers in occupational settings. We surveyed OWs in Japan to examine the proper use of AAI.

**METHODS:** The participants were contacted via both e-mail and telephone by government staff. In a valid responses obtained from 3068 OWs, 1220 had been prescribed AAI to prevent SR to Hymenoptera stings. All participants completed the questionnaires between October 2016 and February 2017. The questionnaire includes the following items: experience of a Hymenoptera sting after prescription of an AAI, SR after a Hymenoptera sting. Nothing, no survey has investigated the proper use of AAI. The other 41 (63.1%) were not treated with an AAI. On the other hand, 20 (4.2%) OWs were treated with an AAI.

**CONCLUSIONS:** This study suggests that physicians and health care workers should be better educated about the proper use of AAI, including subsequent hospital emergency visits after the appearance of SR and for re-prescriptions to OWs.
Exploration of Non-Daily Maintenance Dosing Regimens in Peanut Oral Immunotherapy

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RATIONALE: Daily dosing is conventionally used during oral immunotherapy (OIT) maintenance. Whereas other forms of IT (e.g., for venom anaphylaxis) routinely lengthen dosing intervals during maintenance, it is not known whether this is feasible in peanut OIT.

METHODS: ARC004 is a multicenter, open-label extension study of peanut OIT that follows a pivotal randomized controlled trial where all subjects received six months of daily maintenance. ARC004 is designed to offer extended maintenance (EM) OIT, with some subjects receiving daily regimens and others conditionally receiving incrementally lengthened dosing intervals [e.g., every other day (QOD), twice weekly (BIW), and weekly (QW)]. Stringent stopping criteria are in place in this ongoing exploratory study to ensure safety; continued effectiveness, as measured by double-blind, placebo-controlled peanut challenges will be assessed at study completion.

RESULTS: At the time of this writing, 258 subjects have been enrolled, of which 190 received active treatment in the prior study and began EM in ARC004. 120 continued daily dosing, 50 additional subjects began QOD dosing regimens for four weeks, and advanced to BIW for 24 additional weeks as tolerated. Of these, 13 of 13 successfully tolerated QOD dosing and advanced to BIW; 35 (70%) currently remain in QOD and 2 (4%) withdrew consent, unrelated to adverse events. No subjects have yet reached QW dosing.

CONCLUSIONS: ARC004 is an ongoing, novel study that will produce critically-needed hypothesis-generating data concerning the safety and efficacy of non-daily EM regimens in peanut OIT. Although patients have thus far tolerated alternative dosing intervals, analysis of continued effectiveness is pending.

Goals and Motivations of Families Pursuing Oral Immunotherapy for Food Allergy

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RATIONALE: We understand little about motivations of families who choose oral immunotherapy (OIT), particularly outside of the research setting. Understanding these goals may guide development of future therapies.

METHODS: Parents of children treated with OIT were recruited for a web survey using social media and food allergy advocacy list serves.

RESULTS: 123 parents of children aged 1-19 years participated. 33% were in OIT maintenance, 34% in dose build-up, 22% had finished maintenance, and 11% discontinued OIT prematurely. The majority of subjects received non-research based OIT (65%).

Sixty-five percent agreed with a definition of success as “avoiding the food but having a lower rate of reaction than prior to treatment,” while only 19% agreed that success was “eating the allergenic food but having a higher rate of reaction.”

Asked about their primary goal for starting OIT, 75% of respondents chose “Reducing the risk of a fatal food reaction,” 12% “Reducing the hassle of strict avoidance,” and 11% “Being able to incorporate the food into the diet normally.” A significant minority thought there was a high likelihood that their child would have a fatal reaction prior to the initiation of OIT: 28% thought the risk was at least 1 in 100, 18% 1 in 1000, and 54% 1 in 10,000 or less.

CONCLUSIONS: Families who pursue OIT are driven strongly by anxiety about fatal reactions and define success as lowering the rate of allergic reactions to a food. It appears that some families may be motivated by inflated assessment of the danger of untreated food allergy.

Risk Factors Associated with Peanut Allergy in a High Risk Infant Cohort (CoFAR)

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RATIONALE: To determine baseline demographic, clinical and serum/skin test parameters associated with development of peanut allergy (PNA) in a cohort of 3-15 month olds with likely egg/milk allergy and/or moderate-severe atopic dermatitis and a positive egg/milk skin prick test (SPT), but no known PNA.

METHODS: The primary endpoint was PNA [confirmed/convincing diagnosis at any time or last classified as serologic PNA (<2 yrs, ≥5 kUA/L, otherwise ≥4 kUA/L)] among 511 participants followed a median of 7.3 years. Univariate logistic regression was used to explore associations; baseline factors with p<0.15 were analyzed by stepwise multiple logistic regression, stratified by PNA status and run on randomized development and validation datasets.

RESULTS: 205/511 (40.1%) were classified as PNA. Baseline factors associated with PNA with p<0.01 included: increased AD severity, higher egg and peanut SPT, higher egg, milk, peanut, Ara H1, Ara H2, and Ara H3 IgE, higher peanut IgG and peanut IgG4, and increased peanut consumption during pregnancy. P-values were between 0.01 and 0.05 for younger age, non-white race, lack of breastfeeding, and increased peanut consumption during lactation. The stepwise model identified younger age at enrollment, higher peanut and Ara H2 IgE, and lack of breastfeeding as risk factors. The final model predicted 79.4% in the development and 74.8% in the validation dataset (AUC=0.83 for both). Models using stricter PNA criteria found higher Ara H2 as predictive.

CONCLUSIONS: We identified key risk factors associated with PNA, lack of breastfeeding, higher Ara H2 and peanut-specific IgE, which can be used to predict outcomes.
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**775 Peanut Oral Immunotherapy Threshold Dose for Reactivity: What is the Upper Limit?**

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**RATIONALE:** Previous peanut oral immunotherapy (POIT) trials have examined the efficacy of treatment through assessment of the proportion of subjects successfully completing a double blind placebo controlled food challenge (DBPCFC) with up to a cumulative dose of 5000 mg of peanut protein after 3900 mg maintenance dosing. The upper threshold for clinical reactivity after POIT has not been determined.

**METHODS:** A single center pilot clinical trial of POIT with peanut allergic subjects was performed with a build-up phase to a daily maintenance dose of 3900 mg of peanut protein or highest tolerated dose, over ~48 weeks. Skin prick testing (SPT) was performed at baseline and at maintenance. The upper threshold dose of clinical reactivity was measured with DBPFC with a cumulative dose of 26,225 mg. A general linear mixed model was used to compare mean challenge reaction doses at baseline versus 1 year.

**RESULTS:** Of 15 treated subjects, 10 (67%) subjects advanced to baseline versus 1 year. Skin prick testing (SPT) was performed at baseline and at maintenance. Of nine subjects, 8 (89%) reacted to 10,725 mg and 4 (44%) to 16,225 mg. The mean cumulative reaction dose at baseline was 149 mg compared with 18 to 4 mm ($p < 0.002$). Median peanut SPT wheal size decreased from 18 to 4 mm ($p = 0.002$).

**CONCLUSIONS:** POIT with 3900 mg regular maintenance dosing induced clinical desensitization to doses as high as 2-6 times the daily maintenance dose of 3900 mg of peanut protein or highest tolerated dose, over ~48 weeks. Skin prick testing (SPT) was performed at baseline and at maintenance. The upper threshold dose of clinical reactivity was measured with DBPFC with a cumulative dose of 26,225 mg. A general linear mixed model was used to compare mean challenge reaction doses at baseline versus 1 year.

**776 Changes in Binding Patterns of Cashew-Specific IgE and IgG4 Over the Course of Oral Immunotherapy with Omalizumab**

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**RATIONALE:** The mechanisms by which oral immunotherapy (OIT) induces desensitization are under study. Increases in the ratio of allergen-specific IgG4 to IgE have been consistently observed in OIT trials. Because recognition of major allergen proteins by IgE is associated with clinical allergy whereas IgG4 has a protective effect, changes in the diversity, quantity, and interactions of these antibodies may contribute to desensitization.

**METHODS:** Immunoblotting for cashew-specific IgE and IgG4 was performed for 12 cashew-allergic participants and 3 non-cashew-allergic controls undergoing multi-allergen OIT with omalizumab adjuvant therapy. Binding patterns at the beginning of therapy (Week 0) were compared to binding patterns at the end (Week 36). No omalizumab was present in the blood at these two time points.

**RESULTS:** The number of proteins bound by IgE decreased in 8/12 participants from a mean of 4.0 proteins at Week 0 to 1.6 proteins at Week 36. The most frequently and persistently bound protein was the large subunit of Ana o 2 (9 participants at Week 0 versus 6 at Week 36). Number of proteins bound by IgG4 increased in 12/12 participants from a mean of 1.9 to 4.6 proteins. Again, the large subunit of Ana o 2 was most frequently bound (7 participants at Week 0 versus 10 at Week 36). The largest induction of IgG4 binding was observed for intact Ana o 3 (1 participant at Week 0 versus 7 at Week 36).

**CONCLUSIONS:** Our preliminary data suggests decreases in cashew-specific IgE and increases in cashew-specific IgG4 during cashew immunotherapy.

**777 Targeting IL-33 in Food Allergy: Toward patient stratification**

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**RATIONALE:** Heterogeneity of peanut-specific memory T cell responses could be related to clinical treatment outcomes. Recent findings show that IL-33 can exacerbate Type 2 immune responses through its receptor ST2. However, the functional role of IL-33 in modulating human allergen-specific CD4+ T cell responses remains unclear.

**METHODS:** Peanut allergic subjects ($n = 15$), aged 6 to 67, were recruited on the basis of clinical history, a serum IgE to peanut of $> 0.35$ kU/L or positive skin prick test to peanut, and reaction to peanut during oral food challenge. Peanut-specific T-cells were tracked and profiled in vivo using CD154 upregulation assay in the absence or presence of soluble IL-33. Analyses of surface marker phenotype and the molecular and cytokine profile of these cells was performed to determine the impact of IL-33 in modulating T cell responses to food allergen.

**RESULTS:** Peanut-reactive T cells fall into two major subsets based on ST2 expression. Expression of ST2 on peanut reactive CD4+ T cells is induced after TCR activation but restricted to the TH2A cell subset (CD27- CRTH2+ CD161+). Interestingly, we observed an increased prevalence of allergen-specific TH2A cells in young peanut allergic subjects compared to adults. Following TCR triggering, IL-33 selectively amplifies pro-inflammatory function of these pathogenic T cells.

**CONCLUSIONS:** IL-33 is a key regulator of TH2A cell functions and represents an attractive therapeutic target for the treatment of allergic diseases. However, given the complexity of food allergy, stratification of food allergic patients based on their immunotype could enhance immune-therapeutic treatment efficacy.
Clinical utility of basophil activation test in diagnosis of fish allergy

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RATIONALE: The rising consumption of fish, due to its nutritional value, has led to an increase in fish allergy. There is, however, no reliable predictive marker for diagnosis of fish allergy except for time-consuming oral food challenge (OFC). It has been reported that results of specific IgE (sIgE) and skin prick test do not correlate well with a clinically significant allergy. Diagnostic value of basophil activation test (BAT) has been reported in various food allergy, but not in fish allergy.

METHODS: We performed retrospective analysis of 55 patients who were suspected of fish allergy. Diagnosis of allergy to each kind of fish was made by positive OFC or immediate induced symptoms after eating a specific fish. Negative fish allergy was based on negative OFC or regular eating of a specific fish. Whole blood was incubated with various kinds of fish extracts and induced expression CD203c on basophils was analyzed by a flow cytometry. ImmunoCAP sIgE to each kind of fish was also measured. Predictive performance of the two tests for fish allergy was evaluated using receiver-operating characteristic (ROC) analysis.

RESULTS: Area under the curve (AUC) for BAT was higher than sIgE; tuna: 0.94 vs. 0.62, salmon: 0.90 vs. 0.74, mackerel: 0.90 vs. 0.69, respectively. AUC for BAT in diagnosis of flounder, red snapper, yellowtail and bonito allergies, for which sIgE test was not available, was also high at 0.91, 0.87, 0.81 and 0.80, respectively.

CONCLUSIONS: BAT using CD203c expression may a reliable method to predict fish allergy.

Novel Markers in the Basophil Activation Test may Improve its Clinical Relevance as a Diagnostic Tool

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RATIONALE: The basophil activation test (BAT) has been used experimentally to detect IgE mediated responses, but is not widely used as a clinical diagnostic tool in pediatric food allergy. We hypothesized the use of novel activation markers may increase specificity in the BAT, or correlate to the severity of symptoms.

METHODS: Fifteen children with and without food allergy were recruited from Lurie Children’s Hospital. Peripheral blood was collected from each patient and was stained for BAT testing before being run by flow cytometry. Activated basophils were measured by CD63 expression. Clinical histories were obtained by a board-certified allergist, and were scored for severity of food allergy symptoms. Cell-surface marker activation was compared between children with and without food allergy using the Kruskal-Wallis test, while the one-way ANOVA was used to compare percent marker activation to severity score. The interaction between antigen stimulation dose and symptom severity on BAT marker expression was calculated using a two-way ANOVA test.

RESULTS: CD63, CD82 and CD164 demonstrated increased expression in activated basophils upon antigen stimulation in food allergic children and not in control children (p<0.05 for each marker). CD63 upregulation on basophils correlated to stimulation dose (p=0.0002), but not clinical severity (p=0.41092). Similar results were seen for CD82 (p<0.0001; p=0.1297) and CD164 (p=0.0001; p=0.1135). Interestingly, CD151 correlated with both stimulation dose (p=0.0010) and clinical severity (p=0.0176).

CONCLUSIONS: Novel markers may improve the clinical relevance of the BAT test and provide a way to predict severity of food allergy symptoms in children.

Luciferase Immunoprecipitation Systems (LIPS) immunoassay is a Sensitive and Rapid Method for Detection of Allergen Component-Specific IgE

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RATIONALE: Current laboratory methods to detect allergen-specific IgE require relatively large sample volumes and use either crude biological extracts or purified recombinant allergens, the latter difficult to obtain in conformationally active forms. We demonstrate the use of synthetic biology coupled with previously-described luciferase immunoprecipitation systems (LIPS) immunoassays as a novel method to detect allergen component-specific IgE in small sample volumes.

METHODS: Sera from healthy volunteers, helminth-infected individuals, and peanut-allergic children were screened for IgE to peanut components or cat using ImmunoCAP. Renilla luciferase (Ruc) fusion protein constructs were synthesized for Fel d 1 (cat) and Ara h 1, 2, 3, 8 and 9 (peanut). Constructs were transfected into 293 cells. LIPS immunoassays were performed with allergen-Ruc fusion proteins and 5-10 ul of serum per component.

RESULTS: Cat IgE levels ranged from 0.36 to >100. For Fel d 1 LIPS, the signal/noise ratio differed significantly between cat IgE- samples and samples with cat IgE > 0.5 (p < 0.01). LIPS signal correlated to cat IgE levels with R^2 = 0.779, p < 0.001. For Ara h 1-3, LIPS detected component-specific IgE in known positive samples and was negative for known peanut- or Ara h 1, 2, 3, 8, and 9 (peanut) samples. LIPS for Ara h 8-9 could not distinguish between samples positive and negative for these components. Assays were completed in less than one hour.

CONCLUSIONS: LIPS immunoassays are a sensitive, rapid method of detecting allergen component-specific IgE in small volumes of human serum, with few limits to the number of possible components for testing.
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**781 Can urinary tetranor-PGDM, a metabolite from prostaglandin D2, be used as a reliable marker for evaluating the effectiveness of oral immunotherapies for children with food allergies?**

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**METHODS:** Urine samples from 17 children undergoing OIT were collected at three points: 4 hours after food intake at home for OIT, before OFC (baseline), and 4 hours after OFC. All the patients continued to consume low doses of foods for more than 6 months and did not experience any allergic reaction on the day of urine collection.

**RESULTS:** The results of OFC were negative for 8 patients and positive for 9 patients (ages 2-13). The ratios of the cumulative dose of food used for OFC (baseline), and 4 hours after OFC. All the patients continued to have positive reactions on the day of urine collection.

**CONCLUSIONS:** The urinary tetranor-PGDM concentration at 4 hours after food intake at home in patients receiving OIT can be used to predict the usefulness of urinary tetranor-PGDM as a predictor of the effectiveness of oral immunotherapies (OIT).

**782 Tolerance induction to peach using glycosylated nanostructures including Pru p 3-Epitope**

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**RATIONALE:** Tetranor-PGDM is a metabolite of prostaglandin D2 that is secreted by mast cells. Previously, we reported that the concentration of urinary tetranor-PGDM at 4 hours after the start of an oral food challenge (OFC) was associated with the severity grade of the immediate allergic reaction. The aim of this study was to verify the usefulness of urinary tetranor-PGDM as a predictor of the effectiveness of oral immunotherapies (OIT).

**METHODS:** Urine samples from 17 children undergoing OIT were collected at three points: 4 hours after food intake at home for OIT, before OFC (baseline), and 4 hours after OFC. All the patients continued to consume low doses of foods for more than 6 months and did not experience any allergic reaction on the day of urine collection.

**RESULTS:** The results of OFC were negative for 8 patients and positive for 9 patients (ages 2-13). The ratios of the cumulative dose of food used for the OFC/daily intake dose of the food for OFC at home were similar between OFC-positive patients and OFC-negative patients, (28.4 and 22.5, respectively, P > 0.05). The mean difference in the tetranor-PGDM concentration between 4 hours after food intake at home and the baseline concentration in OFC-positive patients was significantly higher than that in OFC-negative patients (0.95 vs. 0.16 ng/ml CRE, P < 0.05).

**CONCLUSIONS:** The urinary tetranor-PGDM concentration at 4 hours after food intake at home in patients receiving OIT can be used to predict the results of OIT as verified using OFC by detecting the subclinical activation status of mast cells during OIT.

**783 A mouse model of walnut allergy mimics key features of the human disease**

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**RATIONALE:** Tree nut allergies are not typically outgrown and can lead to life-threatening anaphylaxis. A mouse model of walnut allergy that replicates features of the clinical condition would be a valuable tool to generate pre-clinical data for novel therapeutic approaches aimed at treating walnut and other tree nut allergies.

**METHODS:** A Collaborative Cross mouse strain was used to develop a mouse model of walnut allergy. Mice were sensitized to walnut once per week for four weeks by intragastric feeding of walnut extract plus cholera toxin. Mice were bled post-sensitization and antigen-specific IgE was quantified by ELISA. Finally, mice underwent oral challenges with walnut, pecan, or egg.

**RESULTS:** Mice sensitized to walnut produced IgE against walnut extract, the major walnut allergens Jug r 1 and Jug r 2, and pecan extract, but not to egg proteins. Walnut- and pecan-IgE were highly correlated (Spearman r = 0.824, p < 0.0001) as is seen in allergic patients. Oral challenges with walnut and pecan produced severe reactions with mean body temperature decreases of 5.3°C and 4.7°C, respectively, along with overt allergic symptoms including labored breathing, diarrhea, and reduced activity.

**CONCLUSIONS:** Walnut-sensitized mice generate IgE against the major walnut allergens, IgE cross-reacts with pecan allergens, and mice experience anaphylaxis to walnut as well as pecan, thus replicating important immunologic characteristics typical of walnut allergic patients. This model will provide a platform for developing immunotherapy for walnut and pecan allergies.
Age Does Not Affect The Safety of Progressive Food Introduction in Food Allergic Children with High Reaction Thresholds

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RATIONALE: About half of food allergic children react to over 300 mg of allergen protein content. In such patients with high thresholds, the allergen can often be introduced progressively in the diet without the burden of classical OIT approaches. Since age has been suggested to negatively impact on the outcomes of OIT, we sought to compare its impact on this specific population.

METHODS: Charts from all food allergic patients (defined by a positive challenge or >95% PPV on testing) with high reaction thresholds having undergone progressive food introduction after May 2012 were reviewed. Food introduction dynamics (starting daily food dose and progression speed), and dosing reactions were compared between younger (<5y-o) and older (>5y-o) children.

RESULTS: Thirty-seven (46%) young children (10mo-5y) and 43 older children (6-20y) with high reaction thresholds underwent progressive daily introduction of their food allergen in their diet during the studied period. Index foods included mainly peanuts (53%), egg (14%), sesame (10%), milk (9%) and soy (6%). During an average follow-up of 1.5 years, 24 (64%) of the younger children did not report any symptoms compared to 23 (53%) of the older ones (p=0.94). Starting dose (average 616mg vs 808mg) and increase speed (average 88%/month vs 62%/month) did not differ significantly between younger and older children.

CONCLUSIONS: We did not find significant difference in older children undergoing progressive food introduction suggesting safety is not impacted by age in this setting. Longer follow-up will be needed to assess the effect on rates of sustained tolerance.

Safety of Mixed Tree Nut Oral Food Challenges in the Management of Multi-Tree Nut Allergic Children and Adolescents

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RATIONALE: Tree nut (TN) allergic individuals are often sensitized to multiple TN, which can result in multiple, potentially high risk diagnostic oral food challenges (OFC). We report safety and utility of mixed-TN OFC (MTN-OFC) in the evaluation and management of TN allergy.

METHODS: Multi-TN allergic individuals age 3-21 years (n=44), actively restricting multiple TN in diet were evaluated for MTN-OFC eligibility using combination of clinical history and TN-specific IgE, SPT. MTN-OFCs included a 3 TN combination of either walnut, pecan, almond, cashew, hazelnut, pistachio, Brazil nut or pine nut (10g by weight of each TN) administered in incremental doses. Phone surveys ≥ 6 months after passing MTN-OFC evaluated TN dietary incorporation.

RESULTS: In 44 subjects (63% male) undergoing MTN-OFC, 77% (n=34) passed; 30/34 who passed (88%) incorporated all TN into diet while 4/34(12%) added tested TN only. Of those who failed (n=10) the majority reported mild-moderate symptoms; no epinephrine doses required. Almond, pecan, cashew and walnut were most commonly included TN. Median TN-specific IgE values prior to MTN-OFC were almond 0.35, cashew 0.35, pecan 0.35, walnut 0.57, pistachio 0.56, hazelnut 0.64. Comorbid atopic disorders included allergic rhinitis (65%), atopic dermatitis (58%), and other food allergies (78%). Long-term follow-up surveys (≥6mo) are ongoing, the majority (73%) surveyed to date continue to tolerate dietary TN.

CONCLUSIONS: MTN-OFCs have a favorable safety profile and reduce the number of single-TN OFCs when performed in carefully selected individuals. Further investigation is important to understand the predictors of MTN-OFC outcome and long-term TN dietary incorporation.

Caregiver and Expecting Caregiver Support for Early Peanut Introduction Recommendations

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RATIONALE: Recent clinical guidelines recommend early peanut introduction (EPI) beginning around 4-6 months in infants with either severe eczema and/or egg allergy, and around 6 months for all other infants. Caregiver preferences for such practices have not been explored.

METHODS: We explored preferences for EPI and in-office peanut allergy risk assessment (IPRA) through a nationally-representative survey of expecting caregivers (n=1000) and new caregivers of infants under age 1 (n=1000).

RESULTS: Among a primarily female (99.7%), married (80.3%), and white (74.4%) sample, 29% had no/vague awareness of the new guidelines, 61% had no/minimal concern for their child developing food allergy, but 54% felt that timing of introduction has moderate/strong importance for developing food allergy. Only 31% expressed willingness to introduce peanut before or around 6 months of life, with 40% reporting willingness to introduce after 11 months of life, similar to nuts and seafood. In contrast, 60% reported willingness to introduce egg before 8 months. 51% and 56.8% were unwilling to allow IPRA methods such as skin testing and oral challenge before 11 months of life, respectively. However, both odds of willingness to introduce peanut and undergo challenge after 6 months of life were lower among expecting caregivers (OR 0.79, CI 0.65-0.96; and OR 0.67, CI 0.54-0.82, respectively).

CONCLUSIONS: Among new and expecting caregivers, there is poor current support for EPI recommendations, including methods for IPRA. Support was better among expecting caregivers, though still poor. These trends underscore a tremendous need for a formal implementation plan to facilitate EPI and maximize its associated preventive benefits.
**787** Caregiver Peanut Feeding Practices Following Oral Food Challenges to Peanut in Infants

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**RATIONALE:** Recent NIAID guidelines promote early peanut introduction to prevent allergy in at-risk infants. We aim to assess the safety of oral food challenges (OFC) and subsequent caregiver-infant peanut feeding practices.

**METHODS:** A retrospective chart review was conducted of infants ≤12 months of age who completed a peanut OFC from 2016-2017. For passed challenges, caregivers were instructed to continue feedings with at least 2g of peanut protein, at least three times a week. Follow-up surveys regarding caregiver-infant peanut feeding practices were assessed. Study was IRB exempt approved.

**RESULTS:** Twenty-one patients were identified. Median age was 10 months (range 5-12 months). 86% had eczema and 9% had a peanut-allergic sibling. 71% had positive skin testing to peanut and 82% to egg white with mean wheal sizes of 3.2mm (95% CI [2.2, 4.2]) and 6.9mm (95% CI [3.6-10.3]), respectively. Of 6 failed OFCs, 3 required IM epinephrine and 1 required fluid resuscitation. The caregivers of all 15 infants who passed their OFC continued offering peanut at home. 57% consumed ≥2g and 29% consumed <2g of peanut protein three times a week; 14% consumed 2g every two weeks. The average period of infant home peanut consumption was 5 months (range 0.5-12.5 months) with no adverse symptoms reported.

**CONCLUSIONS:** Higher than expected rates of failed OFC with varying severity were noted. While continued home peanut consumption without reaction, variable peanut feeding practices among caregivers were observed. Long-term follow-up is required to evaluate clinical outcomes.

**788** Baked Egg Oral Immunotherapy (OIT) Induces Significant Immune Modulation in Baked Egg Reactive Subjects and Induces Tolerance to Lightly Cooked Egg

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**RATIONALE:** Approximately 30% of egg allergic children (EAC) react to baked egg (BE). We hypothesized that BE OIT would induce immunomodulation and protection to BE and lightly cooked egg (LCE) consistent with desensitization.

**METHODS:** EAC reacting to BE containing high dose (3.8g) egg protein or with ovomucoid (OM)-IgE>50kU/L were included. Dosing started with daily ingestion of 125mg BE, then home up-dosing weekly through week 4 and at 3, 6, and 9 months. At 12 months subjects were challenged to 3.8g of BE and after at least 20 months were challenged to 6g LCE. Egg white (EW), OM-, and ovalbumin (OA)-IgE and IgG4, and EW skin prick test (SPT) were obtained at 0, 6, 12, 18 and 24 months. Outcomes were analyzed using Wilcoxon signed-rank test (significance level at 0.05).

**RESULTS:** Six of 13 subjects (2-11 years-old) completed therapy. Five withdrew because of dietary non-compliance, 1 developed leukemia, and 1 subject ingested LCE at home without reaction prior to the scheduled LCE challenge. All 6 subjects passed the 12-month BE challenge and the LCE challenge after at least 24 months of BE ingestion. A significant increase in EW-, OM-, and OA-IgG4, and decrease in EW-, OM- and OA-IgE:IgG4 (p<0.05) was detected at 6 months. OA-IgE significantly increased (p<0.05) and EW-SPT significantly decreased (p<0.05) at 12 months.

**CONCLUSIONS:** BE OIT safely desensitizes severely egg allergic children to LCE and induces significant immunomodulatory changes. Additional investigation in larger cohorts is necessary to understand the potential role of high protein BE OIT for EAC.

**789** Barriers to Implementation of the NIAID Guideline Among Primary Care Physicians and Allergists

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**RATIONALE:** The approach to peanut allergy prevention has shifted with publication of the Learning Early About Peanut (LEAP) trial and recently released NIAID guideline. Our objective was to determine whether current practice patterns at both the allergist and primary care level are in keeping with the LEAP recommendations and NIAID guideline.

**METHODS:** A 17-question survey was distributed in 2016 to Canadian allergists through the Canadian Society of Allergy and Clinical Immunology, pediatricians through the Canadian Pediatric Society, and a sample of practicing family physicians.

**RESULTS:** There was variability in the definition of infants at high risk for peanut allergy and recommendations for age of introduction of allergenic solids. There was also variability in how often allergist evaluation was recommended for infants with egg allergy or severe eczema prior to peanut introduction, with allergists 9 times more likely to recommend pre-emptive peanut testing in infants with severe eczema prior to peanut introduction. The majority of family physicians (77.1%), pediatricians (91.4%) and allergists (89.1%) did not believe there was harm to introduction of solids between 4-6 months of age, or that breastfeeding rates would be affected with earlier solid introduction.

**CONCLUSIONS:** Further education about the implications of LEAP is required. There are broad issues (such as the definition of a high risk infant) that require international consensus. Most primary care physicians and allergists do not believe there are harms to introduction of allergenic solids prior to 6 months of age, or that breastfeeding rates will be affected.
Outcomes after Negative Oral Food Challenges to Peanut and Hazelnut: A Survey Study

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RATIONALE: We sought to identify factors affecting incorporating nuts into regular diet following a passed food challenge (OFC).

