419. Diagnosis and treatment of inflammatory respiratory diseases

P4071

The nose as a research tool: Intra-subject variability in nasal sampling

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Published literature shows that nasal secretions have been collected from the nasal mucosa by modifications of a filter paper/synthetic matrix method for many years (Alam et al. J Immunol Methods. 1992; 155(1):25-9). Inflammatory markers have been measured in samples collected by these methods.

Method: As per our adopted protocol, two Leukosorb (a highly wettable fibrous matrix) strips were applied to the inferior turbinate for 2 minutes then added to a filter tube containing 300µl buffer. Tubes were centrifuged for 20 minutes at 16,000g. Recovered volume was measured. 32 samples were collected from both nostrils of a pool of 5 healthy subjects at 2-4 timepoints. Total protein concentration (TPC) of each sample was measured. TPC of samples from subjects sampled at different timepoints were compared (n=10) as was the variability between nostrils of the same subject (n=12).

Results: The median percentage difference between the maximum and minimum TPC from a nostril of each subject was 46% (range 13-359%).
The median percentage difference between TPC of left and right nostrils at the same sample timepoint was 19% (range 4-186%).

Conclusions: In our study, variation existed in TPC between nostrils when sampled at the same time. We suggest that, at each timepoint, samples from both nostrils should be pooled to create one sample. Intra subject variability exists in our cohort of healthy subjects between timepoints and between nostrils. A larger study is needed to investigate the full extent of this variability, and the influence, if any, of the "nasal cycle" on sample characteristics before inflammatory markers e.g. cytokines can be measured with confidence.

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Specific nasal challenge in the diagnosis of alternaria-induced asthma

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Background: Allergic sensitization to Alternaria has been identified as a risk factor for the development and persistence of asthma and is associated with severe and life-threatening episodes. The interaction between upper and lower airways has not been investigated for Alternaria.

Aims and objectives: To investigate whether specific nasal challenge with Alternaria allergen can be used as a diagnostic tool for Alternaria-induced asthma.

Patients and methods: The study included 15 adults patients with mild, allergic asthma sensitive to Alternaria and two control groups: 1) 8 patients with mild, allergic asthma non-attributed to Alternaria and 2) 7 healthy controls. Diagnosis of asthma was already established by positive both reversibility and methacholine test. Two nasal provocation tests were performed, one with normal saline (placebo) and another with Alternaria antigen (specific nasal challenge, SNC) performed at two different days. FEV_1 was measured during a 12-hour period, at 18 time points (10, 20, 30, 40, 50, 60, 90, 120, 180, 240, 300, 360, 420, 480, 540, 600, 660, 720 minutes) after nasal provocation.

Results: A significant FEV_1 decline >20% from baseline (26.02±2.38%) was recorded after SNC ($p<0.001$ compared to placebo) in 10 out of the 15 patients (66.7%) ($p<0.001$ compared to both control groups). All asthmatic responses were initiated with a mean 8-hour latency, were recorded at more than three consecutive time points and were sustained until the end of the 12-hour time period.

Conclusions: Specific nasal challenge could be a reliable and specific tool for the diagnosis of Alternaria-induced asthma, alternatively to bronchial challenge, in case confirmation of mould implication is necessary.

P4073

Rhinology findings and their clinical usefulness for closer asthma fenotyping

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Background: Our previous study conducted on patients with severe persistent asthma documented a strong correlation between eosinophilic inflammation of upper and lower airways.The aim of presented study was to determine whether there are existing differences between the intensity of eosinophilia and/or polyp presentation in upper airways in patients with eosinophilic astma with no clinically significant allergy versus patients with eosinophilic and allergic asthma.

Methods: 32 patients with severe persistent asthma were included for evaluation. According to markers of eosinophilia (FeNO, ECP, eo in NM, BALTe, IS and FBC) and allergy (SPT, spec. IgE) we devided asthmatics into three groups: I. eosinophilic and allergic, II. eosinophilic but non-allergic and III. non-eosinophilic. We also focused on presence of perrenial allergy and NSAID intolerance. CT scan of paranasal sinuses, rhinology examination and operation history were included for evaluation of nasal polyps (NP) presentation.

