1 A New Patient Operated Sampling Device That Provides Fingerprints of Allergens in Homes to Evaluate Patient Exposure and Improve Asthma Patient Care

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Rationale: We developed a device for patients with allergic asthma or rhinitis to run in their own homes so they may establish an allergen exposure profile of their inhalable air for improved asthma and allergy management.
Methods: The device ran for various times and multiple locations within a home in order to assess the dynamic equilibrium of airflow throughout a house. Then patients diagnosed with allergic asthma or rhinitis and possessing cats and/or dogs ran the device in their bedrooms. Aerial load of twelve common household allergens was determined in a laboratory with MARIA™ multiplex immunoassays kits from Indoor Biotechnologies. The utility of the data obtained was then evaluated as part of the complete picture of patient management.
Results: Each home was found to have a unique allergen fingerprint. Results were consistent with patient reports on degree of pet bedroom access. Non-pet allergens: dust mite, mouse, pollens and molds were found in 13 cases. There were no positives for cockroach, rat or birch pollen reflecting socio-economic group and season. Review of fingerprints together with individual medical records showed actionable information in 17 cases. Areas of utility included discovering unanticipated allergens; prioritizing triggers for environmental management; encouraging individualized and targeted allergen avoidance activity; and improving patient compliance.
Conclusions: The capability of patients to run simple allergen exposure fingerprints unsupervised in their own homes provides physicians with individualized data to make evidence based decisions on asthma patient management.

2 Perceived Stress in Adults with Asthma in an Urban Environment

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Rationale: The prevalence of asthma continues to increase with higher rates of asthma morbidity found in urban populations. A number of factors are likely to contribute to the higher morbidity in urban areas including stress. Stress is a widely unmeasured exacerbating factor in asthma. We sought to determine levels of perceived stress in an urban asthma population and its' impact on asthma control.
Methods: We recruited asthma and healthy control subjects, performed spirometry and administered the validated 10 item Perceived Stress Scale (PSS). Asthma subjects were administered the Asthma Control Test (ACT). Basic descriptive statistics were performed, including a Pearson correlation.
Results: Thirteen asthmatics and 11 controls participated in the study. Mean age of the asthma subjects was higher compared to the healthy control group (44.2±15y vs. 31±12 years old; p=0.03). There was no difference in BMI. FEV_1% in the asthma subjects was lower than in the control subjects (75±15% vs. 89±9%, p=0.008). The mean ACT score in our asthma group was 18.6±1.3. Asthma subjects had higher perceived stress scale than the controls (16.86±1.3 vs. 11.9±1.8; p=0.03). Furthermore, the ACT score and the PSS score were inversely correlated, indicating those with higher perceived stress had impaired control of their asthma (p=0.02).
Conclusions: This study revealed that adult asthmatics from an urban environment had higher perceived stress compared to healthy controls. Moreover, we found that the ACT and PSS were negatively correlated which suggests that there is a link between stress and asthma control in asthmatics that reside in urban environments.

3 Effect of the SQ House Dust Mite Sublingual Immunotherapy Tablet on Rhinitis and Asthma Symptoms in North American Adolescents and Adults: A Randomized, Placebo-Controlled Trial

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Rationale: SQ house dust mite (HDM) sublingual immunotherapy (SLIT) tablet (MK-8237; Merck/ALK) was assessed in North American subjects with HDM allergic rhinitis with/without conjunctivitis (AR/C).
Methods: Subjects aged ≥12 years were randomized to daily 12 SQ-HDM or placebo for up to 52 weeks in this double-blinded, multicenter trial (NCT01700192). Included subjects were those with HDM AR/C with or without asthma requiring, at most, medium-dose ICS. A rhinitis daily symptom score (DSS; 4 symptoms, maximum=12) of ≥6, or ≥5 with 1 symptom being severe, on 5 of 7 consecutive days before randomization was required for inclusion. Primary endpoint was the average total combined rhinitis symptom and medication score (TCRS) during the last 8 weeks of treatment. Average asthma DSS (3 symptoms; maximum=9) was an additional endpoint.
Results: Of the 1,482 randomized subjects, 31% had asthma. Treatment with SQ HDM improved TCRS 17.2% vs placebo (95% CI: 25.0%, 9.7%). In the entire trial population, mean asthma DSS was 1.26 with SQ HDM and 1.56 with placebo, corresponding to a 19% improvement vs placebo. In subjects with asthma, mean asthma DSS was 1.37 with SQ HDM and 1.83 with placebo, corresponding to a 25% improvement. No treatment-related serious adverse events were reported. A treatment-related systemic allergic reaction of moderate intensity occurred on day 1 under medical supervision and was treated with epinephrine. Subjects with asthma generally tolerated active treatment well.
Conclusions: This was the first North American trial with SQ HDM SLIT-tablet to demonstrate a significant improvement in HDM AR/C and asthma symptoms. Treatment was well-tolerated.