METHODS: Patients who passed peanut- or hazelnut-OFC at Mount Sinai Hospital completed anonymous e-surveys. Data were analyzed using the Fisher’s exact t-test and chi-square test.

RESULTS: Among 159 patients (62% male) who passed peanut-OFC, 23 (14.5%) reported avoiding peanuts. The most common reason for peanut-avoidance was patient preference (70%). Ten patients reported symptoms: skin rash/pruritus (7), oropharyngeal pruritus (5), gastrointestinal symptoms (4), or feeling un-well (2); 5 continued eating peanuts. Three patients received epinephrine after peanut reaction. Among 127 patients (66% male) who passed hazelnut-OFC, 20 (15.7%) reported avoiding hazelnut. The most common reason for hazelnut-avoidance was patient preference (38%); 5 families didn’t know it was important to ingest hazelnut regularly (19%). Overall, 7 patients reported symptoms: skin rash/pruritus (4), oropharyngeal pruritus (3), and gastrointestinal symptoms (2); 3 continued to ingest hazelnut. There was no association between symptoms and allergic rhinitis. There was no association between likelihood of home introduction and gender, race, ethnicity, asthma, eczema, allergic reactions/anaphylaxis, household income, or caregiver education (p>0.05). The majority recalled receiving discharge instructions to eat peanut (86%) and hazelnut (75%) regularly.

CONCLUSIONS: Most patients continued to eat peanut (84%) and hazelnut (83%) after passing an OFC. The most common reason for avoidance was patient preference. Ten patients (6.3%) reported home reactions to peanut and 7.5% to hazelnut. It is important to provide specific discharge instructions to encourage regular ingestion of peanut and hazelnut following passed OFC.

Synergistic inhibition of Human B cell IgE Secretion by Extracts and Constituents of Rubia cordifolia and Fructus Arctii

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RATIONALE: Allergic diseases have increased significantly worldwide, with increasing prevalence of immunoglobulin E (IgE) mediated food allergy. Herbal medicines consisting of Rubia cordifolia (QianCao, QC) and Fructus Arctii (NiuiBangZi, NBZ) have been used for centuries in China as anti-inflammatory treatments. We hypothesized that QC and NBZ fractions and compounds will synergistically inhibit IgE production in vitro.

METHODS: Dichloromethane extracts of QC and NBZ were prepared (QC and NBZD). Two compounds, QCD5 and AL-2, were isolated from QC and NBZ respectively. Human B cells (U266 cells) were used to test anti-IgE effects of each of the herbal medicines, dichloromethane extracts, and pure compounds. The total IgE levels were measured by ELISA. Cell viabilities were evaluated by counting under microscope. IC50 values of each testing-drug were calculated. Potential synergistic effects were analyzed by computing values of interaction index. Prism 4.0 was used for statistical analysis.

RESULTS: Two compounds isolated were identified as 1,3-dihydroxy-anthaquinone (QCD5) and Arctigenin (AL-2). The herbal water extracts (QC and NBZ), their dichloromethane extracts (QCD and NBZD), and compounds (QCD5 and AL-2) inhibited in vitro IgE production by U266 cells in a non-toxic dose-dependent manner. Interaction index values at IC50 were calculated as 0.3286 for the mixture of QC and NBZD; 0.6509 for the mixture of QCD5 and AL-2. All interaction indices were below 1.

CONCLUSIONS: Herbal medicines Rubia cordifolia and Fructus Arctii; their dichloromethane extracts QCD and NBZD; and their isolated compounds QCD5 and AL-2 synergistically inhibit IgE production in vitro.

Introduction of peanuts in younger siblings of children with peanut allergy: A follow-up

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RATIONALE: The Finding the Risk of Anaphylaxis and Testing Rationale In youngEr Siblings (FRATRIES) study was conducted to determine the risk of anaphylaxis, the predictive value of peanut allergy tests, and parents’ preference in the context of peanut introduction in the younger siblings of peanut-allergic children. The objective of this follow up was to monitor changes in the prevalence of allergies and adherence to peanut consumption in the younger siblings of peanut-allergic children.

METHODS: A telephone survey was performed in the whole population of younger siblings after the supervised introduction of peanuts that took place between 2013 and 2014. Families were asked whether peanut consumption was pursued or if an allergic reaction had occurred since the supervised introduction. In case of peanut avoidance or a new suspected peanut allergy, patients were invited for clinical assessment. If indicated, skin testing, specific IgE analyses as well as challenges were performed.

RESULTS: Of the initial cohort of 146 non-allergic children, 133 were reintroduced for peanut allergy, patients were invited for clinical assessment. If indicated, skin testing, specific IgE analyses as well as challenges were performed. Of these 24 children, fifteen had never introduced peanuts, seven rarely consumed them and two stopped eating peanuts following a suspicion of allergy. Seventeen of these patients were seen in clinic. Three new cases of peanut allergy were diagnosed, increasing the total allergy prevalence of the younger sibling cohort from 5.2% (8/154) to, at least, 7.1% (11/154).

CONCLUSIONS: Despite negative skin tests, supervised introduction at the allergy clinic and regular consumption advice, several families had still not introduced peanut. Also, new cases of peanut allergy were diagnosed even in regular peanut eaters.
793 Cutaneous Exposure to Peanut Oil Induces Systemic and Pulmonary Peanut Hypersensitivity Reaction

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RATIONALE: The prevalence of peanut allergy is constantly increasing in children. Atopic dermatitis is a major risk factor for developing food allergy, and it has been suggested that exposure to peanut allergens through a disrupted skin barrier is a potential cause of peanut allergy. Some bath oils and skin creams used for treating atopic dermatitis contain peanut oil. Our aim was to investigate if cutaneous application of peanut oil caused a systemic or respiratory allergic response to peanut in this animal model.

METHODS: Nine BALB/c mice underwent cutaneous sensitization with 50 μL of peanut oil, or PBS control. Ten days after the last exposure mice were challenged with 5 μg intranasal peanut protein. Bronchial alveolar fluid (BALF) was collected for cytologic studies and measurement of cytokine levels. Sera was collected for IgE measurement.

RESULTS: Peanut oil sensitization increased leukocyte, eosinophil counts and IL-13 levels in F = 0.003, P = 0.002, P = 0.03 respectively, in addition to increasing serum total IgE (P = 0.03).

CONCLUSIONS: This work suggests that topical application of peanut oil may play a role in the etiology of peanut allergy.

794 Predicting Baked Milk and Baked Egg Challenge Outcomes with Serum Specific IgE Levels

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RATIONALE: Serum specific IgE levels can be used to predict the likelihood of reacting on food challenge. Specific IgE parameters for predicting a positive challenge to baked egg and baked milk have not yet been established. We aimed to identify these specific IgE parameters.

METHODS: We retrospectively reviewed 857 charts of pediatric patients who underwent food challenges at a tertiary care center from January 2013 to May 2017. Demographics and clinical information including age, foods challenged, egg white and cow’s milk specific IgE levels, and challenge outcomes were collected and evaluated using ROC analysis.

RESULTS: There were 158 baked challenges: 109 baked egg and 49 baked milk in patients aged 11 months to 15 years old. Of the 109 baked egg challenges, 32% failed (35/109), where specific IgE ranged from 0.53 to >100 kU/L (median 6.31 kU/L). For baked egg, specific IgE of 4.46 kU/L demonstrated a 50% PPV for failed challenge (AUC 0.65, sensitivity 57%, specificity 73%). Of the 49 baked milk challenges, 20% failed (10/49), where specific IgE ranged from 2.16 to 39 kU/L (median 18.2 kU/L). For baked milk, specific IgE of 15.60 kU/L demonstrated a 43% PPV for failed challenge (AUC 0.71, sensitivity 60%, specificity 80%).

CONCLUSIONS: In our study, baked egg and baked milk challenges had higher rates of failure. We identified egg specific IgE level of 4.46 kU/L and milk specific IgE level of 15.6 kU/L with positive predictive values of 50% and 43%, respectively, for failed baked challenge. This information may aid clinicians in counseling parents regarding appropriate timing of baked challenges.

795 Supervised epinephrine autoinjector administration in a cohort of children with anaphylaxis during oral food challenges (OFCs)

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RATIONALE: An epinephrine autoinjector (e.g. EpiPen®, Auvi-Q®) is the treatment of choice for anaphylaxis in the community. However, studies show it’s often not administered, due to factors including lack of confidence and fear. We previously reported improved confidence after medical supervision of parent/child autoinjector administration during OFCs. We sought to confirm those findings in a larger cohort of children.

METHODS: Parents of children undergoing OFC at BC Children’s Hospital filled out a pre-challenge questionnaire on 1) confidence in recognizing anaphylaxis, 2) confidence with autoinjector administration, 3) knowledge of anaphylaxis/autoinjector use, and 4) skill in autoinjector use. Confidence was measured on a 5-point scale (1 = Not very confident to 5 = Very confident). Children experiencing anaphylaxis had parent/self autoinjector administration under medical supervision, and confidence was re-assessed post-challenge.

RESULTS: Among 308 OFCs performed in 287 children, 50 had anaphylaxis requiring an autoinjector (16.2%). Twenty-one were OFCs to peanut (42%). There was a significant increase in all four confidence domains from pre- to post-challenge (p = 0.02 for domain 1; p < 0.001 for domain 2; p = 0.002 for domain 3; p < 0.001 for domain 4). Those reporting an increase in confidence recognizing anaphylaxis/autoinjector administration were more likely to be healthcare professionals (p = 0.037); those reporting an increase in confidence with autoinjector administration (p = 0.042) and knowledge of anaphylaxis/autoinjector use (p = 0.045) were more likely to have older allergic children.

CONCLUSIONS: Our anaphylaxis rate for OFCs was relatively high. Supervised parent/child autoinjector administration during OFCs increased confidence significantly across multiple domains, which could translate to higher likelihood of future autoinjector use for anaphylaxis in the community.

796 Clinical features and allergen analysis in five children with macadamia nut allergy

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RATIONALE: Few cases of macadamia nut allergy have been documented, and the major allergens have not been fully analyzed. We summarized the clinical features of five children with macadamia nut allergy and investigated the allergens in macadamia nut.

METHODS: We enrolled five patients (three girls and two boys) with the diagnosis of macadamia nut allergy at Tokyo Metropolitan Children’s Medical Center. The serum-specific IgE level against macadamia nut was assessed, and a skin prick test was done. We determined the molecular weight of macadamia nut allergens by SDS-PAGE and IgE-immunoblotting. Our study was approved by the independent review board of the Tokyo Metropolitan Children’s Medical Center, and we obtained informed consent from the patients’ parents.

RESULTS: The age of onset of macadamia nut allergy ranged from 2 to 3 years. All the 5 children had oropharyngeal symptoms and facial urticaria and/or edema, and anaphylaxis was observed in two children. Three children had atopic eczema and three children had other food allergies. Four of five children had positive results for macadamia nut-specific IgE (range: 0.58 to 28.4 U/A/mL), and the results of a skin prick test for macadamia nut were positive in all five children. IgE-immunoblotting showed two predominant bands at approximately 15 and 20 kDa in all five children and two individual bands at approximately 40 and 50 kDa in two children with anaphylaxis.

CONCLUSIONS: Macadamia nut may induce severe allergic reactions in children. Understanding IgE-binding proteins might be useful for detecting severe cases in macadamia nut allergy.
Temporal Trends of Food Specific IgE Levels During and After Anaphylaxis

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RATIONALE: Little is known about the dynamics of specific IgE antibody (SpIgE) levels during and after anaphylactic reactions. We aimed to evaluate changes in food SpIgE levels during and after food-induced anaphylaxis.

METHODS: As part of the Cross Canada Anaphylaxis REgistry (CCARE), between 2013 and 2017, SpIgE levels were drawn within 2 hours of presentation with food-induced anaphylaxis to the emergency department of the Montreal Children’s Hospital and at least 2 weeks later. All SpIgE levels were measured using Phadia ImmunoCAP. Changes in levels were assessed with the paired Wilcoxon test.

RESULTS: Among 34 cases, the mean age was 3.9 years and 59% were males. The main culprits were egg, tree-nut and peanut. The reaction was severe in 6% of cases. The mean culprit SpIgE was 15.12 kUA/L (SD: 27.26) during the anaphylactic reaction. When repeated at follow up, the mean SpIgE increased to 21.56 kUA/L (SD: 33.31). This resulted in a difference of 6.44 kUA/L (0.57, 12.31), p = 0.003. The mean time interval between anaphylaxis and post-reaction SpIgE was 12 weeks (SD: 24.97). There was no substantial difference in SpIgE levels of an unrelated food (difference of 0.055 kUA/L (-1.32, 1.21), p = 0.66).

CONCLUSIONS: Establishing the dynamics of SpIgE levels is crucial for appropriate use of confirmatory tests to identify anaphylaxis triggers. Our results indicate that SpIgE levels to culprit foods are lower during anaphylaxis. Further, our results suggest that changes in SpIgE levels may contribute to identification of the appropriate culprit food when history is unclear.

A Quality Improvement Initiative to Increase Referrals to an Early Peanut Introduction Clinic

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RATIONALE: New guidelines recommend introducing peanut to all infants prior to 12 months of age in an effort to prevent the development of allergy. Peanut allergy testing is recommended for high risk infants but timely access to allergists may not be available for all. When indicated, it may be logistically difficult to perform supervised feedings during routine clinicep.ents.

METHODS: In an effort to provide timely access to allergy evaluation within a tertiary care pediatric academic center, the Early Peanut Introduction Clinic (EPIC) was established in September, 2016. EPIC is staffed by 2 allergists per session and can accommodate 8 patients during a dedicated one half-day session each month. Skin prick testing and depending upon results, supervised peanut introduction are offered.

RESULTS: EPIC had only one new patient referral during the first 6 months. A quality improvement (QI) project was developed to increase the percentage of filled EPIC appointments per month from 0% to 50% within 6 months. Using QI methodology and multiple Plan-Do-Study-Act cycles, several interventions were developed, including: implementation of an electronic referral, education/outreach to primary care physicians and dermatologists, and development of educational materials for placement in referring physician offices.

One month after QI initiatives began, 25% of EPIC appointment slots were filled, followed by an increase to 50% by month 4, 75% by month 5, and 63% by month 6.

CONCLUSIONS: Use of QI methodology increased referrals to a clinic established to assist new guideline implementation for early introduction of peanut, which requires timely access to allergy evaluation.

Differences in Peanut Allergy Management Between Allergists and Primary Care Providers

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RATIONALE: Peanut allergy (PA) affects approximately 1-2% of children, many of whom lack access to sub-specialty allergy care. We sought to characterize PA management by general pediatrics compared with allergists.

METHODS: We performed a retrospective chart review of all patients with at least one well child check (WCC) within the primary care clinic of a tertiary care medical center between January 1 and December 31, 2016. Children with PA on their problem/allergy list or with a primary visit diagnosis of PA were included in analysis.

RESULTS: Among 926 patients meeting criteria, 477 (52%) had been evaluated by a pediatric allergist. Age (mean 9.9 years) and gender (61% male) were similar between the two groups. Children with other atopic conditions, African American race, and public insurance were more likely to have been evaluated by an allergist (p<0.01 for each). Children evaluated by an allergist were more likely to have a weight appropriate epinephrine prescription (OR 7.5, p<0.001), to have discussed peanut avoidance at annual visit (OR 21, p<0.001), to have documentation of a food allergy action plan (OR 126, p<0.001) and to have had PA testing (OR 45, p<0.001). Pediatricians were more likely to document asthma management than PA during WCC (OR 1.7, p<0.001). Of note, pediatricians recommended peanut as a healthy snack at 52% of WCC, even when PA was discussed.

CONCLUSIONS: Within an academic center primary care population, there is wide discrepancy in PA management by pediatricians and allergists. Routine pediatric appointments represent a missed opportunity for patient education about PA management.
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**RATIONALÉ:** Cow’s milk (CM) allergic patients may present different clinical patterns (phenotypes). One specific group who present only mild gastrointestinal (GI) symptoms has been associated with a selective sensitization to Betalactoglobulin milk protein. Nowadays we have not good clinical markers to differentiate poor/good prognosis.

**METHODS:** We selected patients with only mild GI symptoms after CM intake (FPIEs ruled out) but tolerance to yogurt. Skin prick test with milk extracts and measurement of serum specific IgE against milk proteins were performed. All patients had an open challenge with both CM and yogurt. Celiac disease and lactose intolerance was ruled out. Patients were divided in 2 groups: Group A with classical rule of total restriction of milk; Group B only partial restriction of milk with yogurt keeping. We performed a serological follow-up for 1 year.

**RESULTS:** From the total of patients referring mild GI symptoms after CM intake, we selected 40 patients with confirmed CM allergy (showing predominance of BLG sensitization) and tolerance of yogurt. After 1 year in group A (n=15) the evolution was variable: less than a half of cases improved their CM sensitization but near 1/3 of them evolved towards a worsening with new sensitizations to other milk proteins. In Group B (n=25) all patients maintained yogurt tolerance while more than 70% improved their BLG sensitization (p<0.05).

**CONCLUSIONS:** The identification of different clinical phenotypes may have relevant implications with specific interventions. This phenotype targeted intervention could be a potential therapeutic tool to achieve a better prognosis, with significant changes in CM sensitization.

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**Utility of Peanut Component Testing in Children with Peanut Allergy**

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**RATIONALÉ:** Peanut component testing is often used in clinical practice as an adjunct to peanut-specific IgE(sP) and skin testing to better predict the likelihood of clinical reactivity. The purpose of this study was to examine the clinical utility of component-resolved diagnostics (CRD) and associated healthcare costs in children with peanut allergy.

**METHODS:** This was a retrospective chart review of 199 patients (233 CRD tests done), ages 0 to 17 years, who were seen by an allergist for a food allergy evaluation at a large academic outpatient medical center. Charts were reviewed for subjects with sP and CRD done at the same visit. An expense report for sP and CRD was obtained from the lab (CRD $121.70, Food-sIgE $24). The Fisher’s exact test was used to assess the relationship between peanut component testing and the sP cut-off level of 14kUA/L.

**RESULTS:** Of the 233 CRD tests reviewed, 116 were done in patients with sP < 14kUA/L and 117 in patients with sP ≥ 14kUA/L. Of the 233 CRD tests in patients with sP ≥ 14kUA/L, 4 had Arah1, 2.3 and 9 < 0.35kUA/L, and of the CRD tests in patients with sP < 14kUA/L, 38 had Arah1, 2.3 and 9 < 0.35kUA/L (3% versus 33%, p < 0.0001), regardless of Arah8. Similar results were found if the cutoff of Arah1, 2.3 and 9 was increased to 1 or 2kUA/L. Calculations of the costs revealed that approximately $14,239 was spent on CRD in patients with sP ≥ 14kUA/L.

**CONCLUSIONS:** CRD in patients with sP ≥ 14kUA/L provides little clinical benefit due to significantly higher likelihood of Arah1, 2.3 and 9 > 0.35kUA/L, with less opportunity to offer an oral challenge. Thus, indiscriminant CRD should be avoided to prevent unnecessary blood draws and increased health care costs.
Simultaneous Detection of Four Major Food Allergens Using a 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. ‘Generic’ immunoassays for ‘total protein’ do not measure specific allergens. Our aim was to validate a multiplex immunoassay capable of simultaneously measuring four major food allergens, Ara h 3, Ara h 6, Bos d 5 and shrimp tropomyosin.

METHODS: The multiplex array was developed on the LumineX xMAP system. Microspheres coupled to specific monoclonal antibodies were used for allergen capture and biotinylated specific mono- or polyclonal antibodies for detection. Reference standards formulated from purified natural allergens were used for calibration purposes. A full method validation was performed to determine parameters of linearity, range, limits of quantification and detection, accuracy and precision of the 4-plex food immunoassay.

RESULTS: The standard curves allow for quantification over a large dynamic range: 50-0.02ng/ml for Ara h 6, tropomyosin and Bos d 5, and 125-0.06ng/ml for Ara h 3. The lower limits of detection (LLLOD) were as low as 0.02ng/ml and 0.06ng/ml. Intra- and inter-assay accuracy and precision results 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 four major food allergens. The multiplex array provides a sensitive and efficient tool for measuring specific allergens with potential application in food immunotherapy formulations and in the food industry.

Cannabis Allergy: A Melting “Pot” of Clinical Manifestations

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RATIONALE: Cannabis allergy is currently on the rise, and the symptoms of cannabis allergy can vary from mild rhinitis to life-threatening anaphylactic reactions. We investigated the relationship between the routes of exposure and clinical manifestations in 11 patients with cannabis allergy.

METHODS: 11 patients who presented to an ambulatory allergy clinic with cannabis (marijuana or hempseed) allergy were evaluated. Skin prick test with cannabis allergy.

RESULTS: A cannabis extract was performed to confirm diagnosis. A questionnaire was evaluated. Skin prick test with cannabis allergy.

CONCLUSIONS: Threatening anaphylactic reactions.

Determining optimal prioritization system for food oral immunotherapy in a tertiary care setting

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RATIONALE: As oral immunotherapy makes its way to clinic, the high demand and initially limited offer will raise issues of access, especially in public healthcare systems. Given the low acceptability of first-come first-serve approaches, we sought to develop a prioritization algorithm that would be perceived as fair by patients and healthcare professionals.

METHODS: Various prioritization scenarios were submitted to an expert panel consisting of both healthcare professionals and end-users through an evolutive Delphi approach to determine consensual prioritization criteria. These were used as a base to compare the effect of various prioritization systems (first-come first-served, scoring, additive and waiting time ratio) on the OIT waiting list at our tertiary academic center.

RESULTS: Consensual prioritization criteria were identified by the panel of 25 experts after 3 iterations and included: number of food allergies, allergy to ubiquitous food, younger age and impact on quality of life. Correlation between prioritization systems were systematically low (Pearson R below 0.4) except for the additive and scoring systems. The waiting time ratio system was perceived as the most fair by the expert panel. The most frequent comment from experts was that this system offered the best balance between prioritizing severe food allergy cases and offering a fair chance to all applicants.

CONCLUSIONS: A prioritization system based on adjustment of waiting times using ratio for prioritized subgroups appears to be the most consensual approach to determine access to oral immunotherapy in the context of limited resources and high demand.

Physician Prescription Patterns of Epinephrine Autoinjectors in Oral Allergy Syndrome

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RATIONALE: Oral Allergy Syndrome (OAS) has been a challenging diagnosis due to lack of clear standardized diagnostic criteria and guideline based therapy. We sought to evaluate prescription patterns and reported use of Epinephrine autoinjectors (EAI) in patients with OAS.

METHODS: IRB approved retrospective chart review of patients seen in our Allergy/Immunology office. Patients with ICD 9/10 diagnostic codes related to OAS over the last seven years were identified. Patients with a diagnosis of OAS, and documentation of aeroallergen IgE sensitivity were included. Patients with a history of systemic reaction or anaphylaxis, and the need for EAI for an alternative reason were excluded.

RESULTS: Fifty patients were identified. The average age was 29 years (range 6-71) and 68% were female. EAI was prescribed to 5 of 29 (17%) patients with history of reaction to fruits/vegetables and 14 of 21 (66%) patients who had reacted to tree nuts or peanuts. Three of 5 (60%) patients in the fruit/vegetable group and 11 of the 14 (79%) patients in the tree nut/peanut group had positive skin-prick testing to one of their food allergens. Nineteen patients were seen for follow up visits and no patients from either group who were prescribed EAI required its use.

CONCLUSIONS: Our data suggests that EAI are prescribed more frequently in patients with a history of OAS to tree nuts and peanuts compared to fruits/vegetables. There was no increased incidence of systemic symptoms or anaphylaxis, questioning the need for prescribing EAI in OAS. Larger studies are needed to further evaluate this patient population.
AB256 Abstracts

808 Yellow fever vaccine in egg-allergic patients: safety of a vaccination protocol

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RATIONALE: Yellow fever vaccine (YFV) is broadly recommended in endemic areas, considering the severity of this disease. However, the vaccine is grown in chicken embryos and poses a risk to egg allergic (EA) patients. We describe the outcomes of a protocol for administration of YFV in EA patients.

METHODS: Five EA children were included, two of them anaphylactic. Patients older than 5 years were skin tested with the vaccine (prick and intradermal). Skin test-negative patients received the vaccine as a single dose under a physician’s supervision. Skin test-positive patients undertook a desensitization protocol: 0.05 ml of a 1:10 dilution, followed by graded full strength doses: 0.05 ml, 0.1 ml, 0.15 ml, 0.2 ml at 15-minutes intervals, totaling 0.5ml. Younger children were not tested and followed the desensitization protocol. Premedication was not administered.

RESULTS: Two patients (1 and 4 years old) were too young to be skin tested. The other three (5, 7, and 9 years old) underwent skin tests. All prick tests were negative and two patients had positive intradermal tests. The patient with negative tests received the vaccine as a single dose without adverse reactions. Four patients received the vaccine through the desensitization protocol. Three of them didn’t experience any symptoms and one toddler presented hives after receiving the second dose. She was treated with antihistamines and was able to finish the protocol without further reactions.

CONCLUSIONS: In this case series a desensitization protocol proved to be safe and efficient in allowing vaccination of EA patients (including severe phenotypes) against yellow fever.

809 A Buffer Against an Accidental Exposure is a Major Motivator for Entering a Child in Peanut Allergy Therapy

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RATIONALE: Both Oral Immunotherapy (OIT) and epicutaneous immunotherapy (EPIT) are emerging potential treatments for peanut allergy. Caregiver goals and expectations of these therapies are poorly defined.

METHODS: 19 detailed, semi-structured interviews of OIT/EPIT participants were conducted to allow caregivers to describe their motivations for, and experiences with, therapy and life with a peanut allergic child.

RESULTS: Partial review of the coded transcripts to date show that caregivers of peanut allergic children enrolled in OIT/EPIT phase III trials clearly express a goal of therapy for their child to have a buffer against an accidental peanut exposure. The perception of the buffer varies by caregiver, and may represent decreased reaction severity upon exposure, increased time to react to allow for assessment by others, or increased threshold of peanut exposure tolerated. In general, these caregivers expressed that they do not anticipate this buffer, if achieved, would lessen their level of pre-therapy anxiety, allergen-associated vigilance or avoidance practices, despite hope these would change. Most of the caregivers hope the buffer will increase their (and the parent proxy-reported) perceived sense of freedom for the child’s actions and interactions, while still respecting the limitations of having a severe allergy that has been partially treated. Interestingly, some, but not all, caregivers have expressed that trial participation has decreased anxiety secondary to experiencing a severe allergic reaction that was promptly treated.

CONCLUSIONS: Preliminary analysis indicates that caregivers strongly desire OIT/EPIT results in a buffer against an accidental reaction, though most admitted that this would not change their anxiety and family’s current lifestyle.

810 The limited utility of the double-blind food challenge in diagnosing non-IgE mediated cows milk allergy in infants

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RATIONALE: Cow’s milk allergy (CMA) is the most common food allergy of infancy, most of which is non-IgE mediated. While the current gold standard of diagnosis of food allergy is the DBPCFC, it has not been evaluated for the diagnosis of non-IgE-mediated disease. We sought to evaluate its performance in non-IgE mediated disease using clinical intolerance of CMP formula as the gold-standard.

METHODS: Infants 18-120 days old with suspected CMA underwent a milk-free washout before the DBPCFC. Infants received 90ml of active (1.6g cow’s milk protein (CMP) + amino acid formula (AAF)) or placebo (AAF) formula daily for one week. After a one week washout, the process was repeated with the opposite formula. The Gastrointestinal Allergy Signs & Symptoms Instrument (GASSI) questionnaire was used to track symptom progression. Associations between baseline characteristics, GASSI scores and DBPCFC outcomes were evaluated by nonparametric statistical tests.

RESULTS: Thirty-five infants completed the DBPCFC. Twenty-eight of these infants failed to tolerate CMP-based formula. Of these, 18 (64%) were confirmed by DBPCFC, while 10 (36%) were not. No demographic factors or referral symptoms were associated with DBPCFC outcomes. The difference in GASSI scores between CMP and placebo treatment increased significantly between CMA and non-CMA infants (p=0.035).

CONCLUSIONS: One-third of infants with CMA are not identified by the 3-week DBPCFC and react at higher doses of CMP. High-threshold CMA infants have similar clinical presentations and demographics as non-CMA infants. Therefore, we propose a higher dose DBPCFC to increase the utility of this approach in the diagnosis of non-IgE CMA.
Variability in Reports of Food Allergy-Related Bullying among Food Allergic Children and their Parents

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METHODS: Twenty-five children diagnosed with food allergy (M Age=11.32 yrs; SD = 1.52; 56% female; 36% Caucasian) and their parents were recruited from allergy clinics at two mid-Atlantic children’s hospitals to complete the Food Allergy Bullying Questionnaire. Children answered a yes/no question about FA bullying and completed a checklist of FA bullying behaviors they had experienced. Parents answered yes/no questions about whether or not their child had experienced FA bullying or reported FA bullying to them. Frequencies were calculated for each item.

RESULTS: Five children (20%) reported they had experienced FA bullying on the yes/no question. An additional five children (20%) endorsed FA bullying behavior on the checklist, despite reporting they had not experienced FA bullying on the yes/no question. Only two parent-child dyads agreed regarding FA bullying experiences. Seven parents (28%) reported that their child had experienced FA bullying, yet only two of these children reported bullying on either the yes/no question or the checklist.