Results: Significant correlations were found in eosinophil counts in NM and NP presentation (p=0,0012). Intensity of NP correlated mostly with eosinophilic but non-allergic astma (0,0117). Intensity of eosinophilia in NM and presentation of NP correlated in the group I mostly with mould allergy, in the group II with NSAID intolerance ($p<0,05$).

Conclusion: We found presence of nasal polyps as an negativ prognostic factor in patients with severe asthma - in allergic asthmatics indicates the risk for mould allergy (and possible ABPA or SAFS), in non-allergic astmatics for NSAID intolerance. Previous study data were considered (ERS10L1_6353, ERJ, 2010, 36 Suppl. 54). Supp. by VZ MSM 0021620812 grant.

P4074

Mild asthmatic patients consistently respond to natural, low dose, allergen challenge in an EEC

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Introduction: The cat allergen, *Felis domesticus* (*Fel d1*), is a common trigger of allergic rhinoconjunctivitis and asthma exacerbation. Aerosolized *Fel d1* in an Environmental Exposure Chamber (EEC) reproducibly evokes nasal and ocular symptoms in cat allergic patients. Mild asthmatics' respiratory responses inside the EEC were assessed.
Methods: Patients with history of rhinoconjunctivitis and positive SPT to *Fel d1* were exposed to low, well-controlled levels of aerosolized *Fel d1* in an EEC for 3hrs, over 4 consecutive days [V2a, V2b, V2c, V2d]. Total nasal, ocular, and asthma (cough, wheezing, & shortness of breath) symptoms were collected [scale:0-3] pre-EEC and then every 30min. FEV_1 was measured at screening, pre- & post-EEC. Of the patients who met eligibility criteria, 12 patients were mild asthmatics (GINA classification 1). Asthma scores and FEV_1 from these patients were evaluated. FEV_1 measures were analyzed using paired t-test.
Results: A consistent decrease in FEV_1 and an exacerbation of asthma symptoms was observed in mild asthmatic patients over 4 consecutive days. At V2a, there was a decrease of 10.9 to 87.6±4.52% ($p<0.05$) in% predicted FEV_1 with decreases of 10.2 to 87.1±5.25% ($p=0.07$) [V2b], 11.9 to 84.9±5.50% ($p<0.05$) [V2c], and 12.2 to 85.53±5.50% ($p<0.05$) [V2d]. Asthma scores showed consistent increase over 4 consecutive visits with mean maximum asthma scores between 3.4 to 3.7 units.
Conclusion: Low-dose aerosolized cat allergen EEC clinical model provides a safe, consistent and natural exposure environment to exacerbate a clinical response in asthmatic patients indicating that the EEC model may be used for testing putative therapeutics for cat allergy induced asthma.

P4075

Tuberculin skin test sensivity in asthma patients

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Aim: The aim of this study was to evaluate the tuberculin reaction which develops with Th 1 type immune reaction in asthma in which Th2 type immune reaction is dominant.
Material and method: This study included 36 cases with allergic asthma, 64 cases with non allergic asthma and 51 cases without asthma. Tuberculin skin test was applied with Monteux method to all cases and induration diameter developed after 72 hours was recorded as millimeter.
Results: Tuberculin positivity was significantly different between cases with asthma and cases without asthma ($p<0.05$). The tuberculin induration diameter was calculated as 10.9±9.04 mm in cases with asthma and 15.3±5.95 mm in cases without asthma. The difference between them was significant ($p<0.05$). There was no significant relationship between tuberculin induration diameter and BCG scar ($p>0.05$). With respect to tuberculin positivity, significant difference was not present between asthma cases that are allergic and non allergic ($p>0.05$).
Conclusion: While the tuberculin skin test results are evaluated presence of allergic diseases should be taken into consideration.