4 Safetly of Immunotherapy Mix – USP 747 Issues

Joann Catherine Blessing-Moore, MD, Solo Practice, Palo Alto, CA and Tara LaBounty, Joann Blessing-Moore MD, INC

Rationale: We know allergy shots improve patient outcomes and are cost effective. Allergy Immunotherapy mixes are made of the individual allergens to which the patient has proven sensitive. We prepare these mixes in our office and have never had any known problems with infections related to the shots.
Methods: There are 4 dilutions of the mix and treatment is started at the lowest dilution and advanced until a maintenance concentration is reached. We use the standardized preparation technique presented in "Allergen Immunotherapy Extract Preparation Manual from the AAAAI practice Management Resource Guide 2012 edition (Michael Nelson, Linda Cox)". We culture the last dilution.
Results: Since 1991 preparation of these mixes in our office included a culture of the last dilution. We have done test runs with blinded mixes to test for accuracy for reading the cultures. If any positive culture after 3 days the mix would have been remade. No patient cultures have proven positive after 3 days with the presently used method.
Since 1994 as a solo practitioner, we have prepared and tested 760,106 mixes and have not had one contaminated mix after 3 days culture.
Conclusions: Allergy Immunotherapy mixes can be made safely in the office setting. These mixes are essential in the care of our allergy/asthmatic patients and are being prepared in a safe cost effective manner in the allergist's offices. We do not need to revise these present techniques. (USP797)

5 Once-Daily Tiotropium Respimat® Add-on Therapy Improves $FEF_{25-75\%}$ in Children and Adolescent Patients with Persistent Symptomatic Asthma

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Rationale: $FEF_{25-75\%}$ may be a more sensitive parameter than FEV_1 to assess changes in small, peripheral airway function. We report $FEF_{25-75\%}$ responses from 5 Phase II and III trials that investigated once-daily tiotropium Respimat® (tioR) add-on to existing therapy, in patients aged 6–11 and 12–17 years with persistent symptomatic asthma.

Methods: Five randomized, double-blind, placebo-controlled trials: 2 Phase II, incomplete-crossover trials of tioR 5µg, 2.5µg, or 1.25µg in children aged 6–11 years and adolescents aged 12–17 years with moderate persistent symptomatic asthma; 3 Phase III, parallel-group trials of tioR 5µg or 2.5µg in children aged 6–11 years with severe persistent symptomatic asthma and adolescents aged 12–17 years with moderate or severe persistent symptomatic asthma. Study medication was delivered as 2 puffs. Primary endpoint: peak FEV_1 change from baseline (response) within 3 hours post-dosing. Mean $FEF_{25-75\%}$ response was a further endpoint.
Results: 1397 patients were randomized across the 5 trials. Baseline demographics and disease characteristics were balanced between treatment groups. TioR improved peak and trough FEV_1 responses versus placebo; the improvement was statistically significant in the majority of cases, more frequently with the 5µg dose. In each trial, $FEF_{25-75\%}$ responses versus placebo were statistically significantly improved at most time points across all doses. In most cases, the 5µg dose corresponded with larger $FEF_{25-75\%}$ responses.
Conclusions: In children and adolescents with persistent symptomatic asthma, once-daily tiotropium Respimat® add-on to ICS or ICS plus other controller medication improves lung function. Improvements in $FEF_{25-75\%}$ responses are consistent and more pronounced than improvements in peak and trough FEV_1 responses.

6 Impact of Asthma Exacerbations on Lung Function in a Large Cohort of Patients with Severe or Difficult-to-Treat Asthma

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Rationale: Asthma exacerbations contribute to morbidity and mortality, but limited evidence exists about the extent to which such exacerbations may lead to worsening airway obstruction.
Methods: Patients with severe or difficult to-treat asthma were followed observationally for three years in The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR). Percent predicted post-bronchodilator forced expiratory volume in one second ($ppFEV_1$) was collected annually, and asthma exacerbations, defined as an overnight hospitalization, emergency room visit, or steroid burst, were assessed bi-annually. Patients with chronic obstructive pulmonary disease and current smokers were excluded from analyses. Annual change in $ppFEV_1$ was modeled using repeated measures as a function of asthma exacerbations during that year, baseline ppFEV1, age, sex, race/ethnicity, and body mass index.
Results: A total of 2,429 patients (n=1,803 adults ≥18 years; n=394 adolescents ages ≥12-17 years; n=232 children ages 6-11 years) met the entry criteria. After adjustment for covariates, the 12-month change in $ppFEV_1$ was lower in patients with any asthma exacerbation compared with those with no asthma exacerbation (-1.27±0.26 vs. 0.70 ±0.22; net difference: 1.97±0.36; $p<0.001$); in adults (-1.14±0.30 vs. 0.68±0.25; net difference: 1.82 ±0.41; $p<0.001$); in adolescents (-2.46±0.74 vs. 0.46±0.59; net difference: 2.92±0.98; $p=0.004$); in children (-1.05±0.79 vs. 0.99±0.76; net difference: 2.04±1.14; $p=0.081$).
Conclusions: Asthma exacerbations are associated with lung function decline in patients with severe or difficult-to-treat asthma. Together with prior evidence, this research suggests that prevention of asthma exacerbations may limit airway remodeling and declines in irreversible airway obstruction.