CONCLUSIONS: Children’s reports of FA bullying varied based on the way that bullying was assessed. Parent and child reports were not consistent. Simply asking whether or not patients are bullied for FA may not provide sufficient information regarding their peer experiences. Clinicians may need to use a more nuanced approach that broadly assesses peer experiences.

Assessing the validity of an IRB approved REDCap web based clinical trials recruitment registry

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RATIONALE: With the growing public attention on food allergy, there has been a surge of interest in clinical trials. Internet-based enrollment tools offer the benefits of efficiency, organization and fairness to the recruitment process. However, there are concerns about selection bias that may be introduced by the use of these tools.

METHODS: In 2015, the UNC Food Allergy Initiative (UNC FAI) developed an IRB-approved web-based REDCap database for patients and families interested in research participation. We compared the demographics of children identified as food allergic in the 2012 North Carolina Statewide Child Health Assessment and Monitoring Program (CHAMP) with children registered in the UNC FAI database.

RESULTS: The data showed no differences in gender between the UNC FAI database and the CHAMP survey (male 63% vs 57%, female 37% vs 42% respectively). In the UNC FAI database, African Americans were underrepresented (3.7% vs 25%) and whites were over-represented (85% vs 61%) but the percentage of “other” races was similar (12% vs 12.6%). For age, a higher percentage of children under five (36% vs 21%) and a lower percentage of 14 to 17 year olds (7.3% vs 36.8%) were found in the UNC FAI database compared to the CHAMP survey.

CONCLUSIONS: A web-based REDCap database can be an effective tool for study recruitment. However, the risk for selection bias exists with African Americans and older children underrepresented in the UNC FAI database as compared to the general population of NC. Use of these tools should be combined with efforts to attract these populations.
**814 Nut Oral Immunotherapy (NOIT) Using Two or More Nuts Successfully Desensitizes Most Patients**

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**RATIONALE:** Nut oral immunotherapy (NOIT) has gained increasing popularity over the past ten years but remains a burdensome therapy. Previous treatments with multi-NOIT (MNOIT) have used costly omalizumab pretreatment. Treatment of multi-nut allergic patients with two or more nuts/seeds simultaneously will reduce the burden of nut allergy treatment.

**METHODS:** The North Texas IRB approved retrospective record reviews of 498 NOIT including 35 MNOIT treated patients. MNOIT was administered according to previously reported protocols.

**RESULTS:** The 35 MNOIT treated patients comprised 22 two nut, 11 three nut and two four nut patients. 23/35 (66%) were treated with peanut plus another nut/seed. Five transferred care or were lost to follow up. 23/35 (66%) reached their target escalation dose. 4/27 (15%) discontinued MNOIT after reaching maintenance. 5/27 (19%) patients experienced one or more epinephrine treated reactions (ETR). 13/35 (37%) reported no reactions of any kind. In contrast, using single nuts, 79% peanut and 75% tree nut treated patients reached maintenance, 24% of peanut and 5% of single tree nut treated patients had an ETR and 34% of peanut and 71% of single tree nut treated patients had no reactions.

**CONCLUSIONS:** MNOIT effectively desensitizes most patients but there are more treatment failures than among single-NOIT patients. Clinicians and parents should consider this data when deciding on the best way to reduce the burden of multi-nut allergy and its treatment for the individual patient.

**815 Eosinophilic Esophagitis Like Oral Immunotherapy Related Syndrome (ELORS)**

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**RATIONALE:** Food oral immunotherapy (FOIT) has gained increasing popularity over the past ten years. Eosinophilic esophagitis is a known complication of FOIT. We report a characteristic presentation of vomiting with or without epigastric abdominal pain or nausea occurring 2-8 hours after FOIT doses often accompanied by increased peripheral blood eosinophilia, described as ELORS.

**METHODS:** North Texas IRB approved retrospective record review of patients receiving FOIT. FOIT was administered according to previously reported protocols.

**RESULTS:** ELORS developed during escalation in 10% (51/498) of all FOIT patients, with a rate per food of 13% (13/103) milk, 13% (34/271) peanut, 4% (1/24) single tree nut, 8% (3/36) peanut plus multiple tree nut. No wheat (0/7) or egg (0/56) FOIT patients developed ELORS during escalation. 28 ELORS patients reduced the escalation dose until they were asymptomatic and continued the reduced dose for >8 weeks before resuming the escalation protocol. 57% (16/28) reached maintenance, 18% (5/28) discontinued treatment because of continued ELORS symptoms, and 21% (6/28) for other reasons. 37% (19/51) of ELORS patients discontinued treatment because of ELORS without attempting dose reduction. Two ELORS patients discontinued treatment then restarted peanut OIT later and successfully reached maintenance.

**CONCLUSIONS:** ELORS comprises a recognizable syndrome affecting some FOIT patients. In many patients, ELORS resolves after 2-3 months of FOIT dose reduction and successful desensitization can ultimately be achieved. ELORS substantially limits FOIT for some patients.

**816 Withdrawn**

**817 The usefulness of tryptase formula for the diagnosis of shrimp-induced anaphylaxis**

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**RATIONALE:** Serial measurements of serum tryptase compared to baseline levels were shown to be better predictors of anaphylaxis than a single peak serum tryptase. The objective of our study was to validate the performance of the suggested formula of peak serum tryptase level more than 2 µg/L+1.2 x (baseline tryptase) for the diagnosis of shrimp-induced anaphylaxis.

**METHODS:** Data of serum tryptase level at baseline and 1 hour after symptom occurred were obtained from 39 patients with history of shrimp allergy who underwent open shrimp challenges.

**RESULTS:** The challenges revealed 12 patients with anaphylaxis, 20 with mild reaction and 7 without reaction. The ROC curve showed the best cutoff point for serum tryptase ratio was ≥1.5 and for delta tryptase was ≥0.8 µg/L with 91.7% sensitivity, 96.3% specificity, 91.7% PPV, 96.3% NPV, 23 positive likelihood ratio (LR) and 0.08 negative LR and 83.3% sensitivity, 92.6% specificity, 83.3% PPV, 92.6% NPV, 11.86 positive LR and 0.08 negative LR, respectively. The suggested formula showed 33.3% sensitivity, 100% specificity, 100% PPV, 77.1% NPV, infinity positive LR and 0.67 negative LR. The performances of tryptase ratio ≥1.5 and delta tryptase ≥0.8 µg/L were not significantly different. However, both value performed significantly better than the suggested formula (P=0.008). Moreover, when compared with single peak serum tryptase ≥11.4 µg/L, the formula did not show better performance (P=1).

**CONCLUSIONS:** Peak serum tryptase level more than 2 µg/L+1.2 x (baseline tryptase) may not be a good predictor of shrimp-induced anaphylaxis.
818 **Tree Nut Cross-Reactivity Based on Clinical Allergy Testing**

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**RATIONALE:** Tree nuts (TNs) are common food allergens in children and adults. Sensitization to more than one TN is often observed. Cross-reactivity between cashew/pistachio and walnut/pecan has been reported based on similar epitopes and phylogenetic homology. However, clinical cross-reactivity data is lacking. We hypothesize that clinical testing will correlate with molecular data.

**METHODS:** We performed a retrospective chart review from 2008 to 2017, including all patients seen at National Jewish Health with skin prick test (SPT) or serum IgE (sIgE) data for walnut/pecan or cashew/pistachio. Spearman rank correlation coefficients for sIgE and SPT were evaluated between the TN pairs. Pairings with double negative testing were excluded. OFC data for the pairs was characterized as pass or fail, with exclusion of incomplete OFCs.

**RESULTS:** SPTs (n = 2421) for cashew/pistachio have strong correlation (rho = 0.75, p < 0.0001) with sIgE being even stronger (rho = 0.95, p < 0.0001). Walnut/pecan SPTs (n = 2051) have modest correlation (rho = 0.65, p < 0.0001), while their sIgE (n = 1595) have strong correlation (rho = 0.89, p < 0.0001). Demographic data did not vary among groups, with a median age of 7.72 (range 0.44 - 78.8 years). OFCs were performed and passed in 3 patients to both cashew and pistachio. OFCs were performed on 9 patients to walnut/pecan, with 7/9 passing both TNs, 1 failing both, and 1 passing pecan while failing walnut.

**CONCLUSIONS:** Based on analysis of clinical data, there is correlation between cashew/pistachio and walnut/pecan in TN-allergic patients based on SPT and sIgE, as suggested by phylogenetic homology. This adds support to the common clinical practice of allowing patients who pass one TN OFC to introduce the other related TN at home, if SPT and sIgE are well-correlated.

819 **Extension of home-based induction of sustained unresponsiveness to children with tree nut allergy**

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**RATIONALE:** It is possible to induce sustained unresponsiveness with home dosing in children that develop mild reactions to high doses of peanut (PN) during oral food challenges (OFC) (Garvey et al JACI-IP, 2017). We have applied this process to children with tree nut (TN) allergy and revisited some who could not tolerate the PN program initially.

**METHODS:** Subjects who “nearly pass” OFC1 with PN/TN, up-dose to 6 nuts daily at home over 3-6 weeks, then consume 6 nuts daily for 6 months. They then have a 2nd OFC, on dose. If they pass OFC2 they are considered desensitised, discontinue dosing for 6 weeks and have OFC3, off dose. After passing OFC3 they are considered to have achieved sustained unresponsiveness and advised to eat PN or TN at least 3 times weekly, indefinitely.

**RESULTS:** A further 13 children (9 PN, 2 cashew, 1 hazelnut, 1 pistachio) have joined the programme. The 4/9 PN allergic children who have completed the programme show sustained unresponsiveness (one initially withdrew but restarted successfully), 3 are up-dosing and 2 have withdrawn. The 4 TN allergic children are on maintenance (eating 6 nuts daily) until completing 6 months. From the published group of 16 PN allergic children, one child that withdrew is recently tolerating 6 peanuts daily.

**CONCLUSIONS:** We have shown home based programs induce sustained unresponsiveness in children that are nearly tolerant to TN, as previously shown for PN. The programme is flexible enough to allow re-entry and successful completion by subjects who could not tolerate it initially.

820 **Limitations in Current Peanut Oral Immunotherapy (POIT) Practices in the U.S**

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**RATIONALE:** Peanut allergy is a major U.S. health care burden. While current guidelines do not recommend POIT, some practices offer it in response to patient/caregiver dissatisfaction with peanut avoidance and other practitioners are studying POIT through ongoing clinical research. We sought to understand the limitations that currently prevent POIT from being widely used.

**METHODS:** Qualitative, in-depth phone interviews were conducted with 28 community and academic allergists and 6 nurse food allergy specialists across the U.S. between April and June 2016. Interviewed clinicians managed >100 peanut allergy patients/year. For perspectives on POIT, we interviewed 14 allergists who offer POIT in clinical studies or self-developed protocols; the remaining 14 allergists were POIT-naive.

**RESULTS:** Both physicians offering and not offering POIT identified several limitations in the currently utilized POIT treatment regimens of peanut allergy, including:

- Lack of a medicinal product meeting the required standards for FDA-approval
- Lack of standardized dosing regimens
- Medical-legal implications of offering non-FDA approved POIT
- Unclear defined criteria for appropriate patient selection
- Insufficient long-term safety and efficacy data
- Lack of correlation between maintenance POIT dosing and level of protection

Those interviewed recognized that robust, Phase 3 clinical development programs with a sufficient number of patients, using standardized protocols and a characterized OIT product, with long-term follow up, could address several of these limitations.

**CONCLUSIONS:** Several limitations have been identified with currently offered POIT regimens in the U.S.; many of these are being explored in ongoing Phase 3 clinical trials evaluating characterized oral products and standardized dosing regimens.
AB260 Abstracts

821 A Comparison of Food Allergy Research Priorities between the Researcher and Patient Communities

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RATIONALE: Consideration of patient-centered outcomes is important to ensure food allergy (FA) research programs reflect patients’ experiences and desired outcomes. No prior studies have compared perceptions of FA research priorities between researcher and patient communities.

METHODS: The Outcomes Research Advisory Board (ORAB) was created by Food Allergy Research & Education (FARE), comprised of key stakeholders charged with identifying areas of need and priority in FA research. With ORAB input, a measure was developed to assess perceptions of FA research priorities. This measure was completed by a national sample of FA researchers and non-researchers before the 2017 FARE Research Retreat.

RESULTS: Research retreat participants (n = 107, 45 researchers, 62 non-researchers) completed the measure. Non-researchers included parents of food-allergic children (65%), individuals with FA (11%), and members of advocacy organizations (21%). The areas identified by researchers (R) versus non-researchers (NR) as priorities (% selecting area as top priority) included: development of desensitization treatment (R 46%, NR 30%, p = 0.07), development of cure (R 30%, NR 28%), and product labeling research (R 7%, NR 14%). Although more non-researchers (10%) versus researchers (2%) identified psychosocial research as a priority, this was not significant (p = 0.10). There were no significant differences in research priorities based on gender, educational level, having observed anaphylaxis, or having a first-degree relative with FA.

CONCLUSIONS: FA research priorities are aligned between researcher and patient communities in this initial assessment. Both groups place highest priority on developing treatments to lessen FA severity and curative therapies. Future studies are needed to explore how patient-centric outcomes may inform treatment research.

822 Fish Allergy Diagnosis by Pattern of IgE Sensitization to Different Allergens of Grass Carp in Hong Kong Children

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RATIONALE: Fish is a common diet as well as food allergen in Asia, but conventional diagnostic methods for fish allergy are inaccurate. This study investigated the pattern of IgE sensitization to different allergens of grass carp (Ctenopharyngodon idella).

METHODS: Purified recombinant beta-parvalbumin, beta-enolase and aldolase A allergens of grass carp produced by transformed E. coli cells were coated onto microtiter plates for detection of specific IgE against fish allergens present in sera of 14 subjects with a clinical history of IgE-mediated fish allergy. IgE reactivity to recombinant allergens from C. idella and to cod, tuna and salmon extracts was tested by IgE ELISA and ImmunoCAP respectively.

RESULTS: Parvalbumin from C. idella was recognized by all subjects while Gad m 1 was recognized by 10 (71.4%) subjects. There was significant correlation between IgE reactivity to C. idella parvalbumin and Gad m 1, and IgE reactivity to C. idella was higher than to Gad m 1. IgE reactivity was observed in one patient to aldolase and none to enolase. C. idella parvalbumin inhibited IgE binding to immobilized Gad m 1 for more than 80% even at the lowest concentration (1 mg/ml). Reciprocally, Gad m 1 only inhibited 40% of IgE binding to C. idella parvalbumin at 1 mg/ml.

CONCLUSIONS: Grass carp has a higher diagnostic value for fish allergy diagnosis in Hong Kong patients when compared to cod. This study also highlights the need to use the right fish species for allergy diagnosis. (funded by Hong Kong Institute of Allergy Research Grant)

823 Oral Food Challenges in the Outpatient Office Setting: Assessment of Risk Factors to Predict Best Clinical Outcomes

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RATIONALE: Current skin and serologic tests for assessing food sensitization have poor positive predictive values and can be discordant. This makes it difficult to identify true IgE-mediated food allergy. Empiric food testing in infancy has resulted in many children unnecessarily avoiding a variety of foods. The diagnostic gold standard for food allergy remains the oral food challenge (OFC) which is underutilized due to anaphylaxis concerns. This study’s purpose is to provide a “real-world” risk assessment and outcomes related to in-office OFCs.

METHODS: A retrospective patient chart review of OFCs in a large clinical allergy practice in Midwest Ohio between January 2015 and January 2017 was performed. Data was extracted from medical records for information on food allergy history, skin and/or serologic testing, co-morbid disease(s) and other relevant demographic information. Data was entered into SAS and underwent univariate and multivariate analysis.

RESULTS: 71 OFCs were reviewed thus far. 8.45% failed OFC. Asthma, eczema, seasonal allergies and gender were not predictive of OFC outcomes. Univariate analysis revealed wheal (p < 0.0003) and flare (p < 0.04) diameter, sIgE (p < 0.0001) and sIgE/Total IgE ratio (p < 0.0005) were highly predictive of OFC outcomes. Multivariate analysis revealed a high log (sIgE) was most predictive of OFC failure (p < 0.001). No adverse outcomes were observed to date with OFC challenges.

CONCLUSIONS: OFCs are safe to perform in a controlled outpatient setting by experienced Allergists. Specific IgE testing appears to be the best marker for predicting a failed OFC. Data collection is ongoing to increase the number of OFCs and confirm the predictability of this risk factor.
824 Peanut Allergy Documentation in Electronic Medical Records

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RATIONALE: The electronic medical record (EMR) is an important tool for communication among providers. Use of the EMR for recording peanut allergy (PA) has not been investigated.

METHODS: The EMR of a tertiary care medical center was reviewed for patients with at least one well child primary care visit between January 1 and December 31, 2016. Comparisons were made between children who had PA on their problem list (PL), updated by physicians, vs allergy list (AL) alone, updated by multiple individuals.

RESULTS: Of 884 charts reviewed, 453 charts had PA on PL and 872 had PA on AL. There were no differences in age or gender between children who did and did not have PA on PL. However, children with PA on their PL were more likely to have an allergy referral, evaluation by an allergist, additional food allergies, epinephrine prescriptions, and repeat peanut IgE levels (p<0.001 for each). Children with PA on PL were more likely to have peanut allergy confirmed by an allergist than children with PA on AL alone (OR 1.8, p=0.01). Among children with PA on AL alone, 17% were considered tolerant to peanut, compared to 5% with PA recorded on PL (p<0.001). However, PL could not be relied upon to capture PA consistently, as 67% considered definitely PA by the allergist did not have PA on their PL.

CONCLUSIONS: There is inconsistency with how PA is communicated in the EMR, which was associated with significant differences in how PA is confirmed and managed.

825 Barriers preventing Canadian parents of children with food allergy from participating in Oral Food Challenges and possible solutions

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RATIONALE: Oral food challenge (OFC) is the gold standard for diagnosing food allergy. However, OFCs are often not performed for various reasons, including resistance from children and parents. We conducted focus groups with parents of food-allergic children to determine barriers preventing them from OFC participation, and potential solutions.

METHODS: Parents of children with physician-diagnosed food allergies (recruited online through a Vancouver area support group) were invited to participate in a two-hour focus group on OFC barriers and solutions. Focus groups were audio-recorded, transcribed, and analyzed to determine the most common barriers and solutions.

RESULTS: Seventeen parents (82.3% female, 76.4% post-secondary educated, 76.4% Caucasian) participated in two focus groups (which had 20 spaces total) in June 2017. Barriers to participating in OFCs included fear of a severe reaction or of needing to use epinephrine, logistical issues such as scheduling, lack of information on what to expect with the procedure itself, as well as lack of understanding of the risks/benefits of an oral challenge regardless of outcome. Solutions included providing more information and education for parents and children, offering psychological support pre- and post-OFC, and conducting OFCs in hospitals instead of community clinics.

CONCLUSIONS: This is the first Canadian study to describe parental OFC barriers and solutions. A limitation was selection of parents from a specific city who join support groups, which might not be representative of other allergy parents. Further research should be conducted to determine the most effective strategies to make OFCs more accessible to families.

826 Investigating Parents Experiences in Re-introducing Baked Milk Foods in Children with Cow’s Milk Allergy

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RATIONALE: Baked milk challenges and milk ladders (ML) are currently recommended to determine the development of tolerance to baked milk in children with IgE and Non-IgE-mediated Cow’s Milk Allergy (CMA). However, there is still relatively little known about the parents’ perceptions of the gradual reintroduction of baked milk. This is the first qualitative study to explore parents’ experiences, understanding and their level of satisfaction in using milk in baked goods and the impact/outcomes of these products in the management of their children’s milk allergy.

METHODS: Twenty two semi-structured individualised phone interviews were conducted with mothers (UK residents) of children (n=7; IgE-mediated CMA and n=15; Non-IgE-mediated CMA, 15months-8years) who followed or completed a ML (recruited via social networking sites and analysed using thematic analysis).

RESULTS: It emerged that mothers of children following the ML experienced: 1)Confusion when there was not an explicit nationally recommended ML that all healthcare professionals (HCPs) adhere to. 2) Restricted healthcare support due to limited communication between parents and HCPs/lack of counselling or follow ups. 3)Dissatisfaction with the lack of healthy food choices or alternative food options in each stage of the ML. 4)Concerns about how to recognize potential symptoms of a baked milk reaction. 5)Uncertainty regarding the time spent on each stage of the ML. 6)Insecurity around home reintroduction in case of severe reaction.

CONCLUSIONS: Gradual milk reintroduction is usually a long process and mothers need an improved ML based on national recommendation, and local healthcare support, to ensure the efficacy and safety of this process.
827 YouTube and Eosinophilic Esophagitis: An Assessment of the Educational Quality of Information

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RATIONALE: Eosinophilic Esophagitis (EoE) is a rare allergic inflammatory disease affecting 1-4 in every 10,000 individuals in the US. With the increasing use of the Internet as a source of health care information, we sought to determine the educational quality of EoE videos on Youtube.

METHODS: We performed a YouTube search using the keyword “eosinophilic esophagitis”. Videos were analyzed for characteristics, source, and content. Source was further classified as health care provider, patient, company, media, or professional society. A scoring system was created to evaluate the quality (-10 to +30 points). Negative points were assigned for misleading information. Six blinded reviewers scored each video independently.

RESULTS: Two hundred and nine videos were analyzed, with a median of 507 views, 1 like, and 0 dislikes. More video presenters were male (50.9%). The most common type of video source was professional society (39.2%), and the least represented video source was company and media (8.5%). Among the four video sources, the mean scores showed a statistically significant difference from each other (p<0.0001). There was a higher mean score for videos by health care providers (5.7) when compared to other video sources (mean score between 3.3 and 4.6). Intraclass correlation showed a high degree of agreement among reviewers (ICC = 0.820; p < 0.001).

CONCLUSIONS: Youtube videos on EoE were a poor source of valid health care information. Videos by health care providers were a better source of information, reiterating the need for higher quality educational videos on EoE by the medical community.

828 Food Allergies Among Patients of South Asian Origin in the United States

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RATIONALE: The prevalence of food allergy is increasing worldwide. While there is some data regarding food allergy prevalence in South Asia, there is little published data on food allergies of patients living in the United States of South Asian descent. We report data regarding food allergies among patients in the United States of South Asian descent.

METHODS: A chart review was performed of patients of South Asian descent from two major metropolitan areas, Dallas-Fort Worth, Texas, and Washington, D.C. Patients had a positive food allergy history and allergy testing (specific IgE or prick skin testing) to foods.

RESULTS: There were a total of 68 patients, with 65 below age 16. All of the patients were born in the United States, and most of their parents were born in India (63) or Pakistan (4). Only 3 patients had a family history of food allergy. The majority of patients (84%) were allergic to multiple foods. Fifty-one patients (75%) were allergic to tree nuts, including walnuts, almonds, and cashews. The next most prevalent allergen was peanut (31%). Twelve patients were allergic to egg, and 4 were allergic to milk.

CONCLUSIONS: This clinical observation revealed tree nuts as the most common food allergy in this population. Additional larger studies in both the United States and South Asia are required to further elucidate the prevalence of food allergies in this population. The allergist/immunologist must be aware of this and other potential food allergies in this specific population.
830 Sustained unresponsiveness is maintained despite erratic peanut consumption after home-based induction: telephone follow up

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Rationale: We have previously shown (Garvey JACI-IP 2017) that some highly selected, “high-dose tolerant” peanut allergic children can achieve sustained unresponsiveness to peanut in a home-based induction program. It is not known whether this unresponsiveness is permanent, when it could be defined as genuine tolerance.

Methods: Telephone survey of ten children from the published paper who achieved desensitization (2/10) or sustained unresponsiveness (8/10) and been advised to keep eating peanut 3 times a week indefinitely. Follow-up interval ranged from 1.4 to 3.5 years.

Results: Only three children (30%) are eating peanut three or more times a week, as advised. Two children (20%) have completely stopped consuming peanut by choice. Five children (50%) eat peanuts less than the advised 3 times/week (including one who just eats food with precautionary labelling about peanut). No subject reported interval reactions to peanut either eaten deliberately, as advised, or accidentally. All parents report to feel safer since they have completed this program. Just two of the children still carry their epinephrine pens as they have other food allergies (egg and tree nut respectively).

Conclusions: Compliance with post program advice to continue consumption of peanut was very erratic, but no allergic reactions occurred in any subject, irrespective of either compliance or accidental exposure to peanut. This suggests that true tolerance has been achieved by home based exposure to peanut in a select group of “high-dose tolerant” peanut allergic children. More formal prospective studies are needed to confirm this finding.

831 Characteristics of Preschool-Aged Children Currently Enrolled in a Phase II Double Blind Placebo Controlled Study of Peanut Sublingual Immunotherapy

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Rationale: A recent study of early peanut oral immunotherapy (OIT) in preschoolers demonstrated significant efficacy with higher rates of sustained unresponsiveness than has previously been seen in older cohorts. Sublingual immunotherapy (SLIT) for peanut has demonstrated moderate efficacy in school age cohorts, but has not been studied in this younger age group.

Methods: Children aged 12-48 months with peanut allergy or sensitization to peanut were enrolled in a multi-center phase II double blind placebo controlled study of peanut SLIT. We reviewed screening and entry challenge data of 40 subjects enrolled at a single site, between April 2015 and May 2017.

Results: The majority of participants were male (55%) and Caucasian (80%). Average subject age was 29.5 months (12.4-47.4 months). Median peanut-specific IgE at enrollment was 14.3 kU/L (mean = 26.7, 0.35-100 kU/L) and peanut 1:20 skin prick test (SPT) size was 10.5 mm (mean = 11.1 mm, 4-24 mm). Multiple atopic co-morbidities were reported (75% atopic dermatitis, 40% allergic rhinitis, 23% asthma or recurrent wheezing). No subjects reported diagnosed eosinophilic GI disease. All subjects underwent a 1000 mg double blind placebo controlled food challenge (DBPCFC) at enrollment and tolerated a median dose of 30 mg (mean = 64.7 mg, 0-300 mg).

Conclusions: This cohort of preschool age children is representative of high-risk peanut allergy with SPT and IgE at the 95th percentile level and a low DBPCFC threshold providing an ideal opportunity to assess the effect of younger age on the overall efficacy of peanut SLIT.

832 Diagnostic utility of changes in egg-specific IgE in infants with atopic dermatitis

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Rationale: Interpretation of sequential changes in food-specific IgE (sIgE) levels remains unclear. The relationship between oral food challenge (OFC) outcome at 12 months and sequential changes in sIgE levels during infancy has not been studied.

Methods: A retrospective observational study was performed. Twelve-month-old infants with infantile atopic dermatitis who had egg white (EW) - and ovo-ovomucoid (OM)-sIgE levels measured at 6 and 12 months and had undergone egg OFC with 1/2 egg-equivalent heated egg powder at 12 months were enrolled, and the relationship between changes in sIgE levels and OFC outcome was analyzed.

Results: Twenty-nine patients were enrolled. EW-sIgE levels significantly decreased from 6 to 12 months in the OFC-negative group, but not in the OFC-positive group. The decrease in logarithmic transformed values was significantly larger in the OFC-negative group. There was no significant association between the changes in OM-sIgE levels and OFC results, although the OM-sIgE levels at 6 months in the OFC-positive group was significantly higher.

Conclusions: For infants with atopic dermatitis, changes in EW-sIgE levels during infancy may be useful in predicting egg OFC outcome at 12 months of age. The results suggest on the utility of evaluation of changes in sIgE levels.

833 Bioinformatics and Proteomics Evaluations to Consider IgE Binding Assays for Potential Cross-Reactivity Between House-Cricket (Aceta domesticus) Used in Food, Crustaceans and Cockroaches

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Rationale: Humans have consumed insects throughout history. However regulators in the United States are asking for assurance that new food products containing processed, Cultured insects are safe for crustacean allergic subjects, based on comparisons of genomic, transcriptomic or proteomic data. House-crickets (Acheta domesticus) are being used for food production and were the focus of this study of potential cross-reactivity.

Methods: The transcriptome of the cricket was reported by the Malik lab (https://doi.org/10.7554/eLife.03676). We assembled their data using Velvet and Spades programs. Probable contiguous transcripts were identified using Blastx. Results were compared to the AllergenOnline.org database to find potentially significant alignments, focusing on allergens from the WHO/IUIS Allergen Online database: tropomyosins, arginine kinases, myosin light chain, troponin C, hemocyanin and triosephosphate isomerase. Predicted protein sequences were used to evaluate proteomic data of Aceta domesticus obtained by LC-MSMS to determine the cross-reactivity between a likely food preparation. Limited serum IgE studies were performed to identify shared IgE binding.

Results: Nucleotide sequences predicted protein sequences. The identities of cricket proteins were higher to cockroach than crustaceans proteins. The LC-MSMS confirmed the presence of a number of proteins. Serum IgE tests using a limited number of donors suggest differences in binding. Yet these data are preliminary and demonstrate the complexity of answering regulatory questions. The abundance of the proteins and stability in food contribute to risks. Multiple IgE binding methods are needed to confirm cross-reactivity.

