

MONDAY, SEPTEMBER 4TH 2006

pneumonia (HR: 0.81; 95% CI: 0.31-2.12), hospitalisation from pneumonia (HR: 0.79; 95% CI: 0.54-1.17) and overall pneumonia (HR: 0.84; 95% CI: 0.59-1.19). Pneumococcal vaccination did not show any protective effect against death risk from pneumonia (HR: 1.07; 95% CI: 0.39-2.92) or death risk from any cause (HR: 1.15; CI 95%: 0.86-1.52) among overall population with COPD.

**Conclusions:** These results suggest that the pneumococcal polysaccharide vaccine may not be effective to diminish incidence and severity of pneumococcal infections in elderly subjects with COPD.

**P2575****Correlation of regional death rates for asthma and influenza**

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**Background:** Regional differences in asthma death rate still exist in Japan, but it is not fully understood what this depends on. We tried to identify related factors by examining some "vital statistics of Japan", focusing on the relationship between asthma and influenza.

**Methods:** Referring to statistics produced by the Ministry of Health, Labor and Welfare of Japan from 1997 till 2003, we analyzed the correlation of mean death rates for asthma, influenza and other pulmonary diseases in 47 prefectures. Various social data possibly related to regional differences in asthma death, such as the rate of the aged population, the number of pulmonary specialists etc. were also evaluated. Further, the regional death rates for influenza were compared with those for asthma in each year of the study.

**Results:** Correlation coefficients for the mean regional death rate for asthma versus other pulmonary diseases during the period were as follows; vs. influenza 0.71, vs. pneumonia 0.62, vs. COPD 0.62, vs. pulmonary malignancy 0.51. In 2003, the regional rate of asthma death correlated significantly with that of influenza death ( $r = 0.54$ ), aged population ( $r = 0.42$ ), pulmonary disease specialists per hospital ( $r = -0.44$ ), and annual per capita income ( $r = -0.37$ ). Significant correlations between regional death rates for asthma and influenza were the most persistent throughout the period. ( $r = 0.53$  in 1997, 0.53 in 1998, 0.54 in 1999, 0.49 in 2001, 0.54 in 2003). Using rank correlations, significance existed even in 2000 ( $\rho = 0.49$ ) and 2002 ( $\rho = 0.39$ ).

**Conclusions:** These results suggest that regional differences in asthma death are associated with the prevalence of influenza per se, or regional problems encompassing influenza death.

**P2576****Cost-effectiveness of a Brazilian program for severe asthma**

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**Background:** severe uncontrolled asthma results in economical burden to families and health system. Objective: estimate the cost-effectiveness of a program providing free professional care and inhaled medication to severe asthmatics in Salvador, and compare it to the regular asthma management offered by the public system.

**Methods:** pre and post-intervention cohort study of 81 severe asthmatics 12 to 75 years old. Information on doctor visits, exams, medications, hospitalizations, intensive care unit (ICU) stays and visits to emergency rooms (ER) were collected. Family direct and indirect costs were estimated by using a questionnaire validated for this study. Asthma control was evaluated by lung function, and ACQ (Asthma Control Questionnaire) scores, while quality of life was measured by AQLQ (Asthma Quality of Life Questionnaire) scores, before and after enrolment in ProAR.

**Results:** 64 patients, mean age of 45 years, concluded the study. Comparing the year after and before enrolment, we found a reduction of 99% in hospitalization, 100% in ICU usage and 97% in visits to ER. ACQ scores, PEF, VEF1 and AQLQ improved 46%, 32%, 6.3% and 77% respectively. There was a surplus of US\$566.23/patient-year in public health resources in favour of ProAR. The increased cost of medication from US\$170.36 to US\$369.43 was compensated by the reduction in hospital and ER costs from US\$ 776.5 to US\$ 11.17. Mean annual income of families increased US\$213.87 (10%) and their expenses with asthma reduced by US\$ 676.87 (86%).