P4076

Multiplexed IgE determination in relation to asthma, exhaled NO and bronchial reactivity: Results from a population based survey

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Background: IgE sensitization is an important risk factor for the development and management of asthma. The aim of this study was to investigate the IgE antibody profile for a broad spectrum of allergen molecules in asthmatic patients.
Methods: Participants from the European Community Respiratory Health Survey II (n=467) were tested with ImmunoCAP ISAC against 103 allergen molecules. Bronchial responsiveness was measured with methacholine test and bronchial inflammation with $F_ENO_{0.05}$.
Results: A total of 50.7% of the controls and 80.2% of the asthmatics were sensitized against at least one food, pollen, furry animals, mould or latex allergen ($p<0.0001$). Asthma and increased $F_ENO_{0.05}$ were independently related to IgE against pollen and perennial inhaled allergens, while bronchial responsiveness was only independently associated with perennial allergens. Sensitization against perennial allergens was associated with asthma (OR 3.6 CI 95% 1.2-10.6) and bronchial responsiveness. Sensitization to food allergens was related to asthma and increased $F_ENO_{0.05}$ only if IgE against pollen and/or perennial allergens were present. Simultaneous sensitization to perennial, pollen and food allergens involves the highest risk for asthma (OR 14.7 CI 95% 7.1-30.5), bronchial inflammation and responsiveness.
Conclusion: $F_ENO_{0.05}$ values, bronchial responsiveness and risk for asthma increase with multiple sensitization to different allergen groups. IgE against food allergens increases the risk for asthma and increased $F_ENO_{0.05}$ in subjects with simultaneous sensitization to pollen and/or perennial allergens.

P4077

Experience of applying flow cytofluorometry to analyze immune cells in saliva from COPD patients

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The objective was to analyze the composition of immune cells in saliva from smoking patients with early forms of COPD employed at the radiochemical facility. A group of patients with early forms of COPD (144 individuals) employed at the radiochemical facility are under the constant follow-up for the recent ten years, in addition to 264 individuals without signs of COPD, but smokers, matched to the main group by age, gender, working conditions, smoking index and history. The study included 23 individuals from the main group and 10 individuals from the group of comparison. Leukocytes were measured in saliva, mean 2.4×10^6/ml. Cell viability was determined using 7-AAD. A subpopulation of immunocytes was counted in viable cells expressing a marker, CD45. There were no significant differences in total leukocytes and cells expressing markers of granulocytes (CD13+) in saliva between COPD patients and the group of comparison, the CD13+ cells amounted to 0.36% in the main group and 0% in the group of comparison. There was a significant increase in CD3+CD8- cells (25.85% vs 1.4% in the control group, p=0.049), and CD3+CD4+n (3.3% vs 0.6%, p=0.049) in COPD patients, which proved an increase in total T-lymphocytes and T-helpers without any increase in cytotoxic cells in mucosalivary region, which is constantly exposed to tobacco smoke in smoking patients with COPD. The obtained findings allow assuming involvement of CD3+CD4+ lymphocytes in pathogenesis of inflammatory alterations in COPD.

P4078

Basophil activation test as support for distinguishing between aspirin-induced asthma and allergic reaction to ASA

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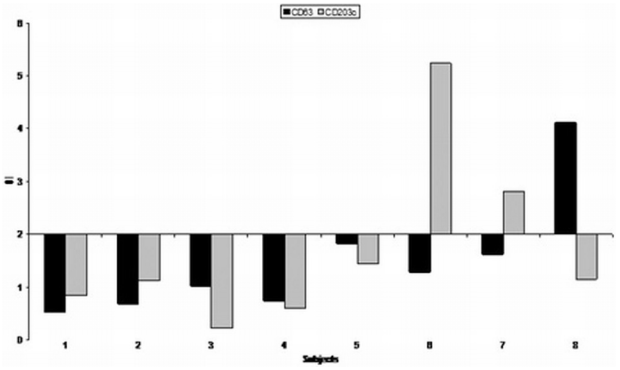
Aspirin-induced asthma (AIA),is a clinical syndrome associated with severe and chronic inflammation in both upper and lower airways.Despite their similarities,AIA is quite distinct from Acetyl Salicylic Acid (ASA) allergy.
AIA remains largely underdiagnosed,mainly for the lack of diagnostic methods to detect ASA sensitisation without risk and to distinguish it from ASA allergy.Here we investigate if it is possible to apply a method designed for allergic sensitization,in order to distinguish hypersensitivity from allergy to ASA.This method is well-known as Basophil Activation Test (BAT),and it consist of *in vitro* blood cells stimulation by ASA and then detection of two activation markers (CD63/CD203c) on basophils,typical of allergic reaction.
We performed BAT on peripheral blood samples from 8 subjects referring respiratory disorders after ASA assumption.The expression of markers were considered positive when the Stimulation Index (SI) was higher than 2,defining SI the ratio between markers on basophils stimulated and unstimulated.BAT evidenced activation in three subjects,indicating that they suffer from ASA allergy.The other five subjects did not show any basophil activation (BA).