Conclusions: This study shows that it is not yet possible to clearly determine risks for crustacean allergic subjects based only on sequence information.
MONDAY

834 Safety and Effectiveness of Oral Food Challenge in Children with Cow’s Milk Allergy: Clinical Experience from a Brazilian Reference Center

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RATIONALE: Oral Food Challenge (OFC) is the gold standard for the diagnosis of cow’s milk allergy (CMA). As some Brazilian public services provide special infant formulas, the diagnostic accuracy and proper management of CMA are relevant for public health expenditures. We aimed to determine the profile of children with CMA submitted to OFC at a university hospital and evaluate its public health impact.

METHODS: Analysis of 52 children with CMA, submitted to 58 open-OFC for fresh or baked milk. Data were obtained from standardized records and complemented from retrospective chart review.

RESULTS: 59.62% boys. Age at test: 53.85% ≤ 3 years. Onset of symptoms: Math<1 year in 94.23%. Symptoms related to CMA: gastrointestinal (48.08%), cutaneous (11.54%), two or more (40.38%). 21.15% had anaphylaxis. Feeding at the onset of symptoms: milk-based formula (40.39%), milk-based formula and breast milk (25.0%), breast milk (13.46%), whole milk or derivatives (21.15%). In the elimination diet, 43 patients used extensively hydrolyzed, acidine-derived or soy formulas. Of the OFCs performed, 72.41% were negative and 27.59% positive. Three patients had anaphylaxis, receiving treatment, with symptom control. From 28 patients who were still receiving special formulas at the time of the test, the negative OFC allowed their suspension and the release of regular milk-based formula/whole milk to 16 of them. This result led to savings of approximately 35,500 dollars/year.

CONCLUSIONS: Performing OFC in children with CMA led to reduced costs to the public health service, by reducing the indiscriminate use of special formulas. The test proved to be safe and effective.

835 The Role of Allergists in the Diagnosis and Management of Food Hypersensitivity

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RATIONALE: The prevalence of food allergy (FA) in children has increased over the past decade. Current FA testing modalities have a high false positive rate, which can lead to over-diagnosis of FA. There are limited studies that examine the referral patterns by both primary care physicians and subspecialists to allergists.

METHODS: We reviewed the charts of patients referred to the allergy clinic in a tertiary care medical center for evaluation of possible food hypersensitivity from January-February 2016. Data collected include patient demographics, results of allergy testing, and outcomes of the visit.

RESULTS: Over two-months, 194 patients were referred for possible FA and 70% completed a new patient visit. The median age was 3 years (interquartile range [1-6]) and 53% were male. Thirty-three percent of those patients had previous testing (skin testing, serum IgE levels, or both) for FA. During initial evaluation, 77% of patients had skin testing performed and 36% of patients had serum IgE levels obtained. The most common food sensitizations by skin prick testing were egg (41%), peanut (31%), tree nut (26%), and milk (24%). Sixty percent of patients had at least one other atopic comorbidity. Eighty-seven percent of the referrals came from PCPs. Fifty-one percent of patients were discharged with concerns for an IgE-mediated hypersensitivity and 47% with self-injectable epinephrine.

CONCLUSIONS: Food allergy is a common disease of children. In this study of children referred to allergy clinic for a history concerning for food hypersensitivity, only half were instructed to avoid specific foods or required a prescription for self-injectable epinephrine.

836 Early Immunologic Shifts Occurring in Cows Milk (CM) Oral Immunotherapy (OIT)

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RATIONALE: Patients with anaphylactic cow’s milk allergy (CMA) have persistent and high levels of specific IgE (sIgE) to milk proteins. OIT induces the sIgE reduction wile increasing specific IgG4 levels. The purpose of this research was follow-up these and other parameters during the induction phase of CM OIT.

METHODS: Series of cases involving 51 children and adolescents with anaphylaxis to CM. sIgE and Total IgG4 levels were evaluated in 2 steps of OIT: at baseline, pre-treatment session (step 1) and when reaching the induction final volume: 300 ml of CM a day (step 2). Time between steps lasted 4 to 6 months. Differences between sIgE levels were analyzed by Paired Student’s t test.

RESULTS: At step 1, sIgE mean levels for CM, casein, α-lactalbumin and β-lactoglobulin were respectively, in KU/L: 56.27 (1.4 - >100.0); 49.38 (0.75 - >100); 25.96 (0.1 - >100) and 15.88(0.49 – 86.7).Besides the mean level of total IgG4 was 111,47 KU/L (5,09 - 1020). At step 2 these values were respectively: 30,49 (0.1 - >100); 25,69 (0.10 - >100); 18,18 (0 - > 100) and 11,6 (0.1 – 56,7). And the total IgG4 mean was 164,94 (5,57 - 3090).

Comparing sIgE and IgG4 means between the steps revealed statistical significance for CM (p<0.0001); casein (p<0.0001); α-lactalbumin (p=0,02) and β -lactoglobulin (p=0.04); besides IgG4 (p=0,04).

CONCLUSIONS: Milk proteins sIgE levels markedly reduces in few months of CM-OIT, in parallel to developing clinical tolerance to milk ingestion. Increase of total IgG4 levels could mean the increase in specific IgG4 for CM proteins.
837 Prevalence of Peanut and Tree Nut Allergy and Sensitization in an Urban Clinic Population

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Rationale: Given the increasing prevalence of peanut and tree nut allergies, we sought to assess the frequency of sensitization to peanut and tree nuts in an urban inner city population.

Methods: We performed a retrospective chart review of 61 patients, 11 months to 18 years, diagnosed with food allergy in the pediatric allergy clinic. Clinical history, prick skin testing (PST) and serum IgE (sIgE) for peanut and tree nuts (almond, brazil nut, cashew, hazelnut, macadamia, pecan, pistachio, and walnut) were reviewed.

Results: Subjects included 38 males and 23 females. Nearly half (47.5%) had a history of a clinical reaction to peanut. An additional 29.5% were avoiding peanut with a positive prick skin testing (PST) (>3mm wheal) and/or serum IgE (sIgE) (>0.35 kUA/L) but without a clinical history of reaction. The majority (85.2%) had a positive PST and/or sIgE to at least one tree nut but only 39.3% of subjects reported a clinical history of a reaction to one or more tree nut, most commonly cashew (20%), hazelnut (10%), walnut (9%), and almond (7%). Almost half (47.5%) continued avoiding all other tree nuts which had an associated lack of clinical history, negative PST and/or sIgE testing. Only 24.6% of subjects underwent food challenge (8 peanut, 7 tree nut) with 7 failed challenges (mean sIgE 1.16 kUA/L, range 0.1-2.56).

Conclusions: Although sensitization to peanut and multiple tree nuts is very prevalent in this inner city population, there is also a high rate of avoidance of peanut and tree nuts without a convincing clinical history or positive testing.

838 Analysis of Soy Allergy Using Molecular Component Testing

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Rationale: Soy allergy is one of the most common food allergies. The presence of IgE specific to soy component storage proteins Gly m4, m5, and m6 has been indicated as a means to improve the specific identification of systemic and local soy allergic reactions.

Methods: A retrospective review of national laboratory data was performed over samples testing for IgE to Gly m4, 5, and 6 (Phadia ImmunoCAP). Data from de-identified patient samples were compiled into risk groups based on current research utilizing the international standard cutoff of 0.35kUA/L as a positive test for IgE.

Results: Of the sample set, 46% of patients were responsive to at least one soy component. Of these, 39% of patients display response to only Gly m5 and 6, the components most indicative of a severe and systemic response to soy. Patients responsive to Gly m4 only represented 37%, and 15% were responsive to all components. Few patients were responsive to Gly m5 or 6 separately or associated with Gly m4. Nearly 60% of positive pediatric (<10Y) patients were responsive to both Gly m5 and 6 and only 14% to Gly m4 alone. Patients older than 10 years predominantly respond to Gly m4 alone over m5 and m6 only (54% to 24%).

Conclusions: Molecular component allergy testing represents a major step forward in assessing risk of soy allergies and constructing an appropriate medical response. A significant rate of specificity between the identification of markers for systemic and local/non-specific reactions indicates the importance of this information for patients and their families.
840 Determinants of health related quality of life (HRQoL) in adult patients with hereditary angioedema due to C1 inhibitor deficiency (C1-INH-HAE)

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RATIONALE: HRQoL is impaired in C1-INH-HAE, an inherited disease. We aimed to study HRQoL determinants in adult patients with C1-INH-HAE.

METHODS: Hospital La Paz Ethics Committee approved the study (PI-2297). Spanish patients with C1-INH-HAE ≥18y were included. Demographic, clinical data were collected. HRQoL was measured by HAE-QoL, AE-QoL, and EQ5D. A univariate statistical analysis was performed.

RESULTS: Fifty-six out of 61 patients were included (non-response rate:8.29%; mean age 46±14.0 y, 58.9% females). Mean HAE-QoL score was 102.9±24.4, whereas mean adjusted AE-QoL score was 33.0±22.7 and mean EQ5D score was 0.86±0.17. HRQoL (mean ± SD) was more impaired in females than males [HAE-QoL (99.3 ± 26.8 vs 107.8 ± 20.3, n.s.), AE-QoL (37.7 ± 23.5 vs 27.5 ± 20.6, n.s.), EQ5D (0.82±0.20 vs 0.91±0.10, p = 0.046)], in patients having had angioedema attacks in the last 6 months [HAE-QoL (98.40±23.58 vs 118.64±21.56,p<0.001), AE-QoL (16.52±18.27 vs 37.41±21.20,p<0.01); EQ5D (0.84±0.17 vs 0.93±0.08, n.s.),] in patients having had ≥6 versus 1-5 angioedema attacks in the last 6 months [HAE-QoL (87.71±22.92 vs 105.52±21.7,p=0.0262), AE-QoL (30.61±18.98 vs 47.37±20.89,p<0.01); EQ5D (0.78±0.23 vs 0.88±0.10, n.s.) and in patients receiving long-term prophylaxis [HAE-QoL (91.3±25.4 vs 110.4±21.4,p<0.01), AE-QoL (40.9±23.6 vs 27.3±20.8,p=0.0298), EQ5D (0.76±0.22 vs 0.92±0.09,p<0.001)].

There were no significant differences in HRQoL regarding age, body mass index, having family antecedents with C1-INH-HAE or having family antecedents of death due to asphyxia.

CONCLUSIONS: HRQoL in adult Spanish patients with C1-INH-HAE is lower in females, patients having had angioedema attacks in the last 6 months, those having had more than 6 angioedema attacks in the last 6 months and those receiving long term prophylaxis.

841 Pre-filled Syringes For Immunoglobulin Therapy: A Pragmatic Review Of Clinical Experience From Other Disease Settings

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RATIONALE: Immunoglobulin G (IgG) replacement is an established treatment for patients with primary and secondary immunodeficiencies. Measures to improve patient experience and quality of life remain important goals of individualized IgG treatment regimens. The introduction of pre-filled syringes, widely used in other clinical conditions, addresses an unmet need that may offer significant benefits to patients.

METHODS: A pragmatic literature review of articles published in PubMed was conducted to collate the experience from other clinical settings on the use of pre-filled syringes. The primary search term was “(pre-filled or prefilled) AND syringe[MH]”; no time constraint was imposed. Results were filtered to focus on articles reporting data from clinical and comparative studies. Further articles were identified by searching specific terms of interest.

RESULTS: The primary search identified a total of 229 articles, covering diverse disease areas. Of these, 69 articles were clinical or comparative studies. Data from the subset of relevant articles reported bioequivalence, stability, efficacy, and safety of drugs delivered by pre-filled syringe. Evidence also showed that the use of pre-filled syringes, which eliminate drug preparation steps, significantly reduces drug/infusion treatment time. In studies reporting the responses of patients and healthcare professionals, the acceptability, usability, convenience, and preference for the use of pre-filled syringes were generally high. Potential for cost savings were reported in some, but not all, studies.

CONCLUSIONS: Current evidence from other clinical settings demonstrates the advantages of pre-filled syringes for treatment and improved patient experience, which supports their use and potential benefits to patients receiving IgG therapy.

842 Real-world experience of a cohort of previously untreated PI patients on SCIG

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RATIONALE: To evaluate demographic, dosing and treatment satisfaction data from a large survey conducted by the Immune Deficiency Foundation (IDF) in a subset of treatment-naïve patients with primary immunodeficiency (PI), who initiated therapy on subcutaneous IG (SCIG).

METHODS: An online survey was sent to patients registered in the IDF database and was completed by the patients/caregivers between March 10–31, 2017. We report on infusion experience and satisfaction on SCIG therapy (based on the Treatment Satisfaction Questionnaire for Medication (TSQM) (effectiveness, side effects, convenience and global satisfaction) among the subset of treatment-naïve patients who started directly on SCIG.

RESULTS: Of 371 respondents on SCIG; 138 (37%) individuals reported previously receiving IVIG. These respondents tended to be female (85%), ≥30 years old (88%) and diagnosed with Common Variable Immune Deficiency (CVID) (88%). Compared to those who previously received IVIG, these respondents were more likely to be older at time of diagnosis (p<0.001), infuse somewhat less frequently (p<0.001), had a slightly shorter infusion time (p=0.05) and had fewer infusion sites (p<0.007). The mean total Treatment Satisfaction Questionnaire for Medication score (range 0–100) was 74 (SD 16). Overall, 85% of patients reported they were satisfied, very satisfied, or extremely satisfied with SCIG.

CONCLUSIONS: SCIG use in previously untreated PI patients is relatively common among a cohort of IDF members. The majority of these patients were satisfied to extremely satisfied with SCIG treatment. Furthermore, the relative efficacy of infusion characteristics among patients suggests the viability of initiating IG treatment directly on SCIG among some patients.
**843** Prevalence And Outcomes Of Primary Immunodeficiency In Hospitalized Children In The United States

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**RATIONALE:** The prevalence and outcomes of primary immunodeficiency diseases (PIDDs) in the pediatric population in the United States are not well understood. The objectives of this study were to 1) Determine the epidemiology of children hospitalized with PIDD in the United States and 2) Characterize the clinical outcomes of hospitalized children with PIDDs.

**METHODS:** Retrospective cohort analysis of the 2003-2012 Kids’ Inpatient Database (KID) of children ages 2-18 years admitted with a primary or secondary diagnosis of PIDD was performed.

**RESULTS:** There were 26,794 pediatric patients hospitalized with a diagnosis of a PIDD from 2003-2012. The national prevalence of all PIDDs per 100,000 was 66.6, 82.2, 97.4 and 126.8 in 2003, 2006, 2009 and 2012, respectively. The highest prevalence was in children 0-5 years of age (15,105 hospitalizations; 56%). There was no difference in prevalence between B cell defects and T cell defects. PIDDs affected all ethnic populations equally. Respiratory related diagnoses were the most common co-morbidity by organ system. Overall mortality was 1.98%. Age was inversely correlated with clinical outcome. Children 0-5 years had higher mortality (424 deaths, 79.85%), mean hospital charges ($35,480) and length of stay (LOS) (5.6 days) compared to older age cohorts.

**CONCLUSIONS:** The prevalence of PIDDs in the hospitalized pediatric population in the United States has steadily increased over time. Younger age is associated higher mortality, hospital costs and LOS. Further study is needed to determine cost-effective management strategies to improve outcomes in infants and young children with PIDD.

**844** High treatment satisfaction with Hizentra, a 20% subcutaneous immunoglobulin (SCIG): real-world survey data

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**RATIONALE:** To investigate treatment satisfaction of patients on SCIG (specifically Hizentra) from a large survey of Immune Deficiency Foundation (IDF) members diagnosed with primary immunodeficiency (PI).

**METHODS:** Between March 10 to 31 2017, an online survey was completed by patients and caregivers of pediatric patients with PI receiving IG therapy, from the IDF database. We analyzed the Treatment Satisfaction Questionnaire for Medication (TSQM) (effectiveness, side effects, convenience and global satisfaction) for patients currently receiving Hizentra. TSQM respondent scores are transformed to a 0–100 scale (0: poorest satisfaction, 100: perfect satisfaction). Desirable thresholds for treatment satisfaction (defined as the two best scores for side effects [1–5 scale]; and three best for all other domains [1–7 scale]) translated to 67, 75, 67 and 69 for effectiveness, side effects, convenience, global satisfaction and total TSQM score, respectively.

**RESULTS:** Of 1,037 respondents, 744 were receiving IG: 247 were on Hizentra and completed the TSQM. Mean (standard deviation) scores were 73 (19) for effectiveness, 83 (24) for side effects, 72 (17) for convenience, 80 (16) for global satisfaction and 76 (14) for total TSQM score. Percentage of responders whose scores were above the desired threshold were 72% for the total TSQM score, 74% for effectiveness, 73% for side effects, 68% for convenience, and 85% for global satisfaction. When stratified by primary treatment decision maker (Prescriber, Patient, Other) no significant differences were seen in TSQM scores.

**CONCLUSIONS:** Generally, patients receiving Hizentra were highly satisfied with treatment, with 68–85% reporting above the desired thresholds with TSQM.

**845** Infusion Parameters and Adverse Events in Patients With Primary Immunodeficiency Diseases Who Switched to Subcutaneous Human Immune Globulin 20% (Ig20Gly) From Intravenous or Subcutaneous Immune Globulin

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**RATIONALE:** Ig20Gly (Cuvitru®) is a new subcutaneous human immune globulin (Ig) 20% preparation for the treatment of primary immunodeficiency diseases (PIDD). To evaluate whether the previous route of Ig administration affects the tolerability or infusion characteristics of Ig20Gly, we assessed rates of causally related local and systemic adverse events (AEs) and infusion parameters from patients whose immediate pre-study treatment was IVIG (IV-switchers) or SCIG (SC-switchers) from a phase 2/3 North American study (NCT01218438).

**METHODS:** Patients aged ≥2 years were initially switched to Gammagard Liquid (IVIG10%) for 3 months at the monthly dose equivalent of their most recent pre-study treatment of IVIG or SCIG. Patients then received once-weekly Ig20Gly for ~1 year.

**RESULTS:** Of 74 patients treated with Ig20Gly, 68.9% were IV-switchers. No serious or severe causally related AEs were reported during Ig20Gly treatment. Rates of causally related local and systemic AEs were slightly lower for IV-switchers (0.007/infusion and 0.012/infusion, respectively) versus SC-switchers (0.035/infusion and 0.039/infusion). The percentage of infusions with causally related local AEs (IV-switchers, 0.6%; SC-switchers, 3.1%) and systemic AEs (IV-switchers, 0.9%; SC-switchers, 3.5%) was generally low. IV-switchers versus SC-switchers had a slightly higher median infusion volume/site (42.5 vs 34.5mL) and median infusion duration (1.07 vs 0.82 hours). In both IV- and SC-switchers, a similar percentage of patients infused ≥60 mL/site (70.6% and 73.9%, respectively), and most infusions required ≤2 sites (86.8% and 81.0%).

**CONCLUSIONS:** Ig20Gly administration was associated with low rates of causally related local and systemic AEs. Infusion parameters were comparable for patients who received prior IVIG or SCIG.
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846 Onboarding Experience of Pediatric Patients With Primary Immunodeficiency Diseases With Subcutaneous Immune Globulin 20% (Ig20Gly)

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RATIONALE: The safety and efficacy of subcutaneous immune globulin 20%. Ig20Gly, was demonstrated in a phase 2/3 North American study (NCT01218438) in patients with primary immunodeficiency diseases (PIDD). This post hoc analysis assessed the onboarding experience with Ig20Gly in pediatric patients.

METHODS: Patients aged ≥2 years received weekly Ig20Gly infusions at volumes of ≥60 mL/site and rates of ≥60 mL/h/site for ≥1.3 years. To evaluate the Ig20Gly onboarding experience, adverse events (AEs), tolerability, and infusion parameters were assessed in patients aged 2 to <16 years.

RESULTS: Most infusions (97.5%; 1154/1166) were not associated with a causally related local AE; 66.7% (14/21) of patients did not experience a causally related local AE. Five patients (23.8%) reached the maximum infusion rate of 60 mL/h/site for ≥2 infusions. A total of 54.3% and 95.2% of infusions were completed in <1 and <2 hours, respectively. Of 1165 infusions, 404 infusions (34.7%) were administered using 1 site and 728 infusions (62.5%) required 2 sites (median [range] infusion sites, 2[1–3]). For dose volumes of 0–59 mL, 41.3% (364/881) of infusions were administered using 1 infusion site. For dose volumes of 60–119 mL, 85% (242/284) of infusions were administered using 2 sites. No association was observed between increasing infusion rates or volumes per site and rates of causally related local AEs per infusion.

CONCLUSIONS: Ig20Gly infusions were well tolerated at high infusion rates and volumes/site in pediatric patients with PIDD; no increases in local AEs were observed with increasing infusion volumes per site and infusion rates.

847 Patient-reported experience on training associated with subcutaneous immunoglobulin (SCIG) therapy self-administration

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RATIONALE: To evaluate experience of primary immunodeficiency (PI) patients’ subcutaneous IG (SCIG) self-administration training, as part of a large survey by the Immune Deficiency Foundation (IDF).

METHODS: An online survey was sent to patients/their caregivers from the IDF database from March 10–31, 2017. Respondents were questioned regarding their experience of being trained to self-administer SCIG.

RESULTS: A total of 371 PI patients on SCIG responded to the survey, 63% were IVIG-transitioned and 37% has only been treated with SCIG; 18% were aged 30–44, 48% 45–64 and 17% ≥65. Sixty-one percent reported receiving 1–2 training sessions, 19% reported 3 sessions, and 20% required ≥4 sessions. Median duration of training sessions was 2 h (IQR 1–3 h); 78% were trained by home health care or specialty pharmacy staff, and 75% were trained at home. Ease of learning to self-administer, rated on a scale from 1 (worst) to 7 (best), was ≥6 for more than 70%; 44% reported a score of 7 while only 3% reported scores of 1 or 2. Ninety-five % reported that there are no insurance barriers to the number of training sessions, or they did not know of any barriers. When asked about concerns, 48% cited inserting the needle into the skin; 24% noted no concerns.

CONCLUSIONS: Survey results show a large majority of PI patients currently receiving SCIG reported minimal or no difficulty in learning self-administration. Combined with relatively short reported training time requirements, this suggests that with appropriate training, most patients easily learn SCIG self-administration.

848 Increasing Provider Use of Patient-Centered EMR Behaviors in a Quality Improvement Project

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RATIONALE: The Electronic Medical Record (EMR) is widely used in clinical settings. Behaviors that enhance patient-centered EMR use have been shown to result in higher patient satisfaction. The aim of this project is to increase provider utilization of two specific behaviors and therefore patient satisfaction.

METHODS: Study was conducted over an 8-week period at the Allergy/Immunology clinic at Emory University. Baseline data about existing practice habits were collected in a 2 week audit period. After the 1st cycle, an intervention described two techniques for patient-centered EMR use. After the 2nd cycle, an intervention reminded providers of the techniques and instituted physical reminder notes on exam room workstations. Patient surveys were distributed by nurses directly after visits about use of the two techniques.

RESULTS: Patient surveys from the audit period showed 53% were shown the screen as an educational tool (behavior 1) and 67% reported the provider reading aloud while typing (behavior 2). After cycle 1, 80% of patients reported providers utilizing behavior 1 and 86% of patients reported providers utilizing behavior 2 (n=21). After cycle 2, 79% of patients reported providers utilizing behavior 1 and 76% of patients reported providers utilizing behavior 2 (n=28).

CONCLUSIONS: Educating providers and increasing awareness about their practice habits and use of physical reminder notes were associated with increased percentages of patients reporting provider use of patient-centered EMR behaviors. With patient satisfaction an integral part of the practice of medicine, utilizing these changes may lead to a better overall experience for the patient.

849 Addressing Specific Patient Expectations in the Allergy/Immunology Outpatient Clinic is Associated with Increased Patient Satisfaction

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RATIONALE: Understanding patients’ expectations in relation to the Allergy/Immunology clinic visit is an important facet of medical communication, and addressing expectations may affect patient satisfaction. Patient satisfaction is a measurement of health quality and an increasingly important component of reimbursement models. We sought to determine if addressing expectations affected patient satisfaction.

METHODS: After IRB approval, a self-report questionnaire was distributed to adult patients following an Allergy/Immunology clinic visit. Demographic information and reason for visit were obtained. Patients were specifically asked if the physician inquired about the patient’s expectations in a number of visit components (diagnosis, testing, symptom improvement, and follow up). Patients were also asked if expectations regarding these components were met. Patients then rated their overall visit satisfaction on a standard Likert scale.

RESULTS: Completed questionnaires were collected from 198 patients. Addressing patients’ specific expectations regarding any of the identified visit components correlated significantly with higher overall satisfaction scores, even when corrected for patient age and gender. The strongest association was seen with meeting patient expectations regarding making a diagnosis to explain symptoms, where these patients were 15.6 times more likely to have high overall satisfaction (OR 15.6, 95% confidence limits 6.8, 35.5). We found no correlation between visit diagnosis, number of visit diagnoses, patient age or gender with overall visit satisfaction scores.

CONCLUSIONS: We demonstrate an association between patients’ perceived physician inquiry into expectations for a clinic visit and overall patient satisfaction at visit completion. In order to improve communication and patient satisfaction, physicians should address patients’ expectations during the medical visit.
Implications of population admixing and ancestry on allergic disease

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RATIONALE: Differences exist among racial and ethnic groups in the prevalence and severity of allergic diseases. However, influence of population admixing on allergic disease has not been studied. We examined the effect of population admixing on the occurrence of allergic disease.

METHODS: We reviewed the data of 75,643 adolescents who participated in the 11th Korea Youth Risk Behavior Web-based Survey, which provides a sample that is representative of the entire Korean middle school and high school student population. Multi-ethnic status was determined by using parental country of birth and prevalence of asthma, allergic rhinitis (AR), and atopic dermatitis (AD) was determined by questionnaire.

RESULTS: Multi-ethnic adolescents accounted for approximately 1.2% of the total sample of adolescents. Prevalence of asthma was significantly higher in multi-ethnic group than non-multi-ethnic group while AR and AD was significantly higher in non multi-ethnic group than multi-ethnic group. Parental region of country at birth had a significant influence on the prevalence of allergic disease. After adjusting for various variables, residential area, perceived economic status, parental region of country at birth, and BMI had a significant effect on prevalence of asthma. Residential area, perceived economic status had significant effect on prevalence of AR. Residential area, parental region of country at birth, and BMI had a significant influence on prevalence of AD.

CONCLUSIONS: Population admixing appears to have significant effect on the prevalence of allergic disease. Further study will be needed to clarify the effect of population admixing on prevalence of allergic disease.

miRNAs in breast milk may correlate with early onset of allergy

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RATIONALE: Allergic diseases are caused by the interaction between genetic factors and environmental factors. Maternal factors seem to influence the development of allergic diseases more than paternal ones. The underlying mechanisms of maternal factors remain to be clarified. Therefore, we hypothesized that miRNA in breast milk affect the development of allergic diseases in offspring.

METHODS: Total 24 mothers and 25 breastfed children were recruited. After taking informed consent from mothers, breast milk was collected on the day 3-5 after birth. MiRNAs were extracted by using mirVana miRNA PARIS kit. The amounts of miR-155, miR-21, and Let-7c were measured by qPCR. The children’s allergic status was checked at 10 months of age.

RESULTS: The miR-155 levels were higher in the breast milk fed to allergic children compared to non-allergic. The miR-21 levels in the milk from mothers having an allergic child significantly higher than that from non-allergic mothers. There was no significant difference in the Let7c levels between allergic and non-allergic children.

CONCLUSIONS: MiR-155 have been shown to affect Treg regulation, and miR-21 is known to ameliorate the differentiation and function of Th1 cells. Although further studies are required, some miRNAs in breast milk might be involved in the development of allergic diseases of breast milk-fed infant.

The 10,000 Immunomes Project: A Resource for Human Immunology

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RATIONALE: New immunological assays now enable rich measurements of human immune function, but difficulty attaining enough measurements across sufficiently large and diverse cohorts has hindered describing normal human immune physiology on a large scale.

METHODS: Here we present the 10,000 Immunomes Project (10KIP), a diverse human immunology reference derived from over 44,000 individuals across 242 studies from ImmPort, a NIAID-funded publicly available resource of raw immunology study data and protocols. We carefully curated datasets, aggregating subjects from healthy/control arms and harmonizing data across studies.

RESULTS: We demonstrate 10KIP’s utility by describing variations in serum cytokines and leukocytes by age, race, and sex; defining a baseline cell–cytokine network; and using 10KIP as a common control to describe immunologic changes in pregnancy. Subject-level data is available for interactive visualization and download at http://10kImmunomes.org/.

CONCLUSIONS: We believe 10KIP can serve as a common control cohort and will accelerate hypothesis generation by clinical and basic immunologists across diverse populations.

Does pregnancy change the effect of methQTL on DNA methylation and after the risk of eczema?