7 Asthma Carepartners: Embedding an Innovative Community Health Worker Program into Standard Healthcare Delivery

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Rationale: The Asthma CarePartners (ACP) program, an innovative partnership between Sinai Urban Health Institute (SUHI) and a Medicaid managed care organization, aims to improve the health of Chicago children and adults with asthma. Four previous asthma interventions with rigorous results and demonstrated cost savings have proven the effectiveness of SUHI's community health worker (CHW) model, leading to this venture to incorporate the model within standard healthcare delivery.
Methods: ACP utilizes CHWs making home visits to educate patients with poorly controlled asthma about the disease, its triggers and proper management. Participants receive six home visits during the year-long intervention. Education focuses on improving medical management while simultaneously addressing environmental triggers. CHWs conduct

structured home environmental assessments, working collaboratively with families to reduce exposure to home triggers.
Results: Since 8/16/11, 596 participants have completed a baseline visit. Among the 120 participants who completed the 12-month intervention, ED visits were reduced by 71% ($p<0.0001$) between the year prior to and the year following the intervention. Furthermore, nights where sleep was disturbed by asthma decreased from 5.7 nights at baseline to an average of 1.9 over the intervention period ($p<0.0001$). Caregiver Asthma-Related Quality of Life scores improved from 5.4 to 6.6 at the 12-month follow-up ($p<0.05$), a clinically and statistically significant improvement.
Conclusions: Data demonstrate an improvement in asthma control, reduction in symptom frequency and a dramatic reduction in asthma-related health resource utilization. Embedding a CHW home visit asthma intervention into managed care delivery yields cost-savings for the healthcare system and life-changing benefits for participants.

8 Expected Number Needed to Treat with Omalizumab to Prevent an Asthma Exacerbation, Emergency Room Visit, or Hospitalization in Patients with Severe Uncontrolled Asthma

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Rationale: Clinicians use number needed to treat (NNT) to compare therapies. We estimated expected NNT to prevent an exacerbation, hospitalization, or emergency room (ER) visit, if omalizumab was used in patients with severe uncontrolled asthma.
Methods: An anti-IL-5 study in patients with severe asthma and history of 3.6 exacerbations reported background placebo rates of exacerbations (1.74 per year), including those requiring hospitalizations (0.10 per year), and ER visits or hospitalizations (0.20 per year). In omalizumab pivotal trial, relative risk reduction (RRR) for exacerbations (by current ATS guidelines: worsening of asthma symptoms requiring ≥3 days of systemic corticosteroids) was 55% (79% in subgroup of patients on LABA in addition to background therapy). Omalizumab annual RRR for hospitalizations was 84%, a Cochrane meta-analysis) and 56% for hospitalizations or ER visits (systematic literature review).
We calculated expected per-year absolute risk difference: (anti-IL-5 placebo background rates) x (omalizumab RRR)/100. We calculated the expected per-year NNT with omalizumab: 1/(expected absolute risk difference).
Results: For omalizumab, the expected per-year NNT to prevent an exacerbation comprised 1.04 (1/0.957) for all enrolled patients or 0.73 (1/1.375) for only patients treated with LABA. The expected NNT comprised 11.9 (1/0.084) for asthma-related hospitalizations and 8.9 (1/0.113) for asthma-related hospitalizations or ER visits.
Conclusions: With the contemporary definition of an asthma exacerbation and background therapy, clinicians would expect to treat ~1 patient with severe uncontrolled asthma for a year with omalizumab to prevent one asthma exacerbation, ~12 patients to prevent a hospitalization, or ~9 patients to prevent a hospitalization or an ER visit.

10 Burden of Allergic Status in Patients with Severe Asthma: A Matched-Cohort Real-World Evidence Study

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Rationale: Allergic asthma comprises a well-recognized phenotype; the burden of allergic status in severe asthma needs elucidation.
Methods: This propensity-score matched cohort study used insurance claims (Truven MarketScan) to identify 6+ year old patients with severe asthma: 1 inpatient or 2 outpatient claims for asthma plus step 6 NHLBI therapies in baseline year. Evidence of allergic asthma included: ≥1 ICD-9-CM code for extrinsic asthma plus ≥1 code for allergic comorbidity (sinusitis, rhinitis, conjunctivitis, nasal polyposis, anaphylaxis, eczema/dermatitis, food allergy, urticaria/angioedema, atopic dermatitis). Allergic and non-allergic patients were matched 1:1 by baseline characteristics: demographics, provider specialty, year, comorbidities, and asthma medications.
Results: Matched severe asthma patients with (n=1,523) and without (n=1,523) evidence of allergic status [mean (SD) age 36.1 (20.9) years, 62.1% female] were well-balanced at baseline, except more chronic conditions, cough, and upper respiratory infections in the allergic group. Medication use in patients with vs without evidence of allergic