**Conclusion:** a program providing free medication for severe asthmatics in a developing country is highly cost-effective. It results in decrease in morbidity and reduction in public and family costs with better quality of life.

**P2578****Serious shortcomings in the management of children with anaphylaxis in Scottish schools: national survey**

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**Objective:** To assess the provision of care for the prevention and treatment of anaphylaxis in Scottish schools.

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## 239. Bronchial asthma – issues in inflammation, prevention and management

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**P2574****Effectiveness of polysaccharide pneumococcal vaccination among subjects with chronic obstructive pulmonary disease**

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**Aim:** The present study assessed the effectiveness of the 23-valent pneumococcal polysaccharide vaccine to prevent pneumococcal disease, pneumonia and death in older adults with chronic obstructive pulmonary disease (COPD).

**Methods:** A prospective cohort study was conducted between January 2002 and April 2005, including all individuals >65 yrs with COPD assigned to 8 Primary Care Centres in Tarragona, Spain (n=1,299). The primary outcomes were invasive pneumococcal disease, pneumococcal pneumonia, overall pneumonia (hospitalised or outpatient) and death from pneumonia. All pneumonias were validated by checking clinical records. The association between the pneumococcal vaccination and the risk of each outcome was evaluated by means of multivariate Cox proportional-hazard models, adjusted by age, sex, influenza vaccination status, comorbidity and immunological status.

**Results:** Pneumococcal vaccination did not alter the risk of invasive pneumococcal disease (HR: 1.14; 95% CI: 0.20-6.40). The pneumococcal vaccination was associated with a non significant reductions in the risks of pneumococcal

**Method:** National postal survey of a representative sample of 250 Scottish schools, enquiring about the prevalence of anaphylaxis, approaches to minimising the risk of food-related allergic reactions developing and emergency treatment provisions if reactions do occur.

**Results:** We obtained responses from 60% (n=149) of schools, 61% (95%CI 53-68) of which reported having one or more child known to be at high risk of experiencing anaphylaxis. Most (80%, 95%CI 71-87) schools with children known to be at high risk, reported having personalised care plans in place and invariably had at least one member of staff trained in the emergency management of anaphylaxis, with access to adrenaline on-site in 97% (95%CI 91-99) of these schools. However, only 48% (95%CI 36-61; p<0.001) of schools with no children known to be high risk had a trained member of staff; access to adrenaline was very poor in these schools (12%, 95%CI 6-23; p<0.001). Overall, 59% (95%CI 51-66) of respondents did not feel confident in their school's ability to respond in an emergency situation, with 78% (95%CI 70-84) expressing the need for detailed guidance on appropriate standards of care. Development and implementation of policies to minimise risk of triggering reactions were poor in most schools.

**Conclusions:** Many schools are under-prepared should an emergency arise, which is concerning considering the severe, unpredictable nature of first attacks. There is an expressed need for detailed national guidelines concerning the prevention and treatment of anaphylaxis in schools in Scotland.

#### P2579

##### Asthma Control Test™ in assessing the asthma control

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**Background.** According to our survey in 2003 the prevalence of asthma in R. Macedonia in the age group 20-44 was found to be 5.4% suggesting more than 100,000 subjects with asthma.

**Objective:** To assess the usefulness of the Asthma Control Test™ (ACT) for identifying patients with poorly controlled disease.

**Methods.** ACT was completed by 264 patients with asthma (123 males and 143 females, aged 18 to 64 years, mean age 37.7±12.5) classified and treated according to the GINA 2004 recommendations. The disease control in the same patients was also evaluated by spirometry.