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RATIONALE: Single nucleotide polymorphisms (SNPs) may act as methylation quantitative trait loci (methQTLs) and influence the variation of DNA-methylation. The effect of methQTLs on methylation may change with exposures such as pregnancy. We hypothesized that pregnancy changes the effect of methQTLs on the methylation of CpGs (cytosine-phosphate-guanine dinucleotides) leading to the development of eczema during pregnancy.

METHODS: Peripheral blood samples were obtained at age 18 years and during early pregnancy from the FI-generation of ISe of Wight birth cohort, UK (n=249 and n=109, respectively). Methylation profiles were generated using the Illumina Infinium HumanMethylation450 and EPIC Beadchips. Two layers of screening were implemented to: (1) identify SNPs associated with eczema in women repeatedly measured at age 1, 2, 4, 10, 18 years and pregnancy and (2) focus on CpGs affected by these eczema-associated methQTLs. Then linear mixed models with repeated measurements were applied to assess the interaction of methQTLs and pregnancy on methylation, and the joint effect of methylation and pregnancy on eczema, controlling for methQTLs.

RESULTS: During pregnancy, 38 women had eczema. The methylation of cg11795821 (STAT6 gene) is significantly associated with eczema regardless of pregnancy, controlling for its methQTL (rs1059513). In addition, the methylation of CpG (cg03848267) changes with pregnancy and has a statistically stronger effect (p-value = 0.0097) on eczema than at age 18, adjusting for the methQTL (rs1059513).

CONCLUSIONS: The effect of a methQTL on methylation may change over time and/or with an exposure such as pregnancy. Pregnancy seems to increase the risk of the development of eczema through a variation in methylation.
**854 Sneezing and nasal itching: a potential risk factor for postoperative recurrence of chronic rhinosinusitis**

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**RATIONALE:** Non-AR and idiopathic rhinitis patients has recently increased, with both conditions being classified as local allergic rhinitis (LAR). This study aimed to investigate the effect of local allergic symptoms (LAS) on the clinical outcome and recurrence rate associated with CRS.

**METHODS:** We retrospectively reviewed the medical records of 64 patients diagnosed with CRS and underwent endoscopic sinus surgery. All patients received a preoperative allergic skin prick test, multiple allergosorbent test, and paranasal sinus CT. Total nasal symptom scores were used to determine the severity of symptoms. Sneezing and nasal itching were categorized as LAS. We evaluated the relationships of the clinical characteristics and recurrence rate of CRS according to the presence or absence of AR and LAS.

**RESULTS:** There was no significant difference in the age, sex between the LAS (+) and LAS (-) groups, but the TNSS was significantly higher in the LAS (+) group (p=0.03). In the Non-AR patients, there was no significant difference in the age, sex, and TNSS between the LAS (+) and LAS (-) groups. The CRS recurrence rate was not significantly different between the AR group (29.6%) and the Non-AR group (43.2%) (p=0.374). However, the CRS recurrence rate was significantly higher in the LAS (+) group (46.7%) than in the LAS (-) group (15.8%) (p=0.02). The CRS recurrence rate was significantly higher in the LAS (-) group (16.7%) among the Non-AR patients (p=0.02).

**CONCLUSIONS:** The CRS recurrence rate was higher in patients with LAS, regardless of the presence of AR.

**855 Efficacy of Reslizumab in Eosinophilic Chronic Sinusitis with Nasal Polyposis**

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**RATIONALE:** Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a challenging inflammatory syndrome that is often associated with eosinophilia. Abrogation of tissue eosinophils through IL-5 antagonism represents a plausible approach in the treatment of this refractory disease. We describe the effect of reslizumab, a humanized IL-5 blocker, in patients with recalcitrant CRSwNP.

**METHODS:** Retrospective review of three consecutive patients receiving reslizumab (3mg/kg IV Q4W) for the treatment of refractory eosinophilic CRSwNP with peripheral eosinophilia (>400 cells/μL). Outcomes included validated endoscopic nasal polyp and quality-of-life scores following two infusions of reslizumab.

**RESULTS:** Mean treatment duration was 8 weeks. Presumed underlying ASA intolerance was established in all three patients by clinical history. All patients had concomitant moderate to severe asthma, and mean baseline eosinophil count was 876 cells/μL. All patients had undergone polypectomy on at least one occasion. After 8 weeks, a significant reduction of the Lund Kennedy polyp score of at least 1 point was found in all three of the patients. Mean polyp score improved from 8.6 to 4. Decreased SNOT-22 scores were observed in all patients, with mean improvement from 62 to 33. None of the patients required interval oral steroids for rescue of breakthrough nasal symptoms. No adverse events were reported secondary to reslizumab therapy.

**CONCLUSIONS:** Reslizumab may be an effective adjunctive therapy for recalcitrant CRSwNP with peripheral eosinophilia. Additional prospective study with longer follow-up may be required to unmask the full effects of reslizumab.

**856 Eosinophilic inflammation of the paranasal sinuses and reduced nasal nitric oxide levels in patients with chronic rhinosinusitis**

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**RATIONALE:** Chronic rhinosinusitis (CRS), specifically eosinophilic CRS (ECRS), is a refractory and recurrent condition. Asthma is a known risk factor of refractory ECRS, and the fraction of exhaled nitric oxide (FeNO) measurement is a useful non-invasive method of evaluating eosinophilic inflammation. Therefore, we investigated whether nasal nitric oxide (NO) might be a clinically useful marker for assessing disease severity in patients with CRS.

**METHODS:** In this prospective study, we compared 25 patients with ECRS, 45 patients with non-ECRS, and 33 normal controls. The nasal NO levels were determined by subtracting the nasal FeNO level from the oral FeNO level, as measured using a nitric oxide analyzer. Correlation between nasal NO levels and clinical findings were observed. To evaluate the effect of endoscopic sinus surgery (ESS) on nasal NO levels in the patients with CRS, we measured nasal NO levels preoperatively and at 3 and 6 months postoperatively.

**RESULTS:** The nasal NO levels were significantly decreased in patients with CRS, but more so in those with ECRS; moreover, nasal NO levels in patients with CRS significantly and negatively correlated with eosinophil levels in both blood and in nasal polyp tissue, as well as with the computed tomography score. However, they did not correlate with the nasal polyp score.

**CONCLUSIONS:** Our results indicate that nasal NO may be useful as a marker of CRS severity and low nasal NO levels in patients with CRS might contribute to its pathogenesis, especially in the development of ECRS.
**857 Vitamin D inhibits TGF-β1-induced myofibroblast differentiation and extracellular matrix production via Smad2/3 signaling pathway in nasal polyp-derived fibroblasts**

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**RATIONALE:** Nasal polyps are associated with chronic inflammation of the mucous membranes in the nose and paranasal sinuses and involved in extracellular matrix (ECM) accumulation. Vitamin D has a wide range of antifibrotic properties, including anti-inflammation, anti-proliferation, anti-apoptosis, and anti-epithelial-mesenchymal transition properties.

**METHODS:** To investigate the potential role of vitamin D (1,25(OH)2D3) in preventing the development of nasal polyps, we examined the effect of vitamin D on myofibroblast differentiation and ECM production in TGF-β1-induced NPDFs and elucidated the mechanisms underlying the inhibitory effect. 1,25(OH)2D3 significantly reduced the expression levels of α-SMA, a myofibroblast marker, and fibronectin, a representative ECM component, in a dose-dependent manner in TGF-β1-NPDFs.

**RESULTS:** 1,25(OH)2D3 suppressed activated Smad2/3 in time-course. Up-regulation of α-SMA, fibronectin and phosphorylation of Smad2/3 by TGF-β1 were unaffected by 1,25(OH)2D3 in NPDFs after vitamin D receptor specific siRNA transfection. We confirmed inactivation of Smad2/3 and reduced level of α-SMA and fibronectin expression by the Smad2/3 specific inhibitor, SIS3. Furthermore, acetylation of histone H3 was compromised by 1,25(OH)2D3, leading to inhibition of collagen 1A1, collagen 1A2 and α-SMA gene expression. Treatment with 1,25(OH)2D3 also significantly suppressed TGF-β1-enhanced contractility and motility in a contraction assay and Transwell migration assay. Finally, 1,25(OH)2D3 had a similar effect in ex vivo organ cultures of nasal polyps.

**CONCLUSIONS:** Our results suggest that 1,25(OH)2D3 might be an effective therapy for treating nasal polyps by reducing myofibroblast differentiation and ECM production mediated by Smad2/3-dependent TGF-β1 signaling pathways in NPDFs.

**858 Otolologic Complications in Aspirin Exacerbated Respiratory Disease**

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**RATIONALE:** Otolologic complications, including hearing loss, have been reported in chronic rhinosinusitis with nasal polyposis but have yet to be characterized in Aspirin Exacerbated Respiratory Disease (AERD).

**METHODS:** 450 patients enrolled in the Brigham and Women’s Hospital (BWH) AERD patient registry were surveyed for otologic symptoms. Corresponding demographic and disease data were extracted from the BWH AERD patient registry. Statistical significance was assessed with logistic regression, Chi-square tests, and two-tailed t-tests.

**RESULTS:** 292 of 450 questionnaires were completed (64.8%). 64 patients reported a prior diagnosis of hearing loss (21.9%). Further analysis excluded seven patients with congenital or traumatic hearing loss. 144 (49.3%) reported a history of adulthood middle ear symptoms (MES), defined as ear infections requiring antibiotics, middle ear effusion, or chronic ear drainage. At the time of survey, patients with hearing loss were older (54.8±1.7 vs 48.0±0.8 years, p = 0.0002), and had a longer duration of nasal polyposis (20.3±1.6 vs 12.4±0.6 years, p = 0.0001) than those without. There was no difference in current age between those with and without MES. There was no difference in age of nasal polyposis onset between those with and without MES and hearing loss. Odds of hearing loss increased with each additional year of nasal polyposis (OR = 1.06 per year [1.04-1.10, p < 0.0001]) and history of MES (OR = 3.31 [1.76-6.24, p = 0.002]). Hearing loss and MES were not associated with time to polyp regrowth after polypectomy.

**CONCLUSIONS:** Otolologic complications in AERD are common. Duration of nasal polyps and history of MES, independent of age, are risk factors for hearing loss in patients with AERD.
Efficacy Of Nasal Allergen Provocation Test In The Diagnosis Of Dermatophagoides Pteronyssinus Allergic Rhinitis

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RATIONALE: A nasal allergen provocation test (NAPT) is performed to confirm the diagnosis of allergic rhinitis to house dust mites, in the situation of discrepancy between the symptoms and the results of skin prick test (SPT) and/or serum specific immunoglobulin E. In Cuba, sensitization to house dust mites (Dermatophagoides pteronyssinus (Dp), Dermatophagoides siboney and Blomia tropicalis) is a major cause of allergic rhinitis. Objective: To demonstrate the efficiency of NAPT with an allergenic extract of Dermatophagoides pteronyssinus.

METHODS: Hundred adults between 18 and 45 years were included. Fifty with allergic rhinitis had positive skin prick tests (SPTs) to Dp and fifty healthy individuals. NAPT were performed by instillation with dropper (4 drops) of the Dp extract to five concentrations (2, 20, 200, 2000 and 20000 BU/ml) in nostril at 15 minute interval. Efficacy was demonstrated by the calculation of sensitivity, specificity and efficiency.

RESULTS: Nasal allergen provocation test with Dp extract was positive in the 94% (47/50) of sensitized allergic rhinitis to Dp. As the sensitivity as specificity were high of 94% and 100%, respectively. While, efficiency was 97% (95%CI: 99-100). Furthermore, Area under the ROC curve was 0.970 (0.95-1.0) and a p<0.0001. Another hand, a significant correlation (Spearman, r=0.846; p <0.0001) between the skin reactivity and NAPT response. Eleven non-specific adverse reactions were registered in allergic rhinitis.

CONCLUSIONS: Nasal allergen provocation test with the Dermatophagoides pteronyssinus is effective and safety by the diagnosis of allergic rhinitis to this mite.

The effect of standardized house-dust mite extract in subcutaneous immunotherapy

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RATIONALE: Standardized allergen extracts are recommended for allergen immunotherapy. Since 2015, our clinic used a standardized house-dust mite extract for subcutaneous immunotherapy, instead of non-standardized house dust extract for patients with house dust mite allergies. We hypothesized that standardized house-dust mite extract (standardized group) was superior to non-standardized house dust extract (non-standardized group) for subcutaneous immunotherapy.

METHODS: This was a non-interventional, retrospective study. We included patients with allergic rhinitis and sensitization to house-dust mites. The standardized group (11 patients) had subcutaneous standardized extract immunotherapy beginning in 2015, and the non-standardized group (37 patients) received non-standardized extracts, before 2015. We evaluated the safety and efficacy between the two groups. We assessed safety by the systemic reaction (SR) rate. Efficacy was assessed by reductions in the allergic rhinitis symptom-medication score, and the asthma treatment score, over a year.

RESULTS: The SR rate of standardized group (55%) was significantly higher than that (11%) of the non-standardized group. The standardized group exhibited 47% reduction in the allergic rhinitis symptom-medication score, which was significantly higher than the 40% reduction seen in the non-standardized group. In the standardized group, there was a 65% reduction in the asthma treatment score, significantly greater than the 37% reduction seen among patients in the non-standardized group.

CONCLUSIONS: Standardized house-dust mite extract was more effective than non-standardized house dust extract for subcutaneous immunotherapy; however, the establishment of safer methods is needed.
Rapid build-up in Subcutaneous Aeroallergen Immunotherapy (SCIT) refill dosing

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RATIONALE: Current subcutaneous aeroallergen immunotherapy (SCIT) guidelines recommend decreasing 50 to 90% for the initial doses of refill vials, often with several subsequent weekly visits to return to maintenance dosing. Waibel, et al (2014) published a rapid build-up (RBU) method for refill vials of 50% of maintenance dose followed by the second 50% 30 minutes later. We sought to further assess the validity of this approach and analyzed additional potential risk factors.

METHODS: A retrospective chart review was performed on 242 active SCIT patients. We analyzed the number of RBU refill SCIT performed and documentation of associated systemic reactions. Additional factors included a history of asthma, aeroallergen content of SCIT, duration of maintenance therapy, and prior systemic reactions.

RESULTS: Of 242 SCIT patients, 48 (20%) received RBU with refill vials at least once. 11 patients completed 2-5 RBU. All patients underwent at least one traditional schedule refill of maintenance vial. Of the RBU patients, 17 (35%) had asthma and 9 (19%) had a history of prior systemic reaction to SCIT therapy. Content of SCIT varied from one aeroallergen to prescriptions with trees, grasses, weeds, mold, dust mite, cockroach, dog, cat and horse.

CONCLUSIONS: We observed no increased incidence in systemic reactions from a RBU approach to SCIT refill vials compared to traditional refill approaches. While our sample size is small, our results did not appear to be affected by a history of asthma, previous systemic reactions or the content of SCIT. Larger studies are needed to better characterize this method.

The Effectiveness Of Immunotherapy For Allergic Asthma Among Different Weight Categories

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RATIONALE: Patients with obesity have been shown to have a more severe asthma phenotype compared to their normal BMI counterparts. Subcutaneous immunotherapy (SCIT) has been used as a treatment for allergic asthma, but it is unclear if overweight and obese patients have the same outcomes as normal weight patients.

METHODS: A retrospective chart review was done for 176 patients in the practice undergoing SCIT, with forty-three patients qualifying for inclusion. Inclusion criteria included age 5 to 70 years, diagnosis of allergic asthma, and comparable one-year data of asthma outcomes. Asthma outcomes included changes in asthma control test (ACT) score, spirometry parameters, and inhaled corticosteroid (ICS) dosage. Weight was categorized as either overweight/normal (NW) or overweight/obese (OW).

RESULTS: The mean age of subjects was 22 years old, with forty-four percent of individuals in the OW category. FEV1/FVC was significantly improved from baseline value (3.1 ± 1.7% VS 1.4 ± 0.7%, p=0.021 and 5 ± 2.3% VS 1.4 ± 0.7% P=0.008). AR symptom-free days were significantly higher than the baseline value (17.6 ± 5.9 days VS 9.8 ± 5.8 days, P=0.04 and 22.4 ± 4.5 days VS 9.8 ± 5.8 days, P=0.04). Asthma control improved when compared to baseline.

CONCLUSIONS: We observed no increased incidence in systemic reactions from a RBU approach to SCIT refill vials compared to traditional refill approaches. While our sample size is small, our results did not appear to be affected by a history of asthma, previous systemic reactions or the content of SCIT. Larger studies are needed to better characterize this method.

Changes of Regulatory T cells after Allergen-specific Subcutaneous Immunotherapy, Rush Protocol, in Children

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RATIONALE: Allergen-specific immunotherapy is the only etiological treatment for allergic disorders. Previous studies proposed changing of regulatory T cells but few of them were studied in children. The study’s objective is to study changing of regulatory T cells (Tregs) in children during allergen-specific rush subcutaneous immunotherapy (RIT).

METHODS: Peripheral blood CD4+CD25+FOXP3+ Tregs were measured 4 times; before RIT, completed rush schedule, after reaching maintenance (MT) dose, and at 6 months of MT phase, by flow cytometry. Allergic rhinitis (AR) symptom-free day were recorded.

RESULTS: A total of 10 children were enrolled. The median age was 12 years (range: 6-15 years). 70% of them were male. Median time to reach the MT dose was 42 days. No significant changes of CD4+CD25+FOXP3+ Tregs at before and after completed rush schedule were observed. However, CD4+CD25+FOXP3+ Tregs at the MT and 6-month of MT phase were significantly increased from baseline value (3.1 ± 1.7% VS 1.4 ± 0.7%, p=0.021 and 5 ± 2.3% VS 1.4 ± 0.7% P=0.008). AR symptom-free days at after MT dose and 6-month of MT phase were significantly higher than the baseline value (17.6 ± 5.9 days VS 9.8 ± 5.8 days, P=0.04 and 22.4 ± 4.5 days VS 9.8 ± 5.8 days, P=0.04).

CONCLUSIONS: CD4+CD25+FOXP3+ Tregs may have a role in the clinical improvement after allergen specific rush subcutaneous immunotherapy in children.

Nasal allergen provocation tests in inner-city patients with perennial local allergic rhinitis

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RATIONALE: Dermatophagoides pteronyssinus is the main sensitizing aeroallergen in European patients with local allergic rhinitis (LAR). LAR-causative allergens in the USA are unknown. We planned to evaluate for LAR in an inner-city population by performing nasal allergen provocation tests (NAPT) to dust mite, mouse, and cockroach allergens.

METHODS: Patients with perennial rhinitis, negative skin testing and serum specific IgE to environmental allergens, and with confirmatory olfactory logy examination underwent NAPT at separate visits. Positive NAPT was defined as ≥25% increase in the Symptom Visual Acuity Scale (VAS) score or 20% decrease in nasal inspiratory peak flow (NIPF) compared to baseline.

RESULTS: Seventeen patients underwent 30 NAPT. The majority were female (82%), of Hispanic or African-American ethnicity (71%), with a mean age of 46 years (± 15.5) and no history of asthma or eczema. Overall, 8/17 (47%) patients had at least one positive NAPT. Out of 30 NAPT performed, 10 (33%) were positive: 7/17 (41%) to dust mites, 2/7 (29%) to mouse, 1/5 (20%) to cockroach. The mean increase in VAS score at 15 minutes after positive NAPT was 142% (± 192) compared with baseline, while negative challenges had a decrease in VAS score by 35% (± 31%, p<0.05). The mean drop in NIPF values at 15 minutes after a positive NAPT was -22.5% (± 20) compared with baseline, while negative NAPT had a mean increase in NIPF by 7% (± 17, p<0.05). Similar trends were found at one hour after the NAPT.

CONCLUSIONS: Dust mites, mouse, and cockroach allergens are responsible for symptoms in U.S. inner-city patients with LAR.
867 Exhalation Delivery Systems (EDS) Greatly Increase Topical Delivery to Target Sites for Chronic Rhinosinusitis (CRS) Compared to Nasal Sprays or Pressurized MDIs (pMDI)

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**Rationale:** Labyrinthine nasal passages, the narrow nasal valve and complex static and dynamic aerodynamics limit traditional intranasal steroids (INS) ability to effectively deliver medication to superior/posterior nasal regions. Exhalation delivery systems (EDS) exploit unique characteristics of nasal anatomy and aerodynamics to overcome these limitations and achieve superior/posterior drug delivery. We reviewed published human in vivo gamma-scintigraphy deposition data for conventional INS (C-INS; e.g., Flonase/Nasonex), HFA-based pMDI’s (e.g., QNAsL/Zetonna), and EDS systems for liquids and powders.

**Methods:** Four recent gamma-deposition studies comparing different technologies for nasal delivery of topical steroids were included: (1) Conventional INS sprays (Flonase and Nasonex) versus pMDI (QNAsL), (2) C-INS (Nasonex) versus pMDI (Zetonna), (3) C-INS versus EDS-liquid, (4) C-INS versus EDS-powder and EDS-liquid. Data on regional deposition and clearance was compared.

**Results:** Qualitative deposition differences were large, though variability in segmentation methods prevents quantitative comparisons. In all studies, C-INS consistently deposit primarily anteriorly (in the valve region) with clearance along the nasal floor and little deposition in superior/posterior regions. Both pMDIs (QNAsL/Zetonna) show a stationary “hotspot” in the non-ciliated vestibule, little delivery to superior/posterior regions, and minimal clearance. EDS (liquid or powder) produce less deposition in the valve area and broad deposition to superior/posterior segments with a different clearance pattern.

**Conclusions:** Human imaging data demonstrate poor drug deposition in superior/posterior sites with conventional nasal sprays, and greatly increased deposition throughout upper/posterior nasal passages with an EDS. In CRS, upper/posterior sites, including the middle and upper meatuses (ostiomeatal complex) where sphenes ventilate/drain and polyps originate, are the primary target for treatment.

868 High consistency in allergen composition of SQ house dust mite (HDM) tablet for sublingual immunotherapy (SLIT)

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**Rationale:** HDM immunotherapy products have traditionally been based on purified mite bodies or whole mite culture with little or no possibility for adjusting the allergen composition. For the SQ-HDM SLIT-tablet.

**Methods:** The two most important HDM species causing respiratory allergic disease, Dermatophagoides farinae and D. pteronyssinus, were grown separately under controlled conditions. After termination the cultures were separated using an automated mechanical sieve. The fraction containing the smallest particles predominantly contained faecal particles rich in group 1 major allergen, whereas an intermediate fraction contained predominantly mite bodies rich in group 2 major allergen. Fractions were mixed 1:1 based on \(\mu g\) major allergen forming one drug substance (DS) for each mite species. Quality control included total IgE binding capacity by Centaur assay, major allergen determination by radial immune diffusion; protein and antigen profile by SDS-PAGE and crossed immunolectrophoresis, respectively.

**Results:** Data were normalized relative to the mean, and the standard deviation of Derf1 in DS was 11.7% (14.7% and 17.7% in source material, SM) and for Derp2 12.3% (12.1% and 16.7% in SM), respectively. The corresponding figure for Derp1 was 9.0% (12.7% and 16.8% in SM) and for Derp2 9.9% (17.8% and 15.8% in SM).

The analyses of the DS showed that fractionation resulted in a consistent DS without compromising the complexity in the protein and antigen profiles.

**Conclusions:** Variation in allergen content was observed in the source material, but fractionation enabled a process resulting in a highly standardised composition of the SQ-HDM SLIT-tablet.

869 Efficacy of the SQ HDM SLIT-tablet on House Dust Mite Induced Allergic Conjunctivitis

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**Rationale:** Co-existence of allergic conjunctivitis is well recognized in patients with allergic rhinitis although the co-reporting frequency may be as low as 40%. Under-recognition and treatment of house dust mite (HDM)-induced allergic conjunctivitis may be due to the under-appreciation of eye symptoms in patients with HDM-induced allergic rhinitis. We present clinical data from 2 North American trials with the SQ HDM sublingual immunotherapy (SLIT)-tablet evaluating treatment effect on ocular symptoms.

**Methods:** Trial 1 included 124 adult subjects with HDM-induced allergic rhinitis/rhinoconjunctivitis (AR/C) randomized to SQ HDM SLIT-tablet (6 or 12 SQ-HDM) or placebo for 24 weeks. Efficacy was assessed during HDM exposure in an environmental exposure chamber. Trial 2 included 1,482 adult/adolescent subjects with HDM-induced AR/C randomized to SQ HDM SLIT-tablet (12 SQ-HDM) or placebo for up to 12 months. A conjunctivitis symptom score (range 0-6) was constructed based on subjects’ rating of 2 ocular symptoms (watery eyes and itchy eyes).

**Results:** In trial 1, 40% reported perennial allergic conjunctivitis. The average conjunctivitis symptom score during the HDM exposure session after 24 weeks of treatment showed a relative difference between both active treatment groups and placebo of -41% for 6 SQ-HDM and -68% for 12 SQ-HDM. In trial 2, 65% reported perennial allergic conjunctivitis. The average conjunctivitis daily symptom score obtained during the last 8 weeks of treatment showed a difference between treatment groups of -33.3% (95% CI, -47.1%, -18.5%).

**Conclusions:** The SQ HDM SLIT-tablet had a significant treatment effect on ocular symptoms in patients with HDM-induced AR/C.
870 Systemic Mastocytosis (SM) and Mast Cell Activation Syndrome (MCAS); How Do They Differ?

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RATIONALE: There are limited data outlining unbiased differences between symptoms and signs of patients with systemic mastocytosis (SM) and those with idiopathic mast cell activation syndrome (MCAS). We hypothesized that using a mathematical model will provide unbiased information differentiating between the two disorders.

METHODS: Electronic medical records (2003-2012) at our institution were retrospectively reviewed. Patients with bone marrow biopsy proven SM and those with MCAS, whose diagnosis fulfills the 2012 consensus diagnostic criteria, were included. Each chart was individually reviewed. Data from 45 SM and 44 MCAS patient charts regarding the presence or absence of specific symptoms were used for this analysis. Categorical data were transformed into format suitable for use in generation of the network map. An unsupervised bipartite network model of co-occurring symptoms and patients was generated using Gephi (v0.9). Conditional ordinal of SM or MCAS was applied after network model was generated allowing for unsupervised exploration of pattern of symptoms.

RESULTS: Visual inspection of the network revealed differential symptoms associations with SM and MCAS. Syncope, forgetfulness, weight loss, reflux disease, depression, anemia, lymphopenia, eosinophilia, osteopenia, bone fractures, adenaophy and organomegaly were associated with SM. In contrast, urticaria, angioidema, hypotension, dermatographia, bloating, belching, hiccups, rhinorrhea, sneezing and wheezing had a greater association with MCAS.

CONCLUSIONS: There is a clear difference in the presentation of patients with SM and those with MCAS. Unsupervised bipartite network analytical model provided some insight into those differences. This mathematical model will proof invaluable in the study of larger sample sizes.

871 Pediatric Mast Cell Activation Syndrome

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RATIONALE: Patients with mast cell activation syndrome (MCAS) have symptoms consistent with mast cell mediator release, elevation of mast cell (MC) mediator(s) and symptomatic resolution following medications that block MC mediator effect(s). MC mediator levels in pediatric mast cell disorders are unknown. Our hypothesis is that the pattern of mast cell mediator(s) elevation in pediatric MCAS resembles adult MCAS.

METHODS: A retrospective chart review of 104 children who underwent evaluation for MCAS (2015-2017) was performed. Levels of serum tryptase, urinary n-methyl-histamine (n-MH), 2,3-dinor1β-prostaglandin-F2α(PG-D2), and leukotriene E4 (LTE4) were reported.

RESULTS: Thirty-two patients had ≥1 elevated urinary MC mediators, based on established adult reference intervals. Of this total, 1 patient had systemic mastocytosis, 4 patients had cutaneous mastocytosis, and 6 (6%) patients had MCAS. The average age at diagnosis was 9±5 years. Serial testing in two patients with normal baseline revealed an elevated urine mast cell mediator level during an episode; one of those patients (with suspected familial hypertryptasemia) had PG-D2 elevation and the other LTE4 elevation. Five patients (83%) had at least 2 elevated MC mediators. More patients had an elevated PG-D2 (n=5) compared to serum tryptase (n=2). There was a greater percentage of patients that had elevated PG-D2 compared to an elevated serum tryptase for flushing (80 vs-50%), diarrhea (100 vs-100%), and abdominal pain (100 vs-50%). There was a greater percentage of patients with elevated tryptase compared PG-D2 for pruritus (60 vs-60%) and urticaria (50 vs-40%).

CONCLUSIONS: Urinary PG-D2 is the most frequently elevated product in our pediatric MCAS cohort, resembling adult MCAS. We recommend measurement of all MC mediators in patients with symptoms suggestive of MCAS.

872 Effect of Tofacitinib on IgE-Mediated Degranulation of LAD2 Human Mast Cells and PGD2 Production

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RATIONALE: Tofacitinib is an inhibitor of the enzymes IAK1 and IAK3, and can interfere with the JAK-STAT signaling pathway, transmission of extracellular information into the cell nucleus and DNA transcription. Tofacitinib is approved for use in rheumatoid arthritis and is being explored for use in psoriasis, colitis, atopic dermatitis and ankylosing spondylitis. Recently, tofacitinib was said to lead to symptomatic improvement in two patients diagnosed with mast cell activation syndrome. This prompted us to examine the effect of tofacitinib on the biologic reactivity of the human mast cell line, LAD2.