Since BA is a clear sign of allergic reaction,it is plausible to conclude that the subjects who do not respond to BAT are suffering from AIA,so we may assume that BAT is useful to distinguish between AIA and ASA allergy.

P4079

Health related quality of life and sense of coherence in adolescents with asthma

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Aim: To prospectively study adolescents with asthma in transition from child to adult with respect to Health Related quality of life "HRQOL" and Sense of Coherence "SOC".
Method: Teenagers with asthma (n=156) were screened employing spirometry, bronchial challenge, skin prick test and exercise test at the time of referral and after five years. They completed the "Living with Asthma Questionnaire" and the Sense of Coherence "SOC" instrument. Patients with mild-to-moderate asthma were assigned randomly to an adult asthma clinic or to primary care.
Results: At both time-points the HRQOL of the men was better than that of the women ($p<0.001$). HRQOL improved for both men and women. Lung function, atopy, bronchial hyper-responsiveness did not exert any impact on HRQOL or SOC. However poor adherence to the recommended asthma treatment was associated with lower HRQOL (OR= 0.29; 95% CI= 0.11-0.73; $P<0.01$). Young women who exercised regularly exhibited better HRQOL than those who did not ($p<0.001$). Only women with severe asthma demonstrated a poorer HRQOL. Over the five year period the men showed a significant stronger SOC compared to the women ($p<0.05$). Lung function and HRQOL remain stable regardless of the randomization to an asthma clinic or to primary care,
Conclusion: The HRQOL of adolescents with asthma improves with age. Young men with asthma have stronger SOC compared to young women. Adolescents with mild-to-moderate asthma receive appropriate care in the primary care system. The negative impact of poor adherence to asthma treatment on HRQOL emphasizes the importance of healthcare programs including patient education and support for adolescents with asthma and with special attention to young women.

P4080

Quantitative assessment of cysteinyl leukotrienes in human sputum during the allergen-induced asthmatic response and the effect of GSK2190915, a 5-lipoxygenase activating protein (FLAP) inhibitor

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Accurate measurement of the cysteinyl leukotrienes (cLTs) LTC_4, LTD_4, and LTE_4 in human sputum may be useful for assessing airway inflammation. GSK2190915 is a potent FLAP inhibitor that inhibits the synthesis of cLTs. The objective of this study was to assess the effect of GSK2190915 on the production of cLTs in human sputum using ultra pressure liquid chromatography-mass spectrometry.
In this double-blind, placebo-controlled, crossover study subjects took 100mg GSK219095 and placebo orally once daily for 5 days, in randomized order. On Day 3 they had an inhaled allergen challenge and on Days 4 and 5 they had induced sputum collection. Sputum was frozen at –80°C until measurement. For analysis, 200-500µL of sputum supernatant was diluted into 1mL of water spiked with $[^2H_3]$-LTE_4 internal standard and was extracted using an Empore C-18 solid phase extraction disk prior to analysis.
The limit of detection for each analyte was 1pg/mL. LTD_4 and LTE_4 were detected in most samples while LTC_4 was generally below the limit of detection:

Sputum	Treatment	Day	No./No. Imputed	Median (pg/mL)	Interquartile Range (pg/mL)	
LTD_4	Placebo	Screen	17/7	5.880	0.500	30.620
		Day 4 (1hr pre-dose)	16/6	9.270	0.500	21.185
		Day 5 (24hr post dose)	15/7	3.990	0.500	11.720
	915 100mg	Day 4 (1hr pre-dose)	18/9	1.475	0.500	8.460
		Day 5 (24hr post dose)	15/7	1.200	0.500	52.110
LTE_4	Placebo	Screen	17/7	6.820	0.500	49.420
		Day 4 (1hr pre-dose)	16/5	9.195	0.500	32.685
		Day 5 (24hr post dose)	15/10	0.500	0.500	37.970
	915 100mg	Day 4 (1hr pre-dose)	18/12	0.500	0.500	8.920
		Day 5 (24hr post dose)	15/10	0.500	0.500	3.880

Measurement of cLTs using this method allows for the accurate and reliable quantitation in human sputum and may allow a better understanding of the role of these molecules in airway inflammation.
Study funded by GlaxoSmithKline. GSK study LPA111834. Clinicaltrials.gov identifier NCT00748306.