status: LABA (57.1% vs 52.5%; p=0.011), LTRA (46.2% vs 35.1%; p<0.001), and omalizumab (3.4% vs 0.9%; p<0.001). Patients with vs without evidence of allergic status were more likely to experience exacerbations [47.7% vs 43.2% (p=0.012)] and used more annual outpatient visits: all-cause (24.6 [SD 21.0] vs. 16.2 [16.2], p<0.001) and asthma-related (3.2 [4.7] vs 2.1 [2.8], p<0.001). Hospitalization and emergency room use rates were comparable.
Conclusions: Severe asthma patients with evidence of allergic status experience more exacerbations and outpatient visits (overall and asthma-related) than their counterparts without allergic status. Treatments directed at allergic asthma may reduce the burden in this severely-affected population.

11 Montelukast Is a Better Controller in Obese Atopic Asthmatics

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Rationale: The concomitant rise in the prevalence of asthma and obesity has suggested an association between the two. Two phenotypes of obesity-associated asthma exist; early-onset atopic and late-onset non-atopic asthma. Animal and human studies suggest involvement of leptin and leukotrienes in inflammatory pathways. We hypothesized that montelukast is a more effective controller of early-onset atopic asthma in overweight/obese (O) compared to normal (N) weight asthmatics.
Methods: Mild to moderate persistent early-onset asthmatics on inhaled corticosteroids (ICS) were randomized in a double-blind controlled manner to receive montelukast (M) or placebo (P). Active treatment with M was compared to P at week 24 with the primary outcome measure, Asthma Control Test (ACT) scores, and secondary outcome measures (spirometric measures, exhaled nitric oxide, total ICS dose, serum leptin and urinary leukotriene E4 levels). Mean difference was calculated as M group minus P group with corresponding 95% confidence interval.
Results: The two treatment groups were comparable at baseline. At week 24, the O group, but not the N group, treated with M demonstrated a significantly higher ACT score than P (25.0 vs. 15.7 respectively, p<0.01). ACT score differed significantly between M and P groups (24.5 vs. 18.1 respectively, p<0.01), overall, but not for any other clinical or laboratory parameters assessed. There were no significant interactions between treatment group and weight subgroup for the parameters of interest.
Conclusions: Montelukast is a more effective controller medication among obese atopic early-onset asthmatics compared to normal weight asthmatics. These data underscore the need to individualize asthma management in obese asthmatics.

12 A Randomized, Multi-Center, Single Visit Study to Compare Feno Measured with the Niox Mino and the Niox Vero in Subjects with Asthma

Kathleen A. Rickard, Aerocrine

Rationale: Measurement of exhaled Nitric Oxide (FeNO) is useful in the diagnosis and management of asthma. The primary objective of this study was to assess the agreement and repeatability of FeNO measured with NIOX MINO and NIOX VERO.
Methods: Data from two randomized, multi-center, single visit studies were pooled. All Subjects performed two measurements with the NIOX MINO and the NIOX VERO in random order. The primary endpoint was the proportion of subjects with FeNO values within the tolerance limits. The secondary endpoint was to evaluate the agreement of FeNO measured with NIOX MINO and the NIOX VERO.
Results: 109 completed one valid FeNO measurement on each device. 90.8%(99/109) of the subjects were within the tolerance limits for the first valid FeNO measurement. The mean observed paired difference for the first valid FeNO measurement on each device was -4.6 ppb (95% CI: -5.825 to -3.3//; p<0.0001). Weighted Deming Regression Analysis showed slope of 0.842 (95% CI: 0.757, 0.927) and Y-intercept of -0.472 (95% CI: -1.999, 1.055). Paired differences were centered close to 0. Intra-subject repeatability of NIOX VERO was significantly better than NIOX MINO (p= 0.0112).
Conclusions: FeNO measurements using the NIOX VERO were slightly lower than on the NIOX MINO, however, no substantial differences were noted between replicates within age groups, gender groups or randomization sequences and the difference is within the technical specifications of the device. The results support a high degree of intra-

subject repeatability. The same agreement was seen when comparing the first valid measurement and the mean of the two measurements.