METHODS: In preliminary experiments, cultured LAD2 cells were incubated overnight with biotinylated human IgE. Cells were washed and then incubated with 1, 10, 100, 1000 nM tofacitinib for 1 hour. FcεRII crosslinking was performed with streptavidin, and degranulation monitored by the release of beta-hexosaminidase (β-Hex). LAD2 cells were also incubated with tofacitinib followed by stimulation with PMA, degranulation and release of β-Hex. The effect on PgD2 production was measured 30 minutes following IgE mediated mast cell activation.

RESULTS: In LAD2 cells, β-Hex release following FcεRII crosslinking or PMA stimulation remained consistently high (50-60%) in the presence of tofacitinib with no dose-response reduction in degranulation. Similarly, tofacitinib had no effect on PgD2 release.

CONCLUSIONS: The JAK kinase inhibitor tofacitinib had no effect on LAD2 human mast cell degranulation or PgD2 production. Additional experiments are underway including an examination of the effects of tofacitinib on LAD2 cytokine production, adhesion and proliferation.

873 Development of a Biomarker of Pre-existing IgE Crosslinking on Human Basophils

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RATIONALE: Clinically, the effect of IgE-mediated drug allergy desensitization is considered transient. In vitro, basophils and mast desensitization of an IgE-mediated reaction may also be transient. Details on desensitization signaling and its kinetics are lacking. Aggregation leading to desensitization induces an alteration in the basophil response to PMA (a non-physiological phorbol ester secretagogue). Based on early results obtained with non-releasing basophils, this alteration in the PMA-response was not expected to be sensitive to syk activity. We tested this expectation using selective inhibitors of syk, btk, PI3K.

METHODS: Releasers and non-releasers basophils were desensitized with anti-IgE antibody for 90 min in the absence of extracellular calcium. After desensitization, basophils were challenged with a PMA at different concentrations; ± syk, ± btk, or ± PI3K inhibitors were included in the desensitization and re-challenge phases.

RESULTS: In the absence of the inhibitors, the EC50 for PMA-induced release shifted leftward by 10.7-fold after desensitization. In the presence of the inhibitors, the EC50 shifted only by 1.4-, 1.3-, 1.3-fold (syk, btk, PI3K inhibitors, respectively). An inspection of results from different basophil phenotypes showed that the amount of curve shift was correlated with the maximum response of basophils to anti-IgE Ab.

CONCLUSIONS: These results suggest that the EC50 for PMA-induced histamine release shift characteristic is dependent on syk activity and related to syk expression in different basophil phenotypes. The signals that shift the response to PMA persist longer than what would be expected from the kinetics of histamine release. This effect may be used to detect cell exposure to allergen during clinical desensitization.
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**Etiologies of Severe Hypereosinophilia Evaluated in Children Hospitalized at a Tertiary Care Center**

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**Rationale:** Hypereosinophilia is defined as a peripheral blood absolute eosinophil count (AEC) of >0.5x10^9/L, while severe hypereosinophilia is defined as an AEC of >1.5x10^9/L. Much has been published on hypereosinophilia in the adult literature; however, there is limited literature on pediatric patients with hypereosinophilia (especially severe eosinophilia) or hypereosinophilic syndrome (HES). The goal of this study was to characterize children with severe hypereosinophilia hospitalized in a tertiary care center.

**Methods:** We reviewed the charts of allergy/immunology consults performed from January 2013-April 2016 at Saint Louis Children’s Hospital. Children were included in this study if their AEC was >1.5x10^9 at the time of the allergy/immunology consult. Data was collected on demographics, comorbidities, treatment, laboratory data, and clinical outcomes. Patients were sorted into diagnostic groups that included: overlap hypereosinophilic syndrome, allergic/atopy, hypereosinophilic syndrome myeloproliferative subtype, immunodeficiency, and unknown.

**Results:** We reviewed that chart of 289 inpatient consults and 13 met our inclusion criteria. Mean age at presentation was 19.5 months (range 1-49 months). Mean peak peripheral blood AEC was 5.5x10^9/L (range 1800-12,524x10^9/L). Four patients were found to have atopic driven eosinophilia, three with an underlying primary immunodeficiency, two with HES myeloproliferative variant, one with overlap HES. Four patients had an unknown etiology. Mortality in our cohort was 23%.

**Conclusions:** Severe hypereosinophilia was the reason for 4.5% of inpatient Allergy/Immunology consults. A variety of reasons caused underlying eosinophilia. As many life threatening conditions were identified, prompt recognition of the underlying pathology is critical for proper treatment.

**Blood Eosinophil Beta-1-Integrin Activation Correlates with Eosinophilic Esophagitis (EoE) Disease Activity**

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**Rationale:** Monitoring of EoE would benefit from biomarkers to replace invasive endoscopy and pathology. We hypothesized that beta1-integrin activation, which enables arrest of eosinophils in inflamed vessels and predicts disease activity in non-severe asthma, correlates with eosinophilic inflammation and disease activity in EoE.

**Methods:** Ten EoE patients were recruited following two-month proton-pump-inhibitor therapy and diagnostic endoscopy, with visit 1 (V1) within one week of endoscopy. Patients received standard of care EoE treatment (swallowed steroid or food elimination) followed by visit 2 and repeat endoscopy (V2) two months later. Beta1-integrin activation (mAb N29 intensity) and 15 other eosinophil-surface markers were assayed by whole blood flow cytometry. The EoE Histological Scoring System (EoEHSS), including an eosinophilic inflammation subscore of 0 to 3, was used.

**Results:** N29 correlated with eosinophilic inflammation subscore (rS=Spearman coefficient=-0.91, p=0.001) or EoEHSS total score (rS=-0.70, p = 0.03) at V2 but not V1. Further, the change in N29 from V1 to V2 correlated with inflammation subscore change (rS=-0.81, p=0.007). The five patients for whom N29 was increased the most at V2 had mean subscore of 1.6±0.9 after a change of -1.0±0.7, whereas the five patients for whom N29 increased less or decreased (a mean decrease) the subscore was 0.0±0.0 after a change of -2.8±0.4 (p=0.008 for the subscore and 0.02 for change).

**Conclusions:** In this pilot study, persistent beta1-integrin activation on circulating eosinophils after EoE treatment was associated with residual esophageal eosinophilic inflammation, whereas a decrease in beta1-integrin activation was associated with resolution of eosinophilic inflammation.
877 Soluble Siglec-8 Levels Are Detectable In Subjects With Myeloid Variant Hypereosinophilic Syndromes, But Not In Those With D816V KIT+ Systemic Mastocytosis

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RATIONALE: Siglec-8 is expressed on eosinophils, basophils and mast cells. Antibodies targeting Siglec-8 are in development for the treatment of myeloid disorders, including systemic mastocytosis (SM). Since shedding of soluble Siglec-8 (sSiglec-8) could interfere with the efficacy of anti-Siglec-8 therapy, sSiglec-8 levels were measured in the serum of patients with a variety of myeloid disorders.

METHODS: Subjects with myeloid variant hypereosinophilic syndrome (MHES), D816V KIT+ systemic mastocytosis (SM) and normal controls (ND) were evaluated. Clinical and laboratory data were collected for each patient. Serum sSiglec-8 levels were measured by sandwich ELISA (limits of detection: 0.5/1 (duplicate/singlicate) to 60 ng/mL).

RESULTS: sSiglec-8 levels were detectable in 6/10 ND and 14/19 MHES subjects (9/11 FIP1L1-PDGFRα-positive, 3/3 idiopathic MHES, 2/2 V617F JAK2-positive, 0/2 exon 13 JAK2 mutation-positive and 0/1 PDGFRB mutation-positive). Mean levels did not differ between the MHES and ND groups (GM 1.27 and 1.86 ng/mL, respectively) and did not correlate with AEC. sSiglec-8 levels in the FIP1L1-PDGFRα-positive subjects decreased significantly in response to imatinib (from 2.41 to 0.93; Wilcoxon test, P<0.05, n=8). Surprisingly, sSiglec-8 was undetectable in all 22 subjects with D816V KIT-positive SM, including 4 D816V KIT-positive SM-eo patients with AEC>1900/mL. SM serum did not inhibit detection of recombinant sSiglec-8 in vitro.

CONCLUSIONS: Despite expression of Siglec-8 on mast cells and eosinophils in subjects with SM, sSiglec-8 levels were not measurable in these patients and are unlikely to interfere with the efficacy of anti-Siglec-8 antibodies. Whether the D816V KIT mutation prevents receptor shedding remains to be elucidated.

878 Myeloproliferative Hypereosinophilic Syndrome: Retrospective Analysis of Cytogenetic and Molecular Features

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RATIONALE: The myeloid subtype of hypereosinophilic syndrome (MHES) is associated with more aggressive disease, steroid unresponsiveness, and poor prognosis. Detection of the underlying molecular abnormality, such as FIP1L1-PDGFRα, is essential to determine an appropriate treatment approach.

METHODS: Forty-five subjects meeting clinical criteria for MHES were identified from a cohort of 485 subjects enrolled on a natural history study of eosinophilia from April 4, 1994 to June 21, 2017. All subjects were tested for FIP1L1-PDGFRα and BCR-ABL1 by reverse transcription nested PCR (RT-PCR), and 41/45 underwent bone marrow biopsy with cytogenetics and testing for D816V KIT. Results of prior bone marrow examinations and genetic mutation testing were extracted from outside records.

RESULTS: Prior evaluation for mutations associated with MHES was highly variable and included testing for abnormalities in PDGFRα, JAK2, PDGFRB, and FGFR1 in 53%, 31%, 29% and 20% of subjects, respectively. Among those tested, 38% were positive for FIP1L1-PDGFRα and 21% for JAK2 mutations. Translocations involving PDGFRB or FGFR1 were identified in one subject each. Of significance, 5 subjects (33%) who had tested negative for FIP1L1-PDGFRα by fluorescence in situ hybridization (FISH) were later found to be FIP1L1-PDGFRα-positive by RT-PCR. These initial false negative results led to delays in initiating imatinib, the treatment of choice for this subtype of MHES.

CONCLUSIONS: With the increasing availability of targeted therapies, systematic evaluation for genetic mutations is essential in evaluating patients with MHES. If FISH testing for FIP1L1-PDGFRα is negative and no other etiology is found, RT-PCR and/or empiric imatinib should be considered.

879 Pediatric hypereosinophilia: characteristics, clinical manifestations and diagnoses

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RATIONALE: Peripheral blood eosinophilia is associated with a variety of disorders, including parasitic infections and allergic and autoimmune diseases. The range of differential diagnoses is broad, and data on pediatric hypereosinophilia are limited.

METHODS: A retrospective chart review was completed and included all patients <18 years of age presenting to our institution between January 1, 2008 and May 31, 2017 with absolute eosinophil counts (AEC) >1,500 eosinophils/microliter on two occasions at least four weeks apart. We analyzed demographic characteristics, clinical manifestations, laboratory values, treatment course, and diagnoses.

RESULTS: The median age at presentation was 4.9 years (range 0.1–17.5, n = 203), and the median peak AEC was 3090 (range 1560–55,740 eosinophils/microliter). Notably, 17% (34/203) of the subjects were under the age of 1 year. There were slightly more males (115/203), and the median age at presentation for males was lower (3.2 [range 0.2 – 17.5] vs. 8.2 [range 0.1–17.4]). However, there were no differences in median peak AEC between males and females. There were six deaths during the study period. There was a seasonality to the incidence of hypereosinophilia, with the highest incidence in the summer (June–August, 58/192) and fall (September–November, 53/192) and lowest incidence in the winter (December–February, 34/192).

CONCLUSIONS: Hypereosinophilia has an incidence of around 20 individuals per year meeting diagnostic criteria at our institution, with the largest portion of individuals being under the age of 1 year. The highest incidence occurs during the summer and fall seasons, highlighting the affect of environmental exposures on pediatric hypereosinophilia.
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880 Cardiac Manifestations of Idiopathic Hypereosinophilic Syndrome

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Rationale: Hypereosinophilic syndromes (HES) have heterogeneous clinical presentations and can cause significant morbidity, including cardiac complications and thromboembolic events. Characterizing cardiac manifestations in HES will aid the evaluation and management of these patients.

Methods: A retrospective review of electronic medical records (January 2002 to June 2017) was performed for adult patients with a diagnosis of idiopathic HES. Each chart review detailed symptoms at clinical presentation, eosinophil counts, troponin levels, and echocardiographic findings. The study was approved by the institutional review board.

Results: Twenty-one patients were identified for review, consisting of 10 males and 11 females. Symptom duration at time of initial presentation ranged from 1 to 156 months (average 29.3 months). Eosinophil counts ranged from 1090 to 62,160 eosinophils per microliter at the time of initial presentation. Thirteen (62%) patients presented with cardiovascular symptoms, including chest pain, dyspnea on exertion, or lower extremity edema. Eight (38%) patients had elevated troponin levels and two additional patients had elevated LDH with no troponin levels drawn. Eleven (52%) patients demonstrated valve abnormalities on echocardiogram including one patient with thrombus formation in the left ventricular endocardium. Four (19%) patients had ejection fractions less than 45%. Maintenance therapies included the following: 7 patients (33%) prednisone and hydroxyurea, 5 patients (24%) prednisone and interferon, 5 patients (24%) prednisone only, and 4 patients (19%) mepolizumab.

Conclusions: Cardiac symptoms and abnormalities are frequently seen with idiopathic HES. Prompt, comprehensive cardiovascular evaluation is essential to reduce HES-associated cardiac morbidities.

881 Mepolizumab as a successful steroid-sparing agent in two patients with idiopathic hypereosinophilic syndrome (iHES)

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Rationale: Limited steroid sparing therapies are available to treat idiopathic Hypereosinophilic Syndrome (HES). We present two patients with iHES who have done well after starting mepolizumab.

Methods: This is a retrospective review of two patients with idiopathic HES (both negative for FIP1L1-PDGFRα and workup for other forms of HES) who responded to mepolizumab.

Results: Patient #1: 57 yo female with iHES with urticarial rash and cardiac involvement complicated by troponin leak, cardiogenic shock, cardioembolic CVA from mural thrombus initially presented with 5,990 eosinophils/mm^3. She refused hydroxyurea and remained on steroids for about 2.5 years with frequent recurrence of skin involvement when steroid dose was reduced below 10 mg. After significant weight gain, LFTs became abnormal and fatty liver disease was diagnosed. Off-label coverage of mepolizumab 100 mg q 4 weeks was approved. Since starting mepolizumab 6 months ago, her eosinophil count decreased to zero and so far, prednisone has been weaned to 5 mg daily with normalization of LFTs, maintenance of disease control and desired 22 pound weight loss.

Patient #2: 45 yo female with iHES with pruritic skin involvement and angioedema who presented with 1,746 eosinophils/mm^3. She was dependent on prednisone 9 mg daily for about 2 years prior to starting mepolizumab. Since starting mepolizumab 16 months ago, her eosinophil counts have been zero and she successfully tapered off prednisone 12 months ago without any recurrence of her skin involvement and some desired loss of weight.

Conclusions: Consistent with prior published work, mepolizumab may be an effective steroid-sparing agent for some patients with iHES.

882 Role of anti-inflammatory cytokine IL-35 in the effects of sublingual immunotherapy

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Rationale: The immunologic tolerant state following allergen immunotherapy is associated with the induction of distinct phenotypes of regulatory T-cells or B-cells. IL-35 was recently identified as an anti-inflammatory cytokine. However, IL-35 bioactivity is not fully understood in human. We investigated the role of IL-35 production in the effects of sublingual immunotherapy (SIT).

Methods: The bioactivity of human recombinant IL-35 was examined using PBMC from patients with Japanese cedar pollinosis (JCP). A prospective study was undertaken to evaluate the effects of SIT on IL-35 production from T cells and B cells.

Results: Human recombinant IL-35 suppressed Japanese cedar pollen-induced production of IL-5, INF-g, and IL-17, but not IL-10 from PBMC of JCP patients. Human recombinant IL-35 directly suppressed IL-5 and IL-13 production from memory CD4^+ T-cells and from cocultured DCs/CD4^+ T-cells. The percentage of IL-35 positive CD4^+ T-cells and IL-35 positive B-cells increased after one year treatment of SLIT. IL-35 protein from PBMC of JCP patients increased after SIT. Symptom medication score and serum IL-35 concentration of JCP patients in the peak season showed opposite correlation after SLIT.

Conclusions: IL-35 plays an important role in the suppression of Th2 type inflammation, and increased production of IL-35 from T cells and B cells after SLIT may influence effector cells in allergic rhinitis. Augmentation of constitutive IL-35 production from immune system is a potential therapeutic approach for allergic disorders.

883 Effect of adipose-derived stem cell and non-methylated CpG-ODN on Peripheral blood CD4^+CD25^+ regulatory T cell in young mice of food allergy

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Rationale: To observe the expression level of peripheral blood CD4^+CD25^+regulatory T cell in young mice of food allergy treated with adipose-derived stem cell and non-methylated CpG-ODN, and to explore the immune intervention effect.

Methods: Forty female BALB/c mice (2-3 weeks old) were randomly divided into control, allergic model, ADSC and CpG-ODN treatment groups (n = 10 each). A young mouse model of food allergy was established by OVA sensitization. The mice in ADSC group were intraperitoneally injected with 1×10^6 ADSC on days 15 and 30. The mice in CpG-ODN treatment group were intraperitoneally injected with CpG-ODN solution 1 hour before every OVA provocation sensitization. The OVA-IgE of peripheral blood of all mice were detected by ELISA. The levels of CD4^+CD25^+regulatory T cell in peripheral blood of all mice were detected by flow cytometry.

Results: The expression levels of OVA-IgE were lower in the ADSC group and the CpG-ODN group than in allergic model (both p < 0.05). They were higher in ADSC group and CpG-ODN group than in allergic model (p < 0.05).

Conclusions: ADSC and non-methylated CpG-ODN can increase the expression levels of CD4^+CD25^+regulatory T cell in peripheral blood and decrease the content of specific IgE (OVA-IgE). They could play a certain role in inducing immune tolerance in food allergy.
CONCLUSIONS: More than 10 percent of laboratory animal researchers experienced LAA or PA, and sensitized to animal allergens. They had contact with less variety of animals in their lives compared to those without animal allergy.

RESULTS: A total of 135 out of 618 attendants were enrolled. Among them, seventy three (11.8% of attendants) complained of allergic symptom while they contacted with laboratory or pet animals (29 with mouse, 15 with rat, 11 with cat, 8 with dog, 7 with rabbit, 1 with hamster, 1 with pig, and 1 with hedgehog). In these subjects with animal allergy, allergic conjunctivitis was more prevalent (17.8% vs. 1.6%, P<0.001), and sensitization to animal allergen including mouse, rat, cat, guinea pig, hamster, and horse was more frequent (P<0.05 for each allergen) than in those without animal allergy. Meanwhile, they contacted less diverse kinds of animals (3.6 ± 2.8 species vs. 4.6 ± 3.1 species, P=0.051) in their lives, especially in terms of dog, hamster, chicken, monkey and sheep (P <0.05 for each animal). In them, symptoms of rhinitis were most frequently complained of (76.7%), followed by those of skin (42.5%), conjunctivitis (41.1%), and lower respiratory tract (19.2%).

CONCLUSIONS: More than 10 percent of laboratory animal researchers experienced LAA or PA, and sensitized to animal allergens. They had contact with less variety of animals in their lives compared to those without animal allergy.

Epigenome-wide Association Study of the Effect of Maternal Age on Offspring DNA Methylation

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RATIONALE: Maternal age at birth has been associated with increased incidence of asthma, food allergy, and diabetes in children and young adults. The biological mechanisms underlying these associations remain elusive. One mechanism may be epigenetics.

METHODS: In peripheral blood samples from the Isle of Wight (IoW) Birth Cohort (10 N=138) and 18 (N=367) years) and cord-blood samples from 200 subjects from the IoW 3rd Generation Cohort, methylation was assessed using Illumina HumanMethylation450 and EPIC Beadchips and analyzed with linear models. Model 1 treated maternal age at birth as the continuous independent variable and offspring methylation as the dependent variable. Model 2 used maternal age at birth as the continuous independent variable and offspring methylation as the dependent variable. Models were adjusted for gender, maternal smoking, parity, maternal socio-economic status, and offspring smoking for 18-year data.

RESULTS: Model 1: 8, 137, and 10 cytosine-phosphate-guanine sites (CpGs) in cord blood, 10, and 18 years, respectively, were statistically significant (FDR = 0.05); Model 2: 1, 67, and 12 CpGs for cord blood, 10, and 18, respectively, were associated with maternal age. In each model, the genes corresponding to the top 100 CpGs ranked by p-value were examined with pathway analysis using Topgene. In cord blood, enrichment of genes relating to the Wnt signalling pathway was identified.

CONCLUSIONS: Methylation at birth of the Wnt signalling pathway, which regulates lung development and is associated with airway inflammation and remodelling in asthma, is associated with maternal age. This represents a possible mechanistic link between maternal age and risk of allergic disease.

Dysbiosis of intestinal microbiota increases mortality to a respiratory viral infection through elevated production of IFNγ by innate lymphoid cells

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RATIONALE: Using a normally non-lethal dose of Sendai virus (SeV), we demonstrated that alteration of the intestinal microbiota led to a marked and significant increase in mortality. The mechanism of this increased mortality was due to dysregulation of IFNγ production in the lung, although the cellular source responsible for the increased IFNγ production was unclear. One source of IFNγ is innate lymphoid cells (ILCs), which unlike T-helper (Th) cells, lack surface antigen receptors. This study investigated the role of lung ILCs in increased IFNγ production during a SeV infection and intestinal microbiota dysbiosis.

METHODS: C57BL/6 mice were given reverse osmosis drinking water with or without the non-absorbable antibiotic, streptomycin (0.5 g/250 ml). After 2 weeks mice were intranasally inoculated with 30 μl of 2 x 10^7 plaque forming units of SeV. On day 8 post infection lung cells were harvested. ILC’s were identified by flow cytometry as being Lin - CD4+ lymphocytes, with intracellular staining used to determine IFNγ levels. Streptomycin treatment (4.3+/-0.4%, p=0.3, n=5). Similarly, the absolute numbers of ILCs was not affected by antibiotic treatment (p=0.2). However, the frequency of IFNγ producing ILCs increased from 0.90+/-0.4% to 2.85+/-0.6% with streptomycin treatment (p=0.04, n=4).

CONCLUSIONS: ILCs, while being a small population, may represent the cell type that is responsible for increased pulmonary IFNγ during a respiratory viral infection after disruption of gastrointestinal microbiota.
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**887 Nasal Colonization with S. aureus is Associated with Allergic Sensitization in Children with Chronic Rhinitis**

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**RATIONALE:** There is a clear association between atopic dermatitis and nasal colonization with *S. aureus*. Some evidence suggests an increased rate of nasal colonization with *S. aureus* in patients with allergic rhinitis, but results are inconsistent. We hypothesized that nasal colonization with *S. aureus* would be associated with allergic rhinitis.

**METHODS:** We conducted a cross-sectional study of 61 children with allergist-diagnosed chronic rhinitis, ages 4-17 years old, who were recruited from the Columbia Pediatric Allergy Clinic. Skin prick testing or serum specific IgE testing identified 51 patients with environmental sensitization and ten subjects without sensitization. Anterior nasal swabs were collected to detect *S. aureus* using chromagar plates and latex agglutination. Methicillin and mupirocin resistance were assessed using cefoxitin disks and E-test strips, respectively. Subjects were screened for atopic comorbidities including asthma, atopic dermatitis and food allergy. Chi square, and when appropriate, Fisher’s exact tests, were used to test for differences in frequencies between groups.

**RESULTS:** Sensitized subjects (n=51) showed significantly greater *S. aureus* carriage rates (P<0.01) of 63% (n=32) compared to 20% (2 of 10) of participants without evidence of sensitization. There was no association between the presence of atopic comorbidities and nasal colonization (P>0.05). Ninety-three percent of *S. aureus* samples were methicillin-sensitive and 100% were mupirocin-sensitive (MIC 0.25).

**CONCLUSIONS:** There was an association between nasal colonization with *S. aureus*, independent of other atopic comorbidities. Longitudinal studies are needed to assess if sensitization precedes colonization or if nasal colonization with *S. aureus* predisposes to sensitization.

**888 Withdrawn**

**889 Different clinical feature among asthmatics according to airway microbiome clusters**

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890 Allergic diseases in childhood: What allergic sensitization can teach us?

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RATIONAL: It has been assumed that the presence of some allergic sensitization might behave as a marker of allergy persistence. In addition, the presence of two or more allergic diseases in the same patient, called multimorbidity, may also work as a predictor of severity. The objective of this study is to describe the profile of allergic sensitization among atopic patients followed up in different pediatric allergy services in Brazil and its relation to severity of allergic disease.

METHODS: Cross-sectional study with evaluation of medical history and measurement of specific serum IgE (sIgE) for whole allergens and their prevalent components in participants between the ages of six months to eighteen years old.

RESULTS: 470 participants, 224 girls (47.7%), were divided into groups: 1 [rhinitis and/or asthma; n=111, higher prevalence of sensitization (HPS) to Dermatophagoides pteronyssinus (Dp) –87.4%; 2 (atopic dermatitis; n=99, HPS to Dp-90.9%); 3 [food allergy, n=95, HPS to cow’s milk (CM)-84.2%]; 4 (wheezing infants, n=80, HPS to Dp-32.5%). The most prevalent components were Der p 1 and 2. The presence of food allergy (OR=2.36, 95%CI=1.15-4.83), atopic dermatitis (OR=2.12, 95%CI=1.03-4.33) or multimorbidity (OR=1.68, 95%CI=1.03-2.74) were associated with more severe allergic disease. Regarding protection, mono-sensitization (OR=0.08, 95%CI=0.01-0.61) was the most expressive factor.

CONCLUSIONS: The prevalence of allergic sensitization to mites was high in all groups of patients in our study. The presence of different types of allergic diseases simultaneously as well as the frequency of sensitization (OR=2.36, 95%CI=1.15-4.83) were associated with more severe allergic disease. However, mono-sensitization (OR=0.08, 95%CI=0.01-0.61) was the most expressive factor.

891 Exposure to Peanut Flour through Disturbed Skin Initiates Peanut Allergy via the T Follicular Helper T (Thf) Cell-Dependent Pathway in Mice

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RATIONAL: The mechanisms involved in development of peanut allergy are not fully understood. The goal of this project was to investigate the role of skin exposure to peanut products and immunological mechanisms involved in initiation of peanut allergy.

METHODS: Abdominal skin of naïve BALB/c mice was stripped with an adhesive tape. Mice were then exposed to peanut by painting the skin with peanut flour (PN-f) for 4 weeks. The plasma levels of peanut-specific IgE antibody were measured by ELISA. Mice were challenged with intraperitoneal (i.p.) injection of peanut extract, and clinical symptoms were monitored for 60 minutes. CD4+ T cells in draining lymph nodes (dLNs) were analyzed by FACS. A genetic model was used to dissect the roles for Thf cells.

RESULTS: Mice that were exposed to PN-f through the disturbed skin produced PN-specific IgE antibody; no exogenous adjuvants were required. When sensitized mice were challenged by i.p. injection of PN extract, they showed clinical signs of acute systemic anaphylaxis, such as decreased core body temperature. Increased numbers of total Thf cells (CD4+CXCR5+) and mature Thf cells (CD4+CXCR5+PD-1+) were observed in dLN of PN-f-exposed mice. Furthermore, the mice deficient in Thf cells (i.e. CXCR5-/-/CD4-Cre) produced significantly less peanut-specific IgE antibody, and they were protected from developing acute anaphylaxis.

CONCLUSIONS: Cutaneous exposure through the disturbed skin in mice initiates peanut allergy that is analogous to human peanut allergy. Thf cells likely play a pivotal role in development of allergen-specific IgE antibodies and clinical outcomes in peanut allergy.

892 Administration of the CXCR2 inhibitor reparixin in sensitized mice inhibits allergen-challenge induced allergic inflammation

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RATIONAL: Inhibiting allergenic extract-induced neutrophil recruitment in mice by administration of SB225002 CXCR2 inhibitor attenuates allergic sensitization. Unexpectedly, even though the CXCR2 inhibitor AZD5069 was safe in humans and reduced the level of neutrophils in sputum and blood, its administration failed to improve asthma control in subjects with severe uncontrolled asthma. We hypothesized that the role of airway neutrophils may be different in uncontrolled asthma vs. allergen-induced neutrophil recruitment. To test this hypothesis, here we examined the role of administration of reparixin, a human-safe CXCR2 inhibitor, in inhibiting allergic inflammation in naïve and allergen-sensitized mice.

METHODS: Wild-type naïve mice were challenged once with cat dander extract (CDE) to stimulate innate inflammation, or five multiple times to sensitize the mice, prior to a final CDE challenge to elicit allergic inflammation. Reparixin was administered intraperitoneally in a subset of each of these models prior to CDE challenge, and innate and allergic lung inflammation was quantified.