P4081

Churg Strauss syndrome associated with montelukast treatment – Study case

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Churg Strauss Syndrome is a systemic vasculitis occurring in patients with asthma, blood eosinophilia and vasculitis involving more than two extrapulmonary organs. In the past few years, there have been several reports about leucotriene receptor antagonist (LTRA), therapy implications in the pathogenesis of Churg Strauss syndrome.
We report a case, 62 years old, nonsmoker women with a 20 years history of moderate asthma treated with Fluticasone/Salmeterol (50/500) for 5 year and Montelukast (10mg) for 5 month (had not been on steroid treatment other than inhaled with no decreasing of steroid dose). The patient was admitted in our hospital in December with malaise, fever, headache, wheezing, musculoskeletal and thoracic pain, rhinitis and gastroenteritis. A chest radiograph showed only few reticulonodular infiltrates. Chest CT revealed infiltrates in right superior lobe. The blood eosinphilia was 52% of her total WBC count. Bronchioalveolar lavage showed 14,6% eosinophils; medular biopsy revealed central eosinophils. The gastrointestinal biopsy show eosinophilic infiltration. Serum IgE level was elevated. The patient has more than four of the six diagnostic criteria (developed by ACR in 1990) for Churg Strauss syndrome. We believed that Montelukast use was associated with CSS. Discontinuation of Montelukast and association of oral Prednisone (1mg/kg) generated rapid improvement of the symptoms and favorable outcome.
Respiratory physicians need to evaluated the risk of CSS when treating patients with LTRA. But Montelukast has been associated with CSS in a very small number. The efficacity, lack of major side effects and easy administration make Montelukast a good alternative in asthma management.

P4082

Age-specific background in inpatients with severe asthma exacerbation

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Background: Characteristics resulting in inpatients with severe asthma exacerbation remain unclear. It is considered that characteristics and risk factors in inpatients with severe asthma vary depending on age. However, they are rarely investigated.
Objective: We investigated the differences in characteristics and risk factors in different age groups. We clarified the countermeasures for each age group, and aimed to reduce the number of inpatients with severe asthma exacerbation.
Methods: All asthma inpatients who were hospitalized with SpO2 <90% (on room air), the breathless at rest, the increased respiratory rate and pulse rate >120/min between 2007-2009 were investigated. We compared their characteristics among the young age group, middle age group, and advanced age group.
Results: The total number of severe asthma exacerbations was 75. In the young age group, 55.6% has mild asthma before hospitalization. The group had poor treatment adherence, a high rate of smoking and a high rate of pet ownership. The percentage of continuous ICS users in the group was 22.2%. In the middle age group, 54.8% has severe asthma before hospitalization. The group had high rates of aspirin-intolerant asthma and chronic sinusitis. The percentage of continuous ICS users in the group was 61.3%. In the advanced age group, high rates of hypertention/heart disease and diabetes mellitus were observed. The group had good treatment adherence. The percentage of continuous ICS users in the group was 82.4%.
Conclusions: The characteristics and the risk factors in inpatients with severe asthma vary depending on age. We need to establish countermeasures for asthma exacerbation according to the characteristics and risk factor depending on age.

P4083

Is it useful CD4+CD103+/CD4+ ratio for the diagnosis of lung sarcoidosis?