13 Pulmonary Embolism Is a Patient with Factor V Leiden Mutation, Presenting with Symptoms of Asthma Exacerbation

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Rationale: The differential diagnosis of asthma is extensive. Pulmonary embolism may present with similar symptoms to asthma. We present a case of pulmonary embolism in a patient with moderate persistent asthma and Factor V Leiden mutation who presented with symptoms of an asthma exacerbation.
Methods: Our patient was referred for evaluation and treatment of moderate persistent asthma.
Results: A 52 year old woman with a Factor V Leiden mutation presented with a history of moderate persistent asthma. Symptoms included cough, wheezing, and shortness of breath. She had been previously treated with montelukast with no significant benefit. She could not tolerate medications with long-acting beta agonists due to anxiety side effects. She was placed on fluticasone proprionate 220 mcg two puffs twice daily with benefit. However, after two months, she developed worsening shortness of breath symptoms with wheezing. On exam, she had normal heart rate (80), respiratory rate (12), and blood pressure (110/70). Lung exam was clear to auscultation without any wheezes, rhonchi, or rales. Fluticasone dose was increased with some benefit in two days, however, mild symptoms still occurred. She then developed chest discomfort, which was exacerbated by arm movement. She was referred to emergency department for further evaluation, and CT pulmonary angiography revealed a pulmonary embolism. She was successfully treated with anticoagulant therapy.
Conclusions: This case demonstrates the importance of considering pulmonary embolism in the differential diagnosis of an asthma exacerbation, especially in a patient with a hypercoagulable state, such as Factor V Leiden.

14 Improving Asthma Outcomes Among Adults through a Community Health Worker Home-Based Intervention

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Rationale: Approximately 7% of the U.S population has asthma. Of these 23 million people, 73% are adults. Asthma prevalence and morbidity are highest among African Americans and those living in poverty. Mount Sinai Hospital, located in Chicago's economically challenged, predominantly African American Westside, sees a disproportionate prevalence of asthma among adults. In 2012, Mount Sinai Hospital's 30-day readmission rate for asthma was 8.1%, or 3.2 times the national rate.
Methods: The Helping Chicago's Westside Adults Breathe and Thrive study is one of the first across the country to test the feasibility and effectiveness of a community health worker (CHW) asthma and healthy homes intervention exclusively with adults. The intervention aims to increase asthma control, improve the home environment, and reduce asthma-related morbidity. CHWs make 5-6 home visits in a year to provide comprehensive, individualized asthma education. They also conduct home environmental assessments to identify in-home asthma triggers, and work closely with participants, landlords and management companies to address them.
Results: Two hundred two adults enrolled in the study. Preliminary results, based on 41 participants who completed the year-long intervention, show a significant reduction in daytime symptoms (65%), nighttime symptoms (55%), and days needing rescue medication (42%). Hospitalizations decreased by 50% and asthma-related Emergency Department visits decreased by 57%.
Conclusions: These results suggest the effectiveness of the CHW model in improving asthma outcomes for adults and that the model translates well. Through home visits, CHWs encourage and empower participants to adopt effective asthma control behaviors, such as addressing in-home triggers to create an asthma-friendly home.

16 Association Between Recent and Future Asthma Exacerbations in Pediatric Patients with Severe or Difficult-to-Treat Asthma

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Rationale: To investigate risk of future severe asthma exacerbations (FSE) in pediatric patients with severe or difficult-to-treat asthma who experience a recent severe asthma exacerbation (RSE).

Methods: Pediatric patients (ages 6-11 years) in the TENOR 3-year observational study were analyzed. A RSE was defined as either an overnight hospitalization or emergency department (ED) visit in the 3 months before baseline; a FSE was defined as either an overnight hospitalization, ED visit, or death between month 6 and month 36. A secondary analysis examined steroid bursts as an independent predictor and outcome measure. Generalized estimating equations repeated measures logistic regression models were used to assess risk of future exacerbations adjusting for demographics, clinical variables, asthma severity, and control.
Results: Compared to patients without a RSE, patients with a RSE were over 3 times (OR=3.8, 95%CI: 2.7, 5.4) more likely to experience a FSE. The association persisted after adjusting for demographic and clinical variables (OR=3.1, 95%CI: 2.2, 4.4), asthma severity (OR=3.4, 95%CI: 2.4, 4.8), and asthma control (OR=4.5, 95%CI: 3.1, 7.0). Patients with a recent steroid burst were over 2 times (OR=2.8, 95%CI: 2.2, 3.7) more likely to experience a future steroid burst after adjusting for demographic and clinical variables (OR=2.6, 95%CI: 2.0, 3.4).
Conclusions: RSE's are an important independent predictor of FSE's in pediatric patients with severe/difficult-to-treat asthma and should be considered when determining asthma action plans. Healthcare providers should question patients regarding recent exacerbation history and adapt treatment plans to reduce future risk.