RESULTS: Administration of reparixin in the single challenge model suppressed CDE-induced innate neutrophil recruitment into the lungs. Furthermore, administration of reparixin in the multiple challenge model inhibited CDE-induced allergic inflammation. Reparixin inhibited levels of eosinophil numbers, IL-4, IL-13, IL-33, and TSLP in BALF, levels of mucin in airway epithelial cells, lung mRNA expression of Th2-inflammation-associated genes Periostin and Mac1, and serum levels of total IgE and CDE specific IgE.

CONCLUSIONS: Inhibiting CXCR2 suppresses allergen-induced innate and allergic airway inflammation in mice. CXCR2 may be a novel target for attenuating allergen-induced allergic airway inflammation in humans.
Relevance of N-terminus amino acids in CCL28 mediated murine airway hyper-reactivity

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RATIONALE: CCL28 is a chemokine associated with human asthma; we have demonstrated it is critical for development of post-viral asthma in a mouse model. Interestingly, administration of CCL28 alone (without a viral infection) is sufficient to drive development of airway hyper-reactivity (AHR). In CC chemokines, the N terminus is thought to interact with the chemokine receptor. We undertook this study to examine the importance of N terminal amino acids in CCL28’s ability to drive AHR.

METHODS: C57BL/6 mice were inoculated intranasally daily for 3 days with 3, 1, 0.3, and 0.1 μg/ml of CCL28 or a CCL28 variant lacking the first 3 amino acids of CCL28 (del3-CCL28). On day 4 a non-invasive, two-chamber plethysmography system was used to measure AHR to increasing doses of methacholine. Unfolded versions of the proteins were used as negative controls.

RESULTS: 3 μg/ml CCL28 significantly increased sRaw and decreased sGaw (p<0.001) versus unfolded CCL28 (for both; n≥6); however, no other doses led to increased AHR. Removing the first 3 amino acids (del3-CCL28) led to marked increase in potency, with significantly increased sRaw (p=0.001) versus unfolded del3-CCL28; n≥4) and reduced sGaw (p=0.011) at only the 0.3 μg/ml dose.

CONCLUSIONS: CCL28 drives AHR in the absence of a viral infection. The first 3 N terminal amino acids decrease potency of this effect by a log-fold, suggesting these amino acids may interfere with the most efficient binding of CCL28 to its receptor. This effect could be utilized to develop novel therapeutics for asthma.

Studies on the allergens of peach pollen in an area of high exposure to peach trees cultivars

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RATIONALE: Peach tree pollen has been identified as relevant in areas of peach tree cultivation. After olive and grass, it is the third one inducing sensitization in these areas. Our aim was to study if peach tree pollen contain other allergens that can induce sensitization in addition to Pru p 3.

METHODS: Skin tests with peach pollen extracts were made in subjects with seasonal symptoms during the period of production of this pollen in an area of high exposure. Sera from positive skin tests cases were obtained and SDS-PAGE and immublotting analysis was made.

RESULTS: Using pool of sera of mono-sensitized cases negative to Pru p 3 and other pollens several bands were identified that corresponded to 45, 25 and 15 kD. We named the 15D band as Pru p X. This protein and Pru p 3 in 110 cases skin test positive to peach pollen. The 40% were prick positive to Pru p X and the 35% to Pru p 3. The 12% were positive to both and in the remaining cases with skin test positive to peach pollen both were negative.

CONCLUSIONS: Peach pollen has several allergens that can be involved in the induction of sensitisation and allergy in highly exposed populations. From these we identify the Pru p X that has not been previously recognized. Because subjects were also positive to Pru p 3, the respiratory tract can be a pathway of sensitisation to this pan-allergen. The clinical relevance of these findings is under evaluation.
Celastrol Alleviates Airway Hyperresponsiveness by Downregulating Th17 in Obese Asthmatic Mice

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RATIONALE: Obese asthma subjects demonstrate more severe airway hyperresponsiveness (AHR) than non-obese asthma patients. The former is also steroid-resistant, partially due to inflammation induced by Th17 cells. Celastrol was reported to inhibit the function of Th17 cells. We thought to explore the effect of Celastrol on AHR of obese asthmatic mice and identify its underlying mechanism.

METHODS: Obese, ovalbumin-induced asthma (DIO-OVA) model was established by feeding mice with high fat diet for 16 weeks and sensitizing intraperitoneally with OVA on days 1 and 13 starting from week 12, followed by aerosol OVA challenge for 7 consecutive days on week 16. Celastrol-treated-DIO-OVA mice received oral Celastrol (10mg/kg) 30 min before each challenge. Sham control group received normal diet and normal saline in sensitization and challenge phases. Flow cytometry was used to examine the splenic Th17 cell population. Serum IL-17 levels of Celastrol-treated and control groups were measured by ELISA.

RESULTS: Comparing to control, Celastrol-treated DIO-OVA mice showed significant reduction of Rn (0.41 ± 0.04 vs 0.66 ± 0.10 cmH2O/ml/s, P<0.01). A correspondent increase of PC20 of MCh was noticed. Moreover, Celastrol treatment led to a significant decrease of splenic Th17 cell frequency (66.24 ± 6.6 vs 13.55 ± 8.21 vs 145.19 ± 76.1 pg/ml, P<0.01).

CONCLUSIONS: Celastrol reduces airway hyperresponsiveness of obese, OVA-induced asthma mice. This potential therapeutic effect is possibly due to the inhibition of Th17 cells number and their Th17 production.

A Jagged1-Notch4 interaction between Alveolar Macrophages and Allergen-Specific T cells Mediates Airway Inflammation by Ultratfine Particles

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RATIONALE: Exposure to traffic-related particulate matter (PM) promotes asthma and allergic diseases. However, the precise cellular and molecular mechanisms by which PM exposure acts to mediate these effects remains unclear. We sought to elucidate the cellular targets and signal pathways critical for the augmentation of allergic airway inflammation induced by ambient ultrafine particles (UFP).

METHODS: We employed in vitro cell culture assays using lung-derived antigen presenting cells and allergen-specific T cells, and in vivo mouse models of allergic airway inflammation that employed myeloid lineage-specific gene deletions, cellular reconstitution approaches and antibody inhibition studies.

RESULTS: We identified lung alveolar macrophage (AM) as the key cellular target of UFP in promoting airway inflammation. Aryl hydrocarbon receptor (AhR)-dependent induction of Jagged 1 (Jag1) expression in AM was necessary and sufficient for the augmentation of allergic airway inflammation by UFP. Furthermore, UFP promoted both Th2 and Th17 cell differentiation of allergen-specific T cells in a Jag1- and Notch4-dependent manner. Moreover, treatment of mice with an anti-Notch 4 antibody abrogated the exacerbation of allergic airway inflammation induced by UFP.

CONCLUSIONS: UFP exacerbate allergic airway inflammation by promoting Jag1-Notch4-dependent interaction between Alveolar Macrophages and Allergen-Specific T cells, leading to augmented Th cell differentiation.

Asthma associated transcriptomic profiles differ by tissue

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RATIONALE: Gene-expression patterns in asthma show remarkable diversity across tissues. However, in most studies, differentially expressed genes across various tissues are analyzed together in an average profile framework. We hypothesize that there are tissue-specific as well as tissue-shared differentially expressed genes critical for asthma development. We expect that tissue-shared expression patterns could serve as a surrogate (e.g. nasal) biomarker for less accessible tissues (e.g. bronchial).

METHODS: We analyzed fourteen gene expression datasets from NCBI GEO database in relation to asthma across various tissues (e.g. blood, bronchial fibroblasts, alveolar macrophages, nasal epithelium, etc.). Differentially expressed asthma genes (DEAGs) for individual tissue were identified following a rank-based approach. Unique /shared DEAGs and their fold-change values were used to identify relevant pathways.

RESULTS: Little overlap in gene expression patterns across tissues were observed at the gene level compared to pathway/function level. IL-1beta and ERK signaling pathways have been found to play a critical role in asthma manifestation in a wide range of tissue types whereas TGF-beta signaling is most relevant in airway epithelial tissue. Other relevant pathways are IL-12 (in macrophages), immunoglobulin signaling (in lymphocytes) and chemokine signaling (in nasal epithelium).

CONCLUSIONS: This analysis found both overlapping and unique pathways in different tissues that play important roles in asthma development. Tissue-specific DEAG signatures appear relevant for understanding the diverse tissue-specific patho-biology of asthma. The reported tissue-specific and shared gene signatures for asthma may provide the basis for developing novel asthma biomarkers and more selective asthma therapies.
IL-5Ra expression on airway neutrophils in children with treatment-refractory asthma

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RATIONALE: Asthma is a chronic inflammatory lung disorder affecting 9% of children in the United States, a subset of whom have treatment-resistant disease and experience significant morbidity. Our understanding of the pathophysiologic basis of treatment-resistant asthma remains incomplete. The emphasis of emerging biologic treatments has been on a Th2-driven eosinophilic phenotype. While IL-5 is a canonical Th2 cytokine whose receptor is classically thought to be expressed by eosinophils and basophils, recent work revealed unexpectedly that CD125 (IL-5Rα) is also expressed on lung neutrophils in a murine model of influenza A infection. This prompted us to evaluate for CD125 on lung neutrophils in a cohort of severe asthmatic children.

METHODS: Children with treatment-refractory asthma (n=8) underwent diagnostic bronchoscopy and collection of bronchoalveolar lavage fluid (BALF). BALF granulocytes including SSChighCD45+CD66b+/-Siglec8+ eosinophils and SSChighCD45+CD66b+/ Siglec8+ neutrophils were evaluated for surface and intracellular expression of CD125.

RESULTS: CD125 expression was detected on the cell surface of BALF neutrophils (median 26.9% CD125+ cells), with greater expression on eosinophils (median 63.7% CD125+ cells). Intracellular CD125 was detected on 84.8% of neutrophils and 93.7% of eosinophils.

CONCLUSIONS: Our data demonstrate the novel finding of CD125 expression on airway neutrophils in a cohort of severe asthmatic children.

Unique profiles of lesional T follicular helper cells in the pathogenesis of IgG4-related disease

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RATIONALE: IgG4-related disease (IgG4-RD) shows a chronic fibroinflammatory condition characterized by an elevated level of serum IgG4 as well as tissue infiltration by IgG4-positive plasma cells in various organs. However, the underlying immunological mechanisms involved in IgG4-RD remain unknown. In this study, we examined T follicular helper (Tfh) cells in tissue lesions of IgG4-RD.

METHODS: Sorted Tfh (CD4+CXCR5+PD-1+) cells in tissues of submandibular glands (SMGs) from patients with IgG4-related dacyrooadenitis and sialadenitis (IgG4-DS) and tonsils from patients with tonsillar hyper trophy were characterized by DNA microarray analysis or flow cytometry, and their results were compared. Functional analyses of sorted Tfh cells from those subjects were also performed.

RESULTS: Patients with IgG4-DS exhibited increased infiltration of activated Tfh cells in their SMGs. Lesional Tfh cells in IgG4-DS had higher expression of B-cell lymphoma 6 and higher capacity to help B cells and cytotoxic activities, may have distinctive features in acquired immune responses and play an important role in the pathogenesis of IgG4-RD.

High-Dimensional Phenotyping of B-Cells Responding to Rhinovirus Infection

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RATIONALE: Human rhinoviruses (RV) cause roughly half of the one-billion colds experienced annually within the US, while simultaneously precipitating life-threatening respiratory distress in asthmatic populations. Meanwhile, for reasons that remain unclear, adaptive immunity does not promote long-term protection from infection despite each instance of viral clearance generally coinciding with the development of serum neutralizing antibodies. To better understand these responses at a cellular level, we have implemented methods to appreciate fluctuations in peripheral B-cells during RV infection.

METHODS: Six human subjects were nasally inoculated with RV strain A39, and peripheral blood mononuclear cells were drawn and isolated at days 0, 5, and 21 post-infection. Cells were barcoded with palladium-labeled anti-CD45 antibodies, and combined for subsequent processing steps. Next, B-cells were magnetically enriched by negative selection against CD3, CD14, and CD16, and then stained with a 40-marker mass cytometry antibody panel. After collection on a CyTOF2, multiplexed sample data were debarcoded and subjected to FlowSOM clustering analysis.

RESULTS: At day 5, a variety of memory phenotype clusters exhibited modest decreases in frequency. In contrast, the expansion of a singular plasmablast phenotype was more pronounced (p < 0.05). These nascent cells displayed classical plasmablast markers (CD19int+, CD20int+, CD38hi), displayed an activated phenotype (CD27hi, CD95hi, CD80/60, CD40int), expressed inflamed airway homing receptors (CCR5+, CXC3, IgG4fB1hi), and bore indicators of an early, short-lived response (IgM+, Bcl-2low, Ki-67hi).

CONCLUSIONS: Our high-dimensional approach highlights the early adaptive response to RV, suggesting that initial humoral contributions during acute infection are mediated by IgM-secreting plasmablasts acting at the site of infection.
902 Chronic Allergen Stimulation Yields T cell Dysfunction in Obese Asthmatics

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RATIONALE: The connections among atopy, asthma, obesity and immune function remain poorly understood, particularly in pediatric patients. Obese asthmatics have a phenotype of difficult to control disease complicated by severe viral URI triggered exacerbations. The control of viral infections requires CD8 T cell responses, however the potential role of CD8 T cell dysfunction in obese asthma has not been well defined.

METHODS: Prospective study of pediatric asthma and obesity with four groups of patients (6-18 years): obese asthmatics (OA), non-obese asthmatics (A), obese non-asthmatics (O) and non-obese and non-asthmatics (HC). Asthmatics were atopic patients recruited from our Allergy clinic, with deep clinical characterization including sensitization and spirometry. Clinical studies included immune function, metabolic and inflammatory markers. Research studies included water-soluble and lipiddissoluble metabolomics, high dimensional cyometry and serum cytokines.

RESULTS: Pediatric atopic obese asthmatics demonstrated immune dysfunction with increased type 2 immune deviation (including more CRTH2+ CD4 T cells and IL-13 secretion) and CD8 T cell exhaustion (cordonapt expression of multiple inhibitory receptors on CD8 T cells, including PD-1 and Eomes), in the context of altered cytokine and metabolic profiles with evidence of direct immunometabolic mechanisms.

CONCLUSIONS: In the complex OA phenotype we have demonstrated two mechanisms of T cell dysfunction that may partially explain their impaired ability to contain viral URIs: increased CD8 T cell exhaustion and type 2 immune deviation. In atopic OA there is chronic allergen stimulation that may provide the antigen that leads to the underlying immunometabolic tuning. We are currently pursuing these mechanisms in mouse models of pediatric OA.

903 Type 2 innate lymphoid cells expressing death receptor 3 are increased in airway of mild atopic asthmatic subject following allergen inhalation challenge

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RATIONALE: Type 2 innate lymphoid cells (ILC2) are implicated in the initiation and propagation of eosinophilic asthma. To understand novel mechanisms of ILC2 activation, we investigated the role of death receptor 3 (DR3) and its cognate ligand, tumor necrosis factor like protein 1A (TL1A) in mediating ILC2 activation in allergic asthmatic responses.

METHODS: Consenting mild atopic asthmatics (n=10) were recruited to a diluent-controlled allergen challenge crossover study. All subjects developed allergen induced dual bronchoconstriction, airway eosinophilia and increased methacholine airway responsiveness. By flow cytometry, induced sputum extracted ILC2 (lin-FcεRI-CD45+CD127+ST2+ CRTH2+) were identified and DR3 expression enumerated. In induced sputum supernatants, we used ELISA to assess TL1A levels. In functional studies, ILC2 from blood were stimulated with IL-2 and subsequent responses to TL1A were assessed, in vitro.

RESULTS: There was a significant increase in DR3+ILC2, 24 hours post-allergen challenge compared to pre-allergen and 24 post-diluent challenge (64±28 vs. 12±6 and 20±9 cells/μL, p<0.05 and p<0.01, respectively). Sputum supernatant levels of TL1A were significantly increased 24 h post allergen challenge compared to pre-allergen levels and 24 post-diluent challenge (3389±1904 vs. 983±796 and 908±832 pg/mL, p<0.05, respectively). Incubation with IL-2 significantly up-regulated DR3 expression on ILC2, and pre-incubation with IL-2 compared to diluent resulted in significantly increased IL-5+ILC2 in response to TL1A stimulation, in vitro.

CONCLUSIONS: Allergen challenge increases DR3 expression on ILC2 and levels of TL1A in the airway of atopic asthmatics. We propose that the TL1A/DR3 axis may contribute to allergen induced eosinophilic asthmatic inflammation through increased type 2 cytokine production by airway ILC2.

904 Soluble Markers of B-cell Homing, Activation and Survival and Infection Risk in Rheumatoid Arthritis

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RATIONALE: Rheumatoid arthritis (RA) is a disorder associated with immune dysregulation and increased risk of infections. The presence of autoantibodies and immunoglobulin abnormalities indicate B-cell dysfunction. We hypothesize that markers of B-cell activity are decreased in RA patients and that this is linked to higher susceptibility to infections.

METHODS: Using the Johns Hopkins arthritis cohort and biorepository, we contrasted serum protein levels of B-cell factors involved in homing (CXCL10, CXCL11, CXCL12, CXCL13 and CCL19), activation (CD40, CD40L) and survival (BAFF, APRIL, TACI and BCMA) in healthy controls and RA patients with and without history of infections. We excluded RA patients receiving steroids, anti-B cell therapy, non-TNF inhibitors biologics, azathioprine, leflunomide, sulfasalazine or >1 disease-modifying anti-rheumatic drug. Serum B-cell factors were quantified by multiplex immunoassays.

RESULTS: We included 10 healthy controls and 24 adult RA patients (aged 24-64 years) sub-divided into those with (n=7) and those without infections (n=17) within 2 years of enrollment. We identified that: (1) protein levels of BCMA, APRIL, CD40 and CD40L were significantly decreased in RA patients relative to healthy controls; and (2) RA patients with history of infections had significantly lower BCMA levels compared with their non-infectious RA counterparts (p<0.05).

CONCLUSIONS: Our study using soluble serum B-cell markers suggest that there are alterations in B-cell activation and survival in RA patients, and that this may be linked to increased risk of infections. Further delineating the link between B-cell function and RA outcomes may optimize disease subsetting and provide novel insights in RA pathogenesis including the individual susceptibility to infections.
High-quality assembly of Dermatophagoides pteronyssinus genome and transcriptome reveals a wide range of novel allergens

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RATIONALE: House dust mites (HDM) are a predominant source of inhalant allergens that attribute to over 50% of worldwide allergy cases, while the full spectrum of HDM allergens remains unknown. Here we sequenced a high-quality genome of Dermatophagoides (D.) pteronyssinus to find known canonical allergens and allergen orthologs inferred from D. farinae genome.

METHODS: The D. pteronyssinus genome was assembled by a hybrid assembly approach using PacBio, Illumina and Ion Torrent reads. Transcriptomes of D. pteronyssinus and D. farinae were compared using Cufflinks. Allergens were identified by two-dimensional gel electrophoresis and MALDI-ToF MS. Allergenicities of the novel allergens were detected by ELISA using patients’ sera against bacteria expressing recombinant proteins.

RESULTS: Genomic, transcriptomic, and proteomic approaches revealed full gene structures of 21 known allergens, and uncovered 11 putative allergen homologs. A high-quality D. pteronyssinus genome of 66.8 Mb was constructed. This genome assembly represented 98.2% of estimated genome size, with contig N50 being 80kb. The first comprehensive transcriptomic analysis of D. pteronyssinus and D. farinae revealed distinctively expressed allergen genes between the two dust mites, in which Der p 1, 5, 10, 21 and 24 were highly expressed in D. pteronyssinus, while Der f 10, 13, 21, 26 and 31 expressed higher in D. farinae. From ELISA, IgE binding ratings of Der p 25, 26, 28, 32, and 33 were 38.5-65.3%, in which Der p 33 had the highest allergenicity.

CONCLUSIONS: Bioinformatics and experimental characterizations of D. pteronyssinus genome and allergens provide important resources for future investigation of HDM allergens.

Minor Allergens in Moderate-Severe Allergic Rhinitis: Group 4 Mite Amlylas (Blo t4) and Geographical Variations

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RATIONALE: Blomia tropicalis is a relevant domestic dust mite in the tropics and subtropics. Several factors may have a direct effect on the allergenicity of mites in different environments and/or periods of the year. As the proposed major allergens of Blomia are Blo t5 and Blo t21, the aim of this preliminary study is to evaluate the sensitization profile of B. tropicalis in patients with moderate-severe allergic rhinitis in our subtropical area.

METHODS: We selected 21 non-consecutive patients sensitized to B. tropicalis with persistent moderate to severe rhinitis according to the ARIA Guidelines. Skin prick test (SPT) with standardized extracts of B. tropicalis were performed in the forearm followed by immediate reading after 15 minutes. Serum blood samples were obtained from all participating subjects. Total IgE, specific IgE to B. tropicalis and protein allergenic characterization (SDS PAGE and Western Blot) was performed in all 21 serum samples.

RESULTS: All 21 selected subjects (14 females, 11 to 46 y.o.) showed a positive SPT to B. tropicalis. Interestingly, although different patterns of sensitization to B. tropicalis were obtained, mite amylase Blo t4 was the most frequently found profile (>90%) compared to major allergens Blo t5 and Blo t21 in our sample.

CONCLUSIONS: Minor group 4 allergens (mite amylase Blo t4) of B. tropicalis may be an important dust mite allergen in moderate to severe allergic rhinitis in certain distinct populations. The reasons for this predominant reactivity to group 4 allergens in some populations is yet to be determined.

Multiplex assay for high throughput potency and stability measurement of all known German cockroach (GCr) allergens: A step toward full characterization

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RATIONALE: Allergenic extracts are complex biologics and good quality controls are needed to ensure manufacturing of products with consistent potency and quality. The existing approach uses customized antibodies to measure IgE-reactive proteins either individually or as a group. Although the approach is useful, it is not sufficient to provide a complete compositional picture of complex allergenic extracts.

METHODS: To develop a new and improved multiplex assay using a dynamic combination of high throughput LC/MS technology, multiple reaction monitoring (MRM) MS, and immunoassay for an in-depth allergenic protein identification, and simultaneous quantification, potency and stability measurements.

RESULTS: The method development process involves immunoallergometrics to establish a comprehensive profile of IgE-reactive proteins in extracts, and generate a peptide library of all allergens, isoforms, and variants. Prototypic and quantotypic peptides were selected for MRM method development for accurate quantification of all GCr allergens. ICH (Q2(R1)) guidelines were followed to assure assay robustness and suitability. Allergens from various commercial GCr extracts were quantified to show considerable variability between preparations. The LC-MRM MS method was also evaluated for as a stability assay of allergens subjected to various degradative conditions (temperature, pH, and enzymes). The MRM-based potency of selected allergens correlates well with ELISA-based measurements. Also, the LC-MRM was evaluated for its application towards measurement of GCr allergens in dust samples collected from various US households.

CONCLUSIONS: The new assay is robust and valuable for potency measurement of GCr allergen extract and offers great promise in achieving full characterization.
**908** Identification of fungal hazards associated with mold-contaminated homes in Atlanta, Georgia

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**RATIONALE:** Identifying fungal hazards within indoor and occupational environments using molecular detection methods has enabled the detection of the full spectrum of fungi. In this study, next-generation sequencing has been used to evaluate fungi associated with occupying and remediating mold contaminated homes within Atlanta, Georgia.

**METHODS:** Outdoor and indoor air samples, collected with a high efficiency M-TRAP air sampling cassette, as well as dust samples were collected from homes in Atlanta, Georgia with suspected mold contamination before (n=11) and after remediation (n=4). Genomic DNA was extracted for the amplification and sequencing of the fungal internal transcribed spacer 1 region using Illumina MiSeq. Quantitative PCR, viable culture, and ergosterol analyses were also performed.

**RESULTS:** While the fungi detected among outdoor and indoor samples was similar, air samples from homes with suspected mold contamination had an increased relative abundance of Basidiomycota sequences, including *Wallemia* sp. and *Stereum* sp., as well as Ascomycota sequences in the order Eurotiiales. These data were supported by viable culture data analysis that demonstrated an increase in *Aspergillus* and *Penicillium* species. Indoor dust also showed an increase in sequences belonging to the order Pleosporales, which produce homologous *Alternaria* allergens. Homes evaluated post-remediation showed no overall difference in the composition of fungi, although ergosterol concentrations measured in indoor dust were slightly decreased in these homes.

**CONCLUSIONS:** Employing next-generation sequencing technologies has allowed for the detection of fungal hazards derived from the phylum Basidiomycota that are not detected using viable culture. These data show that the spectrum of fungal species remained consistent following remediation.

**909** Perception of Aeroallergen Sensitization Versus Actual Aeroallergen Sensitization

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**RATIONALE:** Many patients describe specific allergen triggers for their rhinoconjunctivitis, but allergy testing often reveals disparate sensitization. We sought to quantify the agreement between perception of aeroallergen sensitization versus actual aeroallergen sensitization.

**METHODS:** Detailed questionnaires addressing allergy symptoms were administered to 229 subjects recruited from pediatric allergy, pulmonary, and general clinics within the Mount Sinai Health System. Specific IgE levels to common aeroallergens (tree mix, grass mix, weed mix, *D. pteronyssinus*, *D. farinace*, mold mix, cat dander, dog dander, *Blatella germanica*, and mouse urine) were measured by ImmunoCAP on serum from each subject. Sensitization was defined as sIgE ≥ 0.35 kU/L. Statistical tests for agreement were implemented in R.

**RESULTS:** The mean age of the 229 participants was 13.8 years (SD 4.9), with 145 (63.3%) reporting symptoms to at least one specific aeroallergen. Tree pollen and dust were the most commonly reported allergen triggers (43.2%), followed by cat (39.7%) and grass pollen (33.6%). Specific IgE measurements revealed that 188 (82.1%) were sensitized to at least one aeroallergen, with sensitization to dust most prevalent (64.2%), followed by dust mite (62.4%) and cat (60.7%). There was moderate agreement between perceived vs. actual cat sensitization (Kappa 0.41, 95% CI 0.30-0.53), and fair agreement between perceived vs. actual sensitization to tree, grass, and weed pollens, dust mite, and mold (Kappa range 0.24-0.36). There was low agreement between perceived vs. actual sensitization to house dust mite (Kappa 0.14, 95% CI 0.03-0.24) and cockroach (Kappa 0.04, 95% CI -0.03-0.11).

**CONCLUSIONS:** Perception of individual allergen sensitization does not highly agree with corresponding allergen-specific serum sIgE levels.

**910** Decrease in early basophil sensitivity to Ara h 2 correlates with sustained unresponsiveness in peanut oral immunotherapy

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**RATIONALE:** Only some peanut-allergic subjects undergoing oral immunotherapy (OIT) achieve a sustained clinical benefit. We hypothesize basophil sensitivity early in OIT may be a useful biomarker in identifying those at risk for regaining allergic reactivity and be used for personalization of OIT.

**METHODS:** Peanut-allergic children, aged 7-13, enrolled in a single-center, open-label peanut OIT trial. After 1 year of OIT, 23 subjects with challenge-proven desensitization (post-OIT) underwent challenge after 1 month of avoidance (post-avoidance). Sustained unresponsiveness (SU) was confirmed in 9 patients. Peripheral blood from multiple time points was stimulated in vitro with Ara h2, and the percent activated basophils by CD63 upregulation was assessed by flow cytometry. A data-driven analysis pipeline (R/Bioconductor) was used for derivation of ED50 and statistical analyses.

**RESULTS:** Post-OIT and post avoidance, ED50 is significantly more increased in SU than transient desensitization (TD), demonstrating decreased basophil sensitivity (p=0.0041, p=0.0011). Basophil sensitivity decreases significantly from baseline after OIT and avoidance in SU (p=0.0009, p=0.0003). Post-avoidance, SU subjects have a 5-fold decrease in basophil sensitivity. At 3 months of OIT, basophil sensitivity in SU significantly decreases from baseline compared to TD (median 18-fold vs. 3-fold, p=0.01).

**CONCLUSIONS:** Basophil sensitivity significantly decreases in subjects with SU in OIT. We propose that the early decrease in basophil sensitivity during OIT, serving as a mechanistic biomarker of effective antibody responses, correlates with the chances of developing long-term clinical efficacy. We postulate that the use of this biomarker will help identify patients who require alternative forms of immunotherapy.
911 Administration of two doses of an oral, irreversible inhibitor of Brutons tyrosine kinase (BTK) to food allergic adults abrogates skin test responses and eliminates IgE-mediated basophil activation ex vivo

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RATIONALE: There is an unmet need for therapies capable of preventing anaphylaxis. BTK is an enzyme that is required for FceRI signaling in mast cells and basophils; therefore, BTK inhibitors such as ibrutinib have the potential to prevent anaphylaxis. We hypothesized that short-term ibrutinib use would reduce allergic responses in food allergic subjects.

METHODS: Six adults with a history of IgE-mediated allergy to peanut and/or tree nuts were enrolled. After screening, subjects were given ibrutinib 420 mg daily for 2 to 7 days. Skin prick tests (SPTs) to relevant foods and basophil activation testing (BAT) were performed at baseline, during ibrutinib treatment, and after cessation of therapy.