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The diagnosis of lung sarcoidosis relies in part on the observation of alveolar CD4+ cells and the demonstration of an increased CD4/CD8 ratio. This ratio has been proposed as a diagnostic tool for pulmonary sarcoidosis. But this anomaly is also found in other lung diseases too. The search for other pathognomonic criteria allowing the discrimination of sarcoidosis patients (pts.) from patients with CD4+ alveolar lymphocytosis has been disappointing.
We investigated CD103 molecules on the T lymphocytes subpopulations. The expression of these molecules was examined on BAL lymphocytes from sarcoid patients with different radiologycal stages (Ist. – 23 pts; II – 16 pts: III – 9 pts.) and Lefgren's sindrome (25 pts) and patients with other lung disemination (17 pts.). For all patients, the expression of CD3, CD4, CD8 and CD103 was assessed by flow cytometry.
We found that CD4+/CD8+ ratio in I stage was 6,5±4,1; II st. – 4,5±2,3, III st. – 4,1±3,3, Lefgren's sindrome – 8,6±4,9 and other lung disemination – 1,9±1,7. CD4+CD103+/CD4+ ratio in I st. – 0,2±0,1; 0,2±0,1; 0,2±0,1; 0,1±0,1 and 0,4±0,2 respectively. CD4+CD103+/CD4+ ratio differ significally ($p< 0,05$) in all stages of sarcoidosis compared with other lung disemination while CD4+/CD8+ not.
Our findings demonstrate that the combined use of CD4+/CD8+ and CD4+CD103+/CD4+ ratios provides a highly sensitive indicator of lung sarcoidosis in patients with other CD4+ BAL lymphocytosis.

P4084

Premenstrual asthma and leukotriene variations in the menstrual cycle

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Several authors report an increase in leukotriene C4 in the premenstrual phase in women with severe premenstrual asthma, indicating that antileukotrienes could be used in treatment.

Objective: To analyse the role of leukotrienes in premenstrual asthma.

Methods: A questionnaire on respiratory symptoms and peak flow during menstrual cycle was given to women of fertile age to define them as asthmatics who suffered from premenstrual asthma or not, and the degree of asthma severity (GINA 2005). PMA was defined as a clinical or functional deterioration (≥20%) in the premenstrual phase compared with the preovulatory phase. Blood samples to measure leukotriene C4 were taken during the preovulatory and premenstrual phases.

Results: Blood samples were taken in 62 asthmatic women, 34 of whom (54.3%) presented PMA criteria with a premenstrual deterioration of between 20% and 40%. There was no difference in leukotriene C4 levels between the preovulatory and premenstrual phases in the women who suffered from PMA (1.50 ng/mL vs. 1.31 ng/mL; p=0.32) and those who did not (1.40 ng/mL vs. 1.29 ng/mL; p=0.62). Neither were there any differences in leukotriene levels between women with or without PMA. The results were similar for each category of asthma severity.

Conclusions: Our data show that leukotriene C4 does not appear to be involved in the pathogenesis of premenstrual asthma, or support the use of anti-leukotrienes in the treatment of premenstrual asthma, at least in women with a moderate premenstrual deterioration. No differences appeared in any of the categories of asthma severity.

P4085

Chronic exposure to allergen and cigarette smoke induces predominantly features of COPD

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Rationale: Tobacco smoking by asthmatics correlates with disease severity and smoking is a risk factor for COPD. We previously demonstrated in a short-term mouse model that combining allergen with cigarette smoke exposure aggravated allergic airway inflammation. Here we investigated the effects of (very) long-term combined exposure to allergen and cigarette smoke.

Methods: Sensitized C57/Bl6 mice were exposed to ovalbumin (OVA) or saline (PBS) twice a week, combined with air or mainstream cigarette smoke (5 times/week) for 6 months. Bronchoalveolar lavage fluid (BAL) and lung samples were processed for immunological and histological examination.

Results: Six months exposure to OVA/air, PBS/smoke or OVA/smoke induced a pulmonary inflammation with increased macrophages, dendritic cells, lymphocytes and MIP-3α in BAL compared to PBS/air exposure. OVA and/or smoke exposure induced airway wall remodeling (goblet cells, collagen deposition) and lymphoid neogenesis.

Mice exposed to OVA/air had airway eosinophilia, which was absent or strongly reduced in the PBS/smoke and OVA/smoke groups. OVA-IgE was elevated in both OVA/air and OVA/smoke mice, although more pronounced in the former.

In contrast, PBS/smoke and OVA/smoke exposure, but not OVA/air exposure induced a marked neutrophilic inflammation ($314\pm91\times10^3$and $208\pm36\times10^3$ versus $7\pm2\times10^3$ cells in BAL, respectively; $p<0.05$). This neutrophilia was paralleled by increased levels of KC. Both smoke-exposed groups also had emphysema.