17 Childhood Obesity in Difficult to Control Pediatric Asthma Patients in a Tertiary Pediatric Subspecialty Clinic

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Rationale: Identifying clinical features associated with difficult to control asthma will help address overall control and more effective asthma management. Our clinical observation suggested that the proportion of overweight/obesity is significantly higher in difficult-to-control (DTC) than in well-controlled asthmatics.
Methods: This was a retrospective chart review of 400 patients, aged 5 to 18 years. Cases (n=200) were identified as 100 subjects with difficult-to-control severe persistent asthma and an inhaled corticosteroids (ICS) dose of ≥1000 mcg/day and 100 subjects with well-controlled mild and moderate persistent asthma and an ICS dose of ≤500 mcg/day. The control group included 200 subjects without asthma. Multivariable logistic regression models were used to assess the relationships between asthma status and weight status, age, race and gender.
Results: The BMI percentile was significantly higher in the difficult-to-control asthma group than in the well-controlled asthma group and in the control group (74.66 ± 28.19 vs. 54.25 ± 29.92 vs. 55.19 ± 32.54, $p<0.001$). 36% of the difficult-to-control asthmatics were obese (vs. 6% of the well-controlled asthmatics, $p<0.001$, vs. 13% of non-asthmatics, $p=0.002$), and 47% normal weight (vs. 79% of the well-controlled asthmatics, vs. 75% of non-asthmatics, $p<0.001$). Mean age and the proportion of African Americans in the difficult-to-control asthmatics were significantly higher than in the well-controlled asthmatics and in the control group ($p<0.001$).
Conclusions: The results of this study demonstrate a significant association between severe persistent DTC asthma and obesity, age and race. Obese difficult-to-control asthmatics need treatment approaches addressing both asthma control and weight management.

18 Characterization of T Cell Reactivity in Cockroach-Allergic Children with Different Disease Severities

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Rationale: German cockroach (Bla g) allergy is commonly defined by IgE titers to Bla g extract or allergens. It is commonly associated with rhinitis and asthma in inner-city children. Studying Bla g T cell response is of great relevance to understand potential differences as a function of allergic disease and for the development of efficacious immunotherapy approaches.
Methods: Using pools of previously identified Bla g-derived T cell epitopes, we characterized the allergen-specific T cell response of children who exhibited 1) early onset atopy (Bla g-sensitized, n=8) 2) late onset atopy (Bla g-sensitized, n=7) or 3) low atopy (not Bla g-sensitized, n=6). PBMC from Bla g-sensitized children from all 3 groups were analyzed ex vivo for Bla g-specific T cell responses based on cytokine production in response to antigen stimulation measured by Flow cytometry. Additionally, bulk frequency of total Th2A cells, a Th2 cell subset that has been associated with the pathogenicity of allergy and asthma, was assessed by flow cytometric analysis.
Results: Analysis of total Th2A cells in three groups revealed a 2-3 fold increase of the Th2A populations in the atopic children compared to children with low atopy (p=0.01). Bla g-specific IL-5 production in CD4 t cells was significantly higher in children with early or late onset atopy (median 0.38 and 0.58%, respectively) than low atopy (median 0.03%) (p=0.009).
Conclusions: Onset of early and late atopy in cockroach allergic children is associated with an increase in frequency of total Th2A cells and allergen-specific IL-5-producing T cells compared to children with low atopy.

19 Neighborhood Deprivation Is Longitudinally Associated with Childhood Asthma

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Rationale: Although longitudinal studies have shown associations between parental income and childhood asthma development, deprivation has been proposed as a more comprehensive measure of childhood socioeconomic status. We determined the associations between material deprivation and childhood asthma.
Methods: Prospectively-collected administrative data housed at the Institute for Clinical Evaluative Sciences were evaluated for the 1997-2003 Toronto birth cohorts. Neighbourhood material deprivation was reported according to the Ontario Marginalization Index criteria, including no high school graduation, lone parent families, government transfers, unemployment, low income, and homes needing major repairs. Incident asthma was defined by the time of entry into the Ontario Asthma Surveillance Information System (OASIS) database, requiring 2 outpatient visits for asthma within 2 consecutive years or any hospitalization for asthma. We measured risk of incident asthma due to high neighborhood deprivation with Cox proportional and discrete-time hazard models and associations between asthma visits and deprivation by year of life with Generalized Estimating Equations and generalized linear mixed models.
Results: OASIS asthma criteria were met for 21% of the 326,383 children. After adjusting for sex, preterm delivery, obesity, and atopic conditions, children with high birth neighborhood deprivation were at increased risk of any (HR 1.11; 95% CI, 1.09-1.13) and currently-symptomatic (HR 1.11; 95% CI, 1.06-1.15) incident asthma. High deprivation in a given year of life was associated with increased odds of asthma in that year of life (OR 1.10; 95% CI, 1.07-1.12).
Conclusions: Children living in high-deprivation neighborhoods are at increased risk of incident asthma, suggesting possible primary asthma prevention strategies.