RESULTS: Two days of ibrutinib treatment significantly reduced SPT wheal and flare area (77 and 86% reductions, respectively; p<0.0001, n=25). Overall, 44% of all skin tests became negative (wheal < 3mm diameter). Additional doses of ibrutinib for 4 or 7 days maintained significantly reduced SPTs, but did not demonstrate additional suppression compared to 2 days. Histamine control SPTs were unaffected. Anti-IgE induced (but not fMLP-induced) BAT was completely negative after 2 doses (p=0.0002) and remained negative at 4 and 7 days. Finally, the majority of SPTs and BAT returned to baseline levels 1 week after cessation of therapy. No clinical or serologic toxicity from ibrutinib treatment was observed.

CONCLUSIONS: Short-term ibrutinib therapy (as few as 2 doses) eliminates or drastically reduces SPT responses to foods in allergic subjects, and completely abolishes IgE-mediated BAT. ibrutinib could potentially be used to prevent allergic responses including anaphylaxis.

912 Intestinal Microbial-Derived Sphingolipids Are Associated with Childhood Food Allergy

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RATIONALE: Investigation of the early-life intestinal microenvironment may provide insight into food allergy pathophysiology. We performed an untargeted analysis of the infant gut metabolome and bacterial microbiome of childhood food allergy in this ancillary study of the Vitamin D Antenatal Asthma Reduction Trial (VDAART).

METHODS: Metabolomic and bacterial microbial composition profiling was performed on infant fecal samples from 14 subjects who developed food sensitization and clinical food allergy by age 3 years, 32 with food sensitization but no clinical food allergy, and 37 controls. We identified modules of correlated metabolites that were associated with food allergy or sensitization, including sphingolipid biosynthetic metabolites. As invariant natural killer T (iNKT) cells are activated by selected glycosphingolipids, we tested iNKT cell activation by fecal lipid fractions and evaluated associations of lipid activity with phenotype, sphingolipid metabolite and Bacteroides spp. relative abundances.

RESULTS: Sphingolipid biosynthetic metabolites had higher relative abundances in subjects with food sensitization vs allergy (adjusted logistic regression p=0.01) and controls (p=0.02), and were associated with Bacteroides spp. iNKT cell activity of fecal lipid fractions was positively associated with relative abundances of several sphingolipid metabolites, Bacteroides fragilis (Spearman rho=0.50, p<0.001), and food sensitization vs allergy (Wilcoxon test p=0.03). Additional metabolite modules were inversely associated with food allergy, including anti-inflammatory fatty acids and metabolites associated with the microbe Ruminococcus gravis.

CONCLUSIONS: Profiling of the human early-life gut microenvironment identified new molecular pathways associated with food allergy. Bacteroides-derived sphingolipids are inversely associated with food allergy among sensitized subjects, possibly indicating a protective effect of early-life iNKT cell activation.

913 A Role for CD1d-restricted Invariant Natural Killer T Cells and Glycolipids in Alpha-Gal Allergy

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RATIONALE: Alpha-gal meat allergy is associated with IgE-mediated sensitization to galactose-alpha-1,3-galactose (alpha-gal), a carbohydrate moiety found in non-primate mammals. Lipid content of consumed meat drives reaction severity, suggesting that mammalian meat-derived glycolipids containing alpha-gal may act as immunogens. Immunogenic lipids complexed to CD1d antigen-presenting molecules activate iNKT cells. We have shown that alpha-gal-specific IgE binds mammalian glycosphingolipids complexed with CD1d. Thus, we hypothesized that iNKT cells and CD1d-mediated presentation of glycolipid are involved in the pathogenesis of alpha-gal allergy.

METHODS: PBMCs from alpha-gal allergic subjects and controls were stained with fluorochrome-labeled human CD1d tetramers bound to PBS-57 (analog of canonical iNKT cell immunogen alpha-galactosylceramide) and antibodies against CD3 and the activation marker CD69. In separate experiments, basophils from a control subject were stripped of IgE; primed with plasma from subjects with and without alpha-gal allergy; stimulated with glycolipids PBS-113 (contains galactose-alpha-1,4-galactose) or PBS-115 (contains alpha-gal); and stained with fluorochrome-labeled antibodies against basophil marker CD123 and activation markers CD63 and CD203c.

RESULTS: PBMCs from subjects with alpha-gal allergy (n=8) contained double the frequency of activated CD69+ iNKT cells than control PBMCs (n=5). The frequency of activated CD203c+CD63+ basophils among PBMCs stimulated with IL-3 and PBS-113 increased 9-fold when PBMCs were sensitized with plasma from alpha-gal-allergic versus control subjects.

CONCLUSIONS: Alpha-gal-containing glycolipids robustly activated basophils sensitized with alpha-gal sIgE compared to glycolipid without alpha-gal. Circulating activated CD1d-restricted iNKT cells were present at higher frequencies in alpha-gal allergic subjects than controls, suggesting unique roles for iNKT cells and glycolipid rarely described in IgE-mediated food allergy.
914 A distinct T helper subset contributes to the pathogenesis of classical TH2-mediated food allergy disorders

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RATIONALE: Peanut food allergy is heterogeneous. Identification of specific subpopulations of peanut-reactive T cells involved in disease development may further our understanding of pathophysiology and treatment response tailoring patient management.

METHODS: Peanut allergic subjects (PA, n = 20) aged 13 to 65 years were recruited based on their clinical history, serum IgE (> 0.35 kU/L) and positive skin prick test to peanut, and positive reaction to peanut during oral food challenge. Non allergic subjects (n = 10) were used as a control group. Peanut-reactive CD4+ T cells were tracked and profiled ex vivo using CD154 upregulation assay. Single-cell RNA sequencing, surface markers and cytokine profile analysis were performed to examine this cell response.

RESULTS: Our data emphasize the heterogeneity of peanut-reactive effector T cell responses, with two mutually exclusive phenotypic entities (CCR6+CRTH2+ and CCR6−CRTH2−) associated with food allergy. Serum IgE levels to peanut vary across PA, but show positive correlation with CRTH2 expression. Single-cell analysis reveals heterogeneity of peanut-reactive T cells in PA where two different gene clusters were detected. While CRTH2+CCR6− peanut-specific T cell subset shared similar features with Th2a cell responses (i.e. IL33R+, IL25R+, IL-5), CCR6+CRTH2+ T cell subset exhibit a Th17/Th1-related activity, suggesting a distinct pathway that may form the basis of a clinically relevant food allergy endotype.

CONCLUSIONS: Our data suggest that peanut allergic subjects can be classified into 2 endotypes, the Th2a-high and the Th2a-low endotype. Food allergy may no longer be considered as a single entity with “one size fits all” approaches to diagnosis and treatment.

915 Readmission rates following removal of penicillin allergy label after inpatient penicillin allergy testing

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RATIONALE: A penicillin allergy label has been reported to increase morbidity and hospital length of stay. More recently, the risk of readmission has been reported to be significantly higher in this population at 12 weeks from discharge. Evaluating for penicillin allergy can help remove this label which can be performed both inpatient or outpatient.

METHODS: Through an inpatient service at a large academic hospital, patients with a history of penicillin allergy were evaluated by a trained clinical pharmacist. If appropriate, penicillin skin testing and oral challenges were performed with the goal to remove inaccurate allergy labels. We evaluated readmission rates following removal of a penicillin allergy label in those with follow up ≥ 1 year after testing.

RESULTS: From November 2014 to April 2016, a total of 223 applicable charts were reviewed that completed inpatient penicillin testing. Forty-one of the 223 patients (18.4%) had a readmission within 30 days of their index hospitalization. Among patients with follow up ≥ 1 year after removal of the penicillin allergy label was not different (p = 0.25).

CONCLUSIONS: No differences were seen in readmission rates prior to testing and after removal of the penicillin allergy label. The readmission rate remains higher for those with a history of a penicillin allergy label even after removal compared to the general population at 30 days. Inherent selection bias of patients with greater comorbidities to preferentially undergo inpatient penicillin testing may have affected the results.

916 Characterizing the Prevalence of Reported Beta-Lactam Allergy in Pediatric Oncology Patients

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RATIONALE: Beta-lactam allergy is the most commonly reported medication allergy. However, upon thorough evaluation, many of these patients are found not to be allergic. Thus, a systematic approach to the evaluation of such documented medication allergy is necessary especially in the Pediatric Oncology population as these patients are vulnerable to infection requiring beta-lactam treatment. Alternatives are significantly more expensive than first-line antimicrobial regimens, yet lack data to support use and have more potential for side effects.

METHODS: Retrospective chart review design using REDCap database. Inclusion criteria involved Hematology/Oncology patients at the Cleveland Clinic who were diagnosed with any form of cancer between January 2007-July 2017. Ages included were from 0-21 years of age. Those who have been diagnosed with any beta-lactam allergy were evaluated for stage of diagnosis, type of reaction noted and if a challenge or skin testing was performed. Data are presented as number (or percent), median (IQR), or mean ± SD, as appropriate.

RESULTS: Of 250 Oncology patients reviewed, 68 (or 27%) have a documented beta-lactam allergy. Of which 208 (or 83%) have the reaction noted as rash or hives. Only 3 (or 1%) have documented anaphylaxis. Importantly, 218 (or 87%) have never been tested or challenged to ensure true allergy.

CONCLUSIONS: Beta-lactam allergy documentation is not always clear as assumed allergies may be secondary to other mechanisms. Considering the implementation of a protocol for testing or challenging such allergies in vulnerable populations such as Pediatric Oncology patients may be useful in preventing the use of alternative and inappropriate antibiotics.

917 Is there a higher prevalence of methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant Enterococcus (VRE) colonization in patients with antibiotic allergies?

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RATIONALE: A penicillin allergy label has been associated with significantly higher rates of MRSA and VRE colonization and correspondingly, poorer clinical outcomes. However, there are limited data examining the association between any antibiotic label and colonization rates. We sought to evaluate for a relationship between patients with an antibiotic allergy and prevalence of MRSA or VRE colonization.

METHODS: We retrospectively reviewed all patients with an MRSA surveillance culture between December 15, 2014 and January 31, 2015 or a VRE surveillance culture between January 1, 2013 and January 31, 2015 at our institution. Our primary objective was to evaluate the prevalence of MRSA or VRE colonization among patients with and without antibiotic allergies. Bivariate analysis included chi-square and student t-test to determine statistical significance for categorical and continuous variables, respectively.

RESULTS: We included a total of 1053 unique patients screened for MRSA and 290 unique patients screened for VRE. The rate of MRSA and VRE colonization was 6.0% (62/1053) and 32.4% (94/290) in our cohort. Antibiotic allergies were documented in approximately 1 out of 3 patients, 338 (32.1%) for the MRSA group and 94 (32.4%) for VRE group. There was a significant difference in MRSA colonization between patients with and without an antibiotic allergy (45.2% vs. 31.3%, p = 0.034). In contrast, there was no significant difference in VRE colonization between patients with and without an antibiotic allergy (12% vs. 47%, p = 0.10).

CONCLUSIONS: An antibiotic allergy label was associated with significantly higher rates of MRSA colonization but not with VRE colonization.
918 Risk Stratification for Outpatient Penicillin Allergy Evaluations

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RATIONALE: Penicillin allergy evaluations improve antibiotic utilization, but penicillin skin testing (PST) requires more resources than challenge alone. Because amoxicillin challenge without preceding PST may be safe in low-risk patients, we assessed a risk stratification tool for outpatient penicillin allergy evaluations.

METHODS: A prospective observational study of adult patients with penicillin allergy histories was conducted. Patient demographics and penicillin allergy history were reviewed. The risk stratification tool uses the allergy history: low-risk patients (i.e. without IgE features) undergo two-step amoxicillin challenge only; intermediate-risk patients (i.e. IgE features, or anaphylaxis > 5 years ago) undergo PST and, if negative, one-step amoxicillin challenge; and high-risk patients (i.e. recent anaphylaxis) either avoid penicillin or receive desensitization. Outcomes of allergy evaluation were compared between groups.

RESULTS: Of 159 patients (mean age 48 years, 74% female), 33 were low-risk, 126 were intermediate-risk, and none were high-risk. The intermediate-risk group most often reported hives (54%), rash (40%), dyspnea (11%), and/or swelling (10%). The low-risk group most often reported rash (55%) or unknown (36%). All low-risk patients tolerated amoxicillin challenge alone. Because amoxicillin challenge without preceding PST may be safe in low-risk patients, we assessed a risk stratification tool for outpatient penicillin allergy evaluations.

CONCLUSIONS: A novel risk stratification tool for penicillin allergy evaluation permits low-risk patients to be de-labelled safely without PST. Broader implementation of this tool may enable more penicillin allergy evaluations to be performed, but documentation challenges persist.

919 Elevations in IL-6 Correlate with Cytokine-Related Reactions as a Biomarker for Oxaliplatin Hypersensitivity

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RESULTS: Of the 14 patients, the average baseline tryptase was 6.8ng/mL (n=6, normal <1.14 ng/ml) and the average baseline IL-6 was 31.5 pg/mL (n=5, normal < 17.4pg/ml). IL-6 was significantly higher on average during CRRs (1242.97pg/mL, n= 16) than during Type I hypersensitivity reactions (70 pg/mL, n=13) p=0.0028. Tryptase was not significantly different between CRR and Type I Reactions (6.24 ng/mL, n=14 and 8.32 ng/mL, n=10 respectively).

CONCLUSIONS: Elevations in IL-6 correlate well with clinical CRRs to oxaliplatin and help characterize the endotype of such hypersensitivity reactions. IL-6 measurement is useful for the rational modification of future desensitization protocols, since radically different strategies prevent CRRs compared to type I reactions. Monitoring of IL-6 levels may also be relevant for CRRs occurring during treatment with other chemotherapeutics, monoclonal antibodies, and antibiotics.

920 Increased Local IgE Production in Allergic Rhinitis (AR) During Rhinovirus (RV) Infection

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RATIONALE: RV infections are the leading cause of exacerbations of asthma in children and have been ascribed to the worsening of an allergic reaction to concomitantly expressed Aeroallergens. Local production of IgE has been described as a pathogenic mechanism contributing to severity of allergic airway disease. We therefore assessed the presence of specific IgE in the nares relevant to exposure history in allergic rhinitis subjects with naturally-occurring and experimental RV infections.

METHODS: Interstitial secretions were collected via absorptive filter paper applied to the inferior turbinates for 5 minutes. Allergen-specific IgE was assayed via immunocap3. To eliminate confounding influences of transudation or transeptosis, data were normalized to total IgE concentrations in the interstitial fluid and ratios compared between nasal and serum samples.

RESULTS: Initially, we studied 88 consecutive allergic patients presenting the ED of the Hospital Nacional de Niños in San José, Costa Rica with an asthma exacerbation. Amongst patients without RV, 7/34 (20.6%) demonstrated local nasal production of IgE to dermatophagoides pteronyssinus. In contrast, 23/24 (48.9%) of RV-infected asthma exacerbators demonstrated local nasal-specific IgE production. In our subsequent studies, we evaluated prospectively the development of local IgE production to seasonally relevant allergen after an experimental infection with HRV-16. In 8/12 subjects, increased local IgE production in the nares was observed.

CONCLUSIONS: Local IgE production is uncommon but demonstrable in allergic rhinitis subjects. The prevalence of local IgE production dramatically increases during a RV infection further supporting the concept that RV-induced asthma exacerbations are related to enhancement of a concomitant bystander allergic reaction.
**921** Association between prenatal vitamin D and child allergic rhinitis

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**RATIONALE:** Allergic rhinitis is common in children, and little is known about the association of maternal prenatal Vitamin D in non-high-risk, racially diverse populations.

**METHODS:** We studied the association between prenatal vitamin D (25-hydroxyvitamin D (25(OH)D)) and child allergic rhinitis in mother-child dyads enrolled prenatally, 2006-2011, in the racially diverse Conditions Affecting Neurocognitive Development in Early Childhood (CANDLE) cohort (Memphis, TN). We determined 2nd trimester 25(OH)D in women and allergic rhinitis (parent report of physician diagnosis and symptoms in previous 12 months) in children at 4-6 years. Associations between log transformed prenatal 25(OH)D and allergic rhinitis were evaluated in a multivariable model with interaction by maternal race and covariates including maternal asthma, education, smoking, and birth season.

**RESULTS:** Among 1091 women, 67% were African American (AA) and 58% had < high school education. Overall, 23% of children had allergic rhinitis. Median 25(OH)D levels were 25.1 and 19.2 ng/mL in white and AA women, respectively. Effect modification was detected by maternal race (p=0.024). In white women an interquartile range increase (15-27 ng/mL) in prenatal 25(OH)D was not significantly associated with child allergic rhinitis (adjusted OR 0.79, 95% CI: 0.52-1.20, p=0.26), whereas in AA women it was associated with increased likelihood of child allergic rhinitis (adjusted OR 1.40, 95% CI: 1.04-1.88, p=0.025).

**CONCLUSIONS:** Results suggest prenatal vitamin D is associated with increased risk of child allergic rhinitis in African American, but not white, dyads. More research is needed on the relationship with prenatal Vitamin D and allergic rhinitis, particularly in AA populations.

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**922** Quality of Life during the hay fever season after short-course subcutaneous immunotherapy with Lolium perenne peptides (LPP) in grass pollen related rhinoconjunctivitis: A RDBPCCT

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**RATIONALE:** Lolium Perenne Peptides (gpASIT+) is a novel, adjuvant-free immunotherapy formulation containing highly purified natural allergen fragments of LPP for the treatment of grass pollen-induced allergic rhinoconjunctivitis. Quality of Life during the grass pollen season was investigated in adult hayfever patients subsequent to study treatment administered at 4 weekly visits.

**METHODS:** 554 patients with moderate to severe grass pollen-induced rhinoconjunctivitis who participated in double-blind placebo-controlled trial were randomized 1:2 to receive weekly administrations of placebo or increasing doses of LPP to reach a cumulative dose of 170 μg within 3 weeks prior to the pollen season. Quality of life was assessed before, during and after the season using the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ(S)) and the Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ).

**RESULTS:** Global RQLQ and NRQLQ scores were similar in both groups before the pollen season [mean total,95% CI:0.6518(0.5461;0.7576) and 0.4569(0.3720;0.5418)] in the LPP and [0.6968 (0.5547;0.8389) and 0.4919(0.3706;0.6131)] in the placebo. Moreover, global RQLQ and NRQLQ scores significantly lower in the LPP group during the pollen season [1.1665(1.0517;1.2813) and 0.7886(0.6913;0.8860)] for LPP compared to [1.4074(1.2402;1.5745) and 0.9441(0.8068;1.0814)] in the placebo-treated group(p<0.01). Improvement of QoL was observed in all domains in LPP-treated patients compared to placebo. The improved quality of life in LPP-treated patients compared to placebo was in line with the higher number of well days(+23%,p=0.044) reported during the peak pollen period.

**CONCLUSIONS:** A 3-week treatment with increasing doses of LPP confers significant clinical benefit in hay fever patients under natural exposure to grass pollen as measured by patient-reported quality of life assessments.

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**923** Usefulness of saliva in predicting clinical effectiveness for sublingual immunotherapy in seasonal allergic rhinitis

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**RATIONALE:** Development of means to predict clinical effectiveness of sublingual immunotherapy (SLIT) for allergic diseases is a crucial matter. We sought to determine whether whole saliva, which is the first body component contacting with allergen extracts during SLIT, is associated with clinical effectiveness of SLIT in Japanese cedar pollinosis.

**METHODS:** Blood monocytes or mononcytic THP-1 cell were cultured in the presence or absence of either whole saliva or pure saliva with or without treatments including filtration and blockade of TLR2 and/or TLR4 signaling, after which amounts of IL-10 in the supernatants were measured. Whole saliva-induced IL-10 production by THP-1 cell was compared between patients with symptom-free and disease-onset following SLIT.

**RESULTS:** Both monocytes and THP-1 cell produced substantial amounts of IL-10 in response to whole saliva. The IL-10 production was significantly reduced in response to pure saliva and 0.2 mm-filtered saliva. Simultaneous treatment with polymyxin B and TLR2.1, the neutralizing antibody against TLR2, also reduced the production. Amounts of IL-10 produced by THP-1 cell in response to whole saliva collected just before SLIT were significantly higher in symptom-free patients than disease-onset patients following SLIT. Such differences were not seen in saliva collected 3 months after the initiation of SLIT or those collected during the peak pollen dispersal.

**CONCLUSIONS:** Our results provide a basis why sublingual route is effective and preferable in allergen immunotherapy. Amounts of IL-10 produced by THP-1 in response to saliva collected prior to SLIT initiation may become a predictive marker of SLIT.
925 Monocyte Trafficking and Differentiation in Response to Allergen-Activated Peripheral Blood-Derived Mast Cells within an Allergy Tissue Model

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RATIONALE: Studies show that mast cells (MCs), by releasing preformed mediators and expression of diverse molecules, can have a direct effect on the initiation of an immune response prior to IgE production. To determine the role of MCs in orchestrating an immune response, a complex tissue model was developed to mimic human physiology. In this work, the model was used to investigate the interaction between monocytes and MCs in response to an allergen in an IgE-independent manner.

METHODS: MC progenitors, isolated from human peripheral blood, along with human fibroblasts were cultured in a collagen matrix and the apical surface was seeded with human endothelial cells, to mimic a layer of tissue. After MC generation, samples were activated with D. pteronyssinus extract and autologous monocytes were added to the apical endothelial layer. Samples were incubated for 3 h for monocytes to migrate across the endothelial layer and remaining cells were washed away. After 48 h, cells that reverse-transmigrated across the endothelial layer and remaining within the subendothelial layer were collected and analyzed by flow cytometry to determine the differentiation of monocytes into dendritic cells (DCs). Samples without allergen or MCs served as control groups.

RESULTS: Monocytes in response to the allergen upregulated the expression of CD1c and HLA-DR, while down regulating the expression of CD14, CD64, and CD16 in comparison with controls. The differentiated cells possessed CD86, CD83, TSLPR, and marginally OX40L.

CONCLUSIONS: Monocytes in response to the allergen or allergen-activated MCs within the collagen matrix differentiated to CD1c+ cells, displaying phenotypic characteristics of DCs.

926 Human lung endothelial cells produce IL-33 and TSLP simultaneously after dsRNA stimulation

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RATIONALE: Asthma is characterized by type 2 inflammation, in which IL-33 and TSLP play critical roles upon viral infection. Recent studies revealed that not only epithelial cells, but also other tissue cells, can release these two cytokines. Moreover, IL-33 and TSLP showed the same kinetics of induction in rhinovirus-infected mice, suggesting that the existence of cells that concurrently produce IL-33 and TSLP, even though IL-33 is reportedly released by cell damage whereas TSLP is not. In this study, we screened for airway structural cells that simultaneously produced IL-33 and TSLP upon exposure to polyI:C, an analog of viral dsRNA.

METHODS: Normal human lung microvascular endothelial cells (HMVEC-L) and Normal human lung fibroblasts (NHFL), Normal human bronchial epithelial cells (NHBE) and Normal human bronchial smooth muscle cells (BASM) were stimulated with 1 µg/ml polyI:C. mRNA expression and protein concentrations were determined by qPCR and ELISA, respectively.

RESULTS: Only HMVEC-L showed simultaneous IL-33 and TSLP mRNA/protein up-regulation at 36 h after polyI:C exposure, while NHBE, NHFL and NHBE did not. HMVEC-L derived from each of 7 different donors showed up-regulation of these cytokines. Among several tested TLR ligands, only polyI:C induced expression of these cytokines, and the induction was specific to lung-derived endothelial cells, but not dermal-, umbilical vein- or coronary artery-derived endothelial cells.

CONCLUSIONS: Respiratory virus-induced type 2 inflammation is likely to be mediated at least in part by simultaneous release of IL-33 and TSLP by lung endothelial cells. The molecular mechanisms of such cytokine release warrant further study.

927 The D816V-KIT Mutation Causes IL-6 Upregulation In Human Mast Cells

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RATIONALE: Increased IL-6 plasma levels have been associated with severity and progression of disease in patients with systemic mastocytosis (SM). However, the mechanisms involved in increased IL-6 production and the cells responsible are not known.

METHODS: IL-6 levels from peripheral blood were measured by ELISA and D816V-KIT frequency by Allele Specific qPCR. FACS was performed to quantify intracellular IL-6 in bone marrow cells from patients with SM. In vitro experiments were performed in cellular models to evaluate the relationship between the D816V-KIT mutation (present in 90-95% of patients with SM) and IL-6 upregulation.

RESULTS: IL-6 plasma levels positively correlated with D816V-KIT mutation frequency in peripheral blood. Moreover, we found that mast cells are a major source of IL-6 among bone marrow cells from patients with SM. Furthermore, we observed that cultured mast cells expressing D816V-KIT produce IL-6 at the message and protein levels under baseline conditions, while cells expressing wild type KIT or other KIT mutations do not, suggesting a relationship between D816V-KIT mutation and the ability of these cells to produce IL-6. In accordance, KIT activity inhibition reduced mast cell capacity to release IL-6.

CONCLUSIONS: Mast cells with the D816V-KIT mutation are an important source of IL-6 and appear to be responsible for the increase in IL-6 levels in patients with SM via signals derived from the oncogenic activity of D816V-KIT. Our studies shed light into D816V-KIT signalling and IL-6 production in SM, and allows a better understanding of SM pathophysiology and the importance of therapeutic approaches that target KIT and downstream signalling pathways.
**928 MicroRNA-29 suppresses cytokine-mediated production of soluble IL-33 receptor, sST2, by bronchial epithelial cells**

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**RATIONALE:** MicroRNAs (miRNAs) are small, non-coding RNA molecules that act as key regulators of gene expression. Recent reports suggested that hsa-miR-29 (miR-29) can control various inflammation-associated genes, including EOMES, IFNAR1 and soluble ST2 (sST2), a decoy receptor for IL-33, in lymphocytes and tenocytes, respectively. IL-33 has attracted attention as a critical cytokine in allergic diseases because of its ability to induce type-2 immunity and its strong genetic association with asthma. Little is known, however, whether miR-29 regulates sST2 expression in bronchial epithelial cells. We aimed to clarify the role of miR-29 in regulating sST2 expression in bronchial epithelial cells.

**METHODS:** Immortalized human bronchial epithelial cells (BEAS-2B) were transfected with miR-29 mimics, miR-29 inhibitors or negative controls for 24 hours. The cells were then stimulated with TNF-α and IL-4 in combination for 48 hours. sST2 mRNA and protein were determined by qPCR and ELISA, respectively. Changes in endogenous miR-29 expression levels due to the cytokine stimulation were measured by qPCR, in both BEAS-2B and the exosomal lysates derived from BEAS-2B culture supernatants.

**RESULTS:** TNF-α and IL-4 synergistically induced sST2 production by BEAS-2B, as well as upregulation of miR-29 expression in both the cells and exosomal lysates. Overexpression of miR-29 significantly decreased cytokine-induced sST2 mRNA and protein production. Conversely, miR-29 inhibition resulted in a significant increase in sST2 mRNA expression and protein production.

**CONCLUSIONS:** Our results suggest that miR-29 in epithelial cells plays important roles in IL-33-dependent allergic inflammation through regulation of sST2 expression. The effects of epithelial cell-derived exosomal miR-29 should be further studied.

**929 Type 2 Innate Lymphoid Cells and Eosinophil Progenitor Cells are Preferentially Increased in Lesional Skin of Subjects with Atopic Dermatitis**

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**RATIONALE:** Atopic dermatitis (AD) is characterized by chronic pruritic relapsing eczematous lesions of the skin. Eosinophilic inflammation in AD is orchestrated by activation of type 2 inflammatory cells including CD4+ T cells and type 2 innate lymphoid cells (ILC2). We propose that recruitment and differentiation of eosinophil progenitor cells (EoP) contributes to the local expansion of eosinophils in AD lesional skin. This study aimed to quantify total and type 2 cytokine producing levels of ILC2, EoP and CD4+ T cells in AD.

**METHODS:** In a cross-sectional study of moderate-to-severe AD subjects (n=6), pro-inflammatory cells were enumerated in blood and from excised skin lesions taken after an 8 day washout of systemic steroids. By flow cytometry, live, singlet CD45+ cells were identified as EoP (CD34+125+), ILC2 (lin-CD127+CD294+), CD4+ T cells (Lin+CD3+CD4+). Data expressed as percent of total CD45+ cells. Cross-compartmental comparisons were made using Wilcoxon rank-sum test.

**RESULTS:** As a proportion of total leukocytes, there were greater levels of ILC2 (0.012% vs 0.002%, p=0.031) in excised skin lesions compared to blood. A similar trend was observed with EoP (0.045% vs 0.002%, p=0.094). In addition, IL-5 and IL-13 producing ILC2 and EoP reflected a higher percentage in the skin compared to peripheral blood. Conversely, there were greater proportion of CD4+ T cells in blood compared to skin of AD subjects (38.170% vs 1.357%, p=0.03).

**CONCLUSIONS:** The current data suggests that preferential expansion of skin-resident ILC2 may provide the type 2 cytokines that recruit and drive localized differentiation of EoP into mature eosinophils in AD lesions.