Conclusion: Chronic exposure to aeroallergens in the presence of cigarette smoke results in a pathology with predominantly features of COPD, albeit limited characteristics of allergy remain present.

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P4086

Passive smoking may influence respiratory allergic reaction

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It has been proven that smoking boosts the symptoms of allergy; the smokers have higher bronchial responsiveness and tobacco smoking provokes a strong immunological imbalance to those exposed.

The aim of our study was to evaluate reactivity and sensitivity of respiratory tract in persons with the symptoms of allergic rhinitis and proven tobacco smoke allergy who are active smokers or passively exposed to tobacco smoke.

Materials and methods: We evaluated 40 patients, average age 34 years divided into two groups: group I - active smokers (with average 16.4±8.7 package years) and group II – passive smokers. All subjects had symptoms of allergic rhinitis, local ORL findings that confirms excluded vasomotor rhinitis, positive Prick test on inhalation allergens of tobacco smoke and normal basal spirometry findings. Non-specific bronchoprovocative testing was done by intermittent inhalation of histamine in progressive grooving doze and result was expressed by the value of provocative doze by which the value of FEV1 was reduced by 20% of basal FEV1. Histamine responsiveness was analyzed using dose-response slope to describe each subject's responsiveness (positive results were considered to be if reactivity was between 520-2000mcg).

Results: Bronchial activity was confirmed in 58.2% in smoking group and 39.5% in non-smoking group. The degree of bronchial hypereactivity didn't differ between groups, although provocative doze was in lower concentrations in smoking group, but difference wasn't significant.

Conclusion: Although we confirmed that smokers have higher degree of hypereactivity than non-smokers, our results in passive smokers group may implicate on significance of passive smoking.

P4087

Effect of dust aerosol in patients with asthma

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Dust storms are said to exacerbate asthma in desert areas. We explored the role of dust component of dust storm in exacerbation of asthma by using equivalent amount of dust administered through an aerosol. Samples of sandy soil were collected from Bikaner, Jaipur and Ganganagar districts. Clay soil was procured from Ganganagar. These are dust storm prone areas of the state of Rajasthan in India. Dust aerosol was created in a specially designed re-suspension chamber to simulate mild to moderate dust storm. Concentration and size of dust particles (0.1 to 10μm) in the chamber was monitored with help of an aerosol spectrometer. Twenty patients with mild asthma having FEV1 more than 70% of predicted, were recruited in the study after obtaining an informed consent. These subjects were challenged with four samples of dust and placebo. The challenge aerosols were administered randomly in single blind cross over design on 5 study days at an interval of at least two weeks. Subjects took three tidal breaths of dust aerosol from the chamber. FEV_1 was measured for next 60 minutes. Dust samples were also analysed for particle size and adhesiveness. The maximal fall in FEV1 was observed 15 min after exposure with all dust samples. Mean fall in FEV_1 for clay, Bikaner, Jaipur and Ganganagar sand dust aerosol samples were (0.69±.08), (0.52±.06), (0.39±.07), (0.32±.04) liters respectively. It was observed that dust sample having higher adhesiveness and higher fraction of small size particles caused maximal fall in FEV_1 ($p<0.05$). It can be concluded that small size dust particles of dust storm with higher adhesive properties have potential of causing aggravation of asthma.

P4088

What does healthy people know about asthma?

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We aimed to assess knowledge about asthma in healthy adults from the general Portuguese population.

Data were collected as part of the Portuguese National Asthma Survey, a nationwide, cross-sectional, list-assisted, random-digit-dialing telephone survey. Adult participants without respiratory symptoms answered a 13-item statements tool with agree/disagree answer format about asthma knowledge.