20 Prevalence of Exercise-Induced Bronchoconstriction Using the 6-Minute Free-Running Test in 5- to 6-Year-Old Japanese Children: A Cross-Sectional Study

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Rationale: Exercise-induced bronchoconstriction (EIB) develops during or after exercise in healthy children, as well as in those with bronchial asthma (BA). However, the definition of EIB varies because of differing criteria among countries, and differences between sexes are poorly understood. This study aimed to investigate the prevalence of EIB using 3 different criteria of positive EIB, taking into account sex, in kindergarteners in Japan.
Methods: Fifty-one 5- to 6-year-old children without BA were enrolled in this cross-sectional study. The children underwent the 6-minute free-running test (6MFRT) for an exercise challenge. Peak expiratory flow rate (PEFR) was measured before exercise and at 0, 3, 10, and 20 minutes after exercise. Positive EIB was defined using 3 criteria: ≥15%, ≥20%, or ≥25% decrease in post-exercise PEFR from pre-exercise PEFR.
Results: Among the children (n=23 boys; n=28 girls), the prevalence of EIB was 54.9% (28/51) in children when a ≥15% decrease in PEFR was used, 41.2% (21/51) when a ≥20% decrease in PEFR was used, and 25.5% (13/51) when a ≥25% decrease in PEFR was used. When EIB was defined as a ≥25% decrease in PEFR, the prevalence of EIB was significantly higher in girls than in boys (39.3% vs 8.7%, p = 0.022).
Conclusions: Regardless of which criteria are used, the prevalence of EIB in Japanese kindergarteners is higher than that observed worldwide, especially in girls. Our results suggest that the criteria for diagnosing EIB in 5- and 6- year-old children should take sex into account.

21 Using Electronic Medical Records (EMR) to Improve Outpatient Quality of Care for Children with Asthma

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Rationale: Poorly controlled asthma is the leading cause of school absenteeism and accounts for billions of dollars in medical costs annually for children. Use of EMR can be helpful with both monitoring asthma control and standardization of care.
Methods: Retrospective chart reviews were completed in two phases. In Phase 1 (2013), outpatient encounters for patients with asthma in general pediatrics and pulmonology were analyzed. Data collected included: severity classification, inhaled corticosteroid (ICS), asthma action plan (AAP) and patient education. Results from Phase 1 were summarized and distributed to attending physicians and residents in individual report cards. Mandatory questions regarding asthma severity and management were added to EMR charts. In Phase 2 (2015), a post-intervention chart review was completed for patients meeting the same inclusion criteria.
Results: In Phase 1, 1229 charts were reviewed and compared to 1672 charts in Phase 2. The rates of documenting severity classification significantly increased from 67.6% (832/1229) in Phase 1 to 91.5% (1530/1672) in phase 2 (p=0.001). Use of ICS significantly improved from 60.1% (739/1229) in Phase 1 to 70.2% (1175/1672) in Phase 2 (p=0.001). Documentation of asthma education improved from 73.1% (898/1229) in Phase 1 to 76.6% (1282/1672) in Phase 2 (p=0.026). The distribution of AAP improved significantly from 48.4% (598/1229) in Phase 1 to 60% (1002/1672) in Phase 2 (p=0.001).
Conclusions: Standardization of documentation in the EMR resulted in significant improvement in documentation of severity classification, utilization of ICS, distribution of AAP and provision of education.

22 Mobile Phone Asthma Action Plan Application; Use in Adolescents

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Rationale: Asthma burden affects mortality, morbidity, quality of life, and the economy. The *British Medical Journal* recently reported that two-thirds of asthma deaths are due to failure to follow recommended guidelines and primary care failings in routine care. Written asthma action plans are standard of care according to national guidelines, but these plans are seldom prescribed. Furthermore, these written care plans are often unavailable at the time of an exacerbation. The purpose of this project was to create an asthma action plan application for smartphones. The goal of the project was improved patient access to their asthma action plan and improved utilization rates among providers.
Methods: A development studio was consulted for support in developing a smartphone application to code the software for the asthma action plan and assist in the design process. Following development of the application, a survey was completed to evaluate design and functionality.
Results: All survey participants agreed that the application was easy to use, could be used without written instruction and was designed for adolescents with asthma of any severity. Patients and providers noted that the app would help provide information about what to do in the event of an asthma exacerbation and that the application would be used frequently.
Conclusions: There was consensus from both patients and providers that this application is not only functional but also helpful in the event of an asthma exacerbation. The project met the goal of creating a mobile phone application that improved patient access to asthma action plans.