**Results.** The mean asthma score was found to be 21.7±3.5, ranging from 12 to 25. The asthma scores 25, 20-24 and less than 20 were obtained in 20.2%, 55.2% and 24.6%, respectively. The highest mean asthma score was obtained in the females aged 18-30 (22.9±1.5), and the lowest one in the males aged more than 45 (20.4±1.4). Self-reported poor disease control was strongly linked to the actual FEV1 value (P = 0.0012). The main cause for the poor disease control was irregular use of the inhaled corticosteroids (51/65; 78.4%) followed by untreated rhinosinusitis (12/65; 18.4%) and gastroesophageal reflux disease (8/65; 12.3%).

**Conclusions.** Our data confirm the usefulness of the ACT as a reliable screening tool for asthma control. Additionally, we emphasize the need of its wide use among the patients with asthma in R. Macedonia.

#### P2580

##### The effect of allergic rhinitis on quality of life and sleep quality in asthmatic patients

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The aim of this study was to determine the impact of allergic rhinitis on asthmatic patients' quality of life and sleep quality.

96 asthmatic patients were included to the study and they were classified according to disease severity. The patients were divided into two groups according to presence of allergic rhinitis.

Adult Quality Life Questionnaire (AQLQ) and Pittsburgh Sleep Quality of Life Index (PSQI) were applied to all patients. There was 87 female (90.6%), 9 male (9.4%) patients. The presence of allergic rhinitis was 37(38.5%).

When the patients were classified according to asthma severity, in allergic rhinitis group there were mild intermittent n=5 (5.2%), mild persistence n=16 (16.6%), moderate persistence n=13 (13.54%), and severe persistence n=3 (3.12%). In non-allergic rhinitic patients mild intermittent n=6 (6.25%), mild persistence n=31 (32.2%), moderate persistence n=20 (20.8%), and severe persistence n=2 (2.08%). In asthmatics inverse correlation was found between pulmonary function parameters and quality of life scores (symptom, activity and emotional functions) (p<0.005). There were more deterioration in activity and symptom scores in moderate and severe asthma (p<0.05). Worsening in activity scores in female patients was detected more than male patients (p<0.05). When the patients were classified according to PSQI, there were 33 patients in healthy sleep (34.3%), 48 patients in bad sleep (50%) and 15 patients (15.65%) in chronic sleep disorder categories.

#### P2581

##### Asthma control deteriorates on a low antioxidant diet

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An antioxidant-rich diet is associated with reduced prevalence of asthma symptoms in some epidemiological studies. However, there has been no direct evidence that altering the intake of antioxidant-rich foods will affect asthma outcomes. This study investigated changes in asthma control resulting from consumption of a low antioxidant diet.

**Methods:** Subjects with asthma (n=15) consumed a low antioxidant diet for 10 days. Asthma medications were kept constant. Changes in asthma status were monitored using spirometry and Asthma Control Score. Total and differential cell counts were performed in induced sputum. Plasma carotenoid levels (β-carotene, lycopene, α-carotene, β-cryptoxanthin, lutein/zeaxanthin) and α-tocopherol were measured by HPLC.

**Results:** Changes in dietary intake resulted in decreased plasma antioxidant levels, in particular carotenoids, in most subjects (11/15, 73%). Subjects who had decreased plasma lycopene levels also demonstrated a worsening of lung function and asthma control score [see Table].

	Visit 1	Visit 2	p
Plasma lycopene (mg/L)*	0.40 (0.08-0.65)	0.18 (0.03-0.57)	0.004
%predicted FEV1†	80.1 ± 4.9	77.5 ± 4.5	0.032
%predicted FVC‡	92.5 ± 4.4	89.5 ± 4.7	0.024
Asthma Control Score†	0.8 ± 0.2	1.4 ± 0.2	0.020
Total Cell Count*	2.07 (0.81-7.65)	2.61 (1.08-3.78)	0.760
%Neutrophils†	22.3 ± 8.5	50.9 ± 10.0	0.004
%Eosinophils*	0.0 (0.0-2.0)	1.0 (0.1-5.2)	0.855

Data is \*Median (IQR) or †Mean ± SEM

**Conclusion:** A low antioxidant diet worsens asthma control and lung function. Increasing dietary antioxidant consumption may alleviate asthma.