The mean (SD) age of the 858 participants included was 56.3 (17.4); 53% (457) female; 47% (401) had up to 4 years (y) of education, 20% (175) 4-9y, 21% (176) 9-12y and 12% (104) had more than 12y; 22% (186) were classified in the low, 73% (619) medium, 5% (44) high socioeconomic strata. The highest frequencies of correct answers were for "Asthma cannot be cured, but it can be controlled" 86% (726); "Asthma is a chronic disease"70% (592) and "People with asthma may exercise, except when having an asthma attack"68% (573). The most frequent errors were on: "Inhaled asthma medication are dangerous" 84% (710), "Asthma starts in childhood or young age" 75% (631) and "The airways are inflamed in asthma, even out of an asthma attack" 67% (563). No one answered correctly to all statements; 19% (158) answered correctly to 10 or more and 23% (192) to 5 or less statements. Knowledge was significantly different across socioeconomic strata, education levels, age (all $p<0.001$) and gender ($p=0.046$)

A wide variation on knowledge about asthma was observed among healthy adults from the Portuguese general population. Some topics such as chronicity and individual impact of asthma seem to be well known, while topics as treatment and persistence of inflammation are poorly understood.

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P4089

Severe asthma: Clinical features and management in Tunisia

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Chronic severe asthma (CSA) is a complex and heterogeneous condition with distinct subphenotypes leading to impaired quality of life and excessive healthcare need. Aim of the study was to describe the different subphenotypes of CSA and to assess its management in Tunisia.

Methods: The clinical data of 54 patients (1998-2011) with CSA were analysed. Three groups were identified according to the CSA WHO definition. G1: untreated CSA due to unavailability of therapy, G2: difficult-to-treat CSA due to compliance issues and inappropriate use of medicines, and G3: treatment-resistant CSA. The latter includes 2 subgroups: uncontroled asthma despite the highest level of recommended treatment (G3a) and asthma which is controled only with the highest level of recommended treatment (G3b).

Results: Patients are distributed as follows: G1: 27 patients (50%), G2: 8 patients (15%), G3: 19 patients (25%) including 9 cases of G3a (17%) and 10 cases of G3b (18%). Treatment included high doses of inhaled corticosteroids in all groups, long acting β2-agonists were available for G2 and G3 but not for G1 due to absence of social coverage. Oral corticosteroids were prescribed in 18 patients (33%), among whom 50% belong to G1. Admissions in intensive care unit for severe exacerbation were recorded in 18 cases (29%) and near-fatal-asthma was diagnosed in 13 cases (21%). CSA aetiologies were allergy: 37 cases, allergic bronchopulmonary aspergillosis: 3 cases, gastro oesophageal reflux: 4 cases and sensitivity to aspirin: 1 case.

Conclusions: Management of CSA in Tunisia hospitals still suffers from unavailability of appropriate therapy for an important proportion of patients, which makes recourse to oral corticosteroids more frequent than in the reported literature.

P4090

Characteristics of 51 asthmatics autopsied in São Paulo, Brazil from 2005-2009

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Introduction: Deaths attributed to asthma in the city of São Paulo, Brazil have decreased since 2005. We have previously reported the clinical characteristics of asthmatics autopsied in the city of Sao Paulo from 1996-2004 (Mauad, 2008). Our aim was to describe the clinical characteristics of 51 fatal asthmatics autopsied in Sao Paulo from 2005 to 2009.

Methods: Fifty-one patients who were autopsied at the Death Verification Service of Sao Paulo from 2005-2009 and had deaths confirmed macro and microscopically as due to status asthmaticus were studied. An interview with the next of kin assessed demographics, history and treatment of asthma and events surrounding the last attack; written informed consent was obtained from the next of kin.

Results: There were 28 females and 23 males, with a median age of 50 years (range 20-73). Thirty-nine patients were whites and 26 patients had at least 8 years of education. Thirty-one individuals were non-smokers, 11 were current smokers and 9 were ex-smokers. The age at onset of asthma <12 years was reported in 51% of the cases and 30 patients did not have regular medical follow-up. Seven individuals used inhaled corticosteroids and 45 used regular short-acting bronchodilators. Seventeen patients had been hospitalized due to asthma in the previous year and 8 had been admitted to an intensive care unit. The duration of the last exacerbation was >24 hours for 55% of the patients. These characteristics are similar to those described for asthmatics deceased from 1996-2004.

Conclusion: Fatal asthmatics deceased in the city of São Paulo from 2005-2009 have similar characteristics to those deceased from 1996-2004, despite of a decreasing number of asthma deaths.