23 Inhaled House Dust Programs Pulmonary Dendritic Cells to Promote Type 2 T-Cell Responses By an Indirect Mechanism

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Rationale: The induction of allergen-specific T helper 2 (Th2) cells by lung dendritic cells (DCs) is a critical step in allergic asthma development. Airway delivery of purified allergens or microbial products can promote Th2 priming by lung DCs, but how environmentally relevant quantities and combinations of these factors affect lung DC function is unclear.
Methods: We investigated the ability of house dust extract (HDE), which contains a mixture of environmental adjuvants, to prime Th2 responses against an innocuous inhaled antigen in mice.
Results: Inhalational exposure to HDE conditioned lung conventional DCs, but not monocyte-derived DCs, to induce antigen-specific Th2 differentiation. Conditioning of DCs by HDE was independent of Toll-like receptor 4 signaling, indicating that environmental endotoxin is dispensable for programming DCs to induce Th2 responses. DCs directly treated with HDE underwent maturation but were poor stimulators of Th2 differentiation. In contrast, DCs treated with bronchoalveolar lavage fluid (BALF) from HDE-exposed mice induced robust Th2 differentiation. DC conditioning by BALF was independent of the proallergic cytokines IL-25, IL-33, and thymic stromal lymphopoietin. BALF treatment of DCs resulted in upregulation of CD80 but low expression of CD40, CD86, and IL-12p40, which was associated with Th2 induction.
Conclusions: These findings support a model whereby environmental adjuvants in house dust indirectly program DCs to prime Th2 responses by triggering the release of endogenous soluble factor(s) by airway cells. Identifying these factors could lead to novel therapeutic targets for allergic asthma.

24 Neuronal Nitric Oxide Synthase Plays an Important Role in the Early TLR4-Triggered Inflammatory Response Via the SOCS1-p38-AP1 Signaling Axis

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Rationale: Asthma and chronic obstructive pulmonary disease (COPD) are very common inflammatory diseases of the airways. Proinflammatory cytokines play a key role in symphonizing the chronic inflammation and structural changes of the respiratory tract in both asthma and COPD. Therefore, identifying the regulatory mechanisms of

proinflammatory cytokine expression can be useful clinically to mitigate tissue damage and foment repair caused by dysregulated or persistent inflammatory conditions.
Methods: Mice were procured from Jackson laboratory, USA. Microvessel Kfc was measured to determine the pulmonary microvascular permeability to liquids, as described previously (Vogel et al., 2000). Bioluminescence intravital imaging was performed using an IVIS charge-coupled camera (PerkinElmer). NO concentration in the culture medium was assessed indirectly by measuring NO2 accumulation using a 280i Nitric Oxide Analyzer (Sievers Instruments) and reported as nmol NO per mg protein. Measurement of peroxynitrite production was done using Coumarin-7-boronate (CBA; Sigma-Aldrich). Protein localization was determined by LSM 510 META confocal laser scanning microscope (Carl Zeiss). RT PCR was done using 7500 Real-Time PCR System (Applied Biosystems).
Results: We studied that NOS1 regulation of suppressor of cytokine signaling-1 (SOCS1) stability in macrophages as a critical effector of macrophage derived proinflammatory cytokines. Further, increased amounts of SOCS1 in NOS1-/- macrophages leads to decreased p38MAPK activity and ultimately decreased activity of AP-1 and NFkB transcription factors, which impairs expression of pro inflammatory cytokines.
Conclusions: Our studies suggest that NOS1 is a clinically relevant drug target to suppress inflammatory conditions like Asthma and chronic obstructive pulmonary disease (COPD).

25 Induction of Kruppel-like Transcription Factor (KLF4&5) By Baker's Yeast Mannan in Human Bronchial Epithelial and Smooth Muscle Cells

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Rationale: Mannan derived from *Saccharomyces cerevisiae*(SC-MN) modulates allergic asthma pathogenesis in a mouse model. The purpose of this study is to explore downstream transcription factor(s) involved in SC-MN's beneficial effects in asthma. The KLFs are important transcription factors in epithelial survival, and modulate epithelial mesenchymal transition and smooth muscle proliferation. As KLF4&5 are highly expressed in lung, we hypothesize that SC-MN can induce KLFs in lung cells.
Methods: Primary normal human epithelial cells (NHBEC) and bronchial smooth muscle cells were incubated with SC-MN and examined for KLF4, KLF5, p38MAPK levels and phosphorylation over a time course by Western Blot (WB). Normal human bronchial smooth muscle cells were analyzed for SM22alpha levels by WB and alpha-isoactin by indirect immunofluorescent staining.
Results: Following exposure to SC-MN, protein levels of KLF4 and KLF5 increased in both NHBEC and NHBSM cells over the subsequent 2-18 h. SC-MN–treated bronchial smooth muscle cells, but not in NHBEC, showed biphasic activation of p38MAPK (5-120 min and 8 h) that is known to lead to KLF phosphorylation in vascular smooth muscle cells. In addition, SC-MN increased smoooth muscle specific alpha-isoactin and SM22aαlpha at 24 hrs, consistent with a phenotype change.
Conclusions: SC-MN can induce KLF4 or KLF5, transcription factors that are important in epithelial survival and regulation of smooth muscle proliferation.