#### P2582

##### Analysis of cytokines in exhaled breath condensate and induced sputum using electrochemiluminescence multi-array assay

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**Introduction:** Exhaled Breath Condensate (EBC) is a non-invasive method to assess airway inflammation. However, its reliability has not been well-established. Induced sputum (IS) is the default non-invasive procedure used to study airway inflammation although it may cause bronchospasm. The aim of this study was to analyse inflammatory cytokines in EBC and IS using a novel technique, electrochemiluminescence (ECL) multi-array cytokine assay.

**Methods:** EBC and IS samples were obtained from 6 healthy, non-atopic subjects. Sputum plugs were picked and DTT treated. Supernatants were stored at -80°C. Samples were analysed by ECL multi-array assay.

**Results:** There were no detectable cytokines in the EBC. IL-1β, IL-2, IL-5, IL-8, IL-10, IL-12p70, IL-13 and TNF-α were found in all sputum samples, while IFN-γ and IL-4 detection was sporadic.

##### EBC and Sputum Cytokine Concentrations

Cytokines	IFN-γ	IL-1β	IL-2	IL-4	IL-5
Detection Limit (pg/ml)	13.92	1.53	0.76	2	0.36
EBC	0 (0-0)	0 (0-2.03)	0 (0-0)	0 (0-0)	0 (0-0)
Sputum	9.1(0-31)	9.1(0.96-86)	5.3 (0.3-37)	6.6 (0-27)	1.8 (0.2-14)

Cytokines	IL-8	IL-10	IL-12p70	IL-13	TNF-α
Detection Limit (pg/ml)	0.13	5.53	1.71	1.85	0.87
EBC	0 (0-0.009)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Sputum	127 (11-934)	96 (22-501)	14 (0.2-157)	13.3 (3-121)	2.8 (0.08-20)

Data shown as medians and ranges

**Conclusions:** IS samples yielded quantifiable cytokine data. EBC samples had no detectable cytokines suggesting that it is not a viable medium to measure inflammatory cytokines.

#### P2583

##### The detection of Th1/Th2 inflammatory cytokines in whole sputum from healthy subjects, using a novel electrochemiluminescence (ECL) multi-array assay

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**Introduction:** Induced sputum is widely used for the analysis of airway inflam-

mation in asthma and COPD. Conventional processing of sputum involves the selection of mucoid plugs followed by treatment with DTT prior to analysis. DTT may alter the structure of cytokine proteins. Utilising a novel technique, ECL multi-array cytokine assay, the aim of the study was to explore the potential to measure markers of airway inflammation - Th1/Th2 cytokines - in untreated whole sputum.

**Methods:** sputum samples were obtained from 6 non-atopic, healthy subjects by induction with hypertonic saline. Each sample of whole sputum was centrifuged at 14,000g for 35 minutes at 20°C. Supernate was collected and analysed for Th1/Th2 cytokines using ECL multi-array assay.

**Results:** IL-1, IL-2, IL-5, IL-8, IL-10, IL-12p70 and IL-13 were detected in whole sputum samples. IFN-, TNF- and IL-4 were mostly below the detection levels of the assay (see table).

#### Cytokine Concentrations in Whole Sputum

Cytokines	IFN- $\gamma$	IL-1 $\beta$	IL-2	IL-4	IL-5
Detection Limit (pg/ml)	13.92	1.53	0.76	2.0	0.36
Whole Sputum (pg/ml)	0.45 (0-36)	14.5 (5.3-103)	40.6 (0-70)	0 (0-27)	0.62 (0-17)

  

Cytokines	IL-8	IL-10	IL-12p70	IL-13	TNF- $\alpha$
Detection Limit (pg/ml)	0.13	5.53	1.71	1.85	0.87
Whole Sputum (pg/ml)	264 (80-1306)	147 (8-1324)	2.4 (0-136)	20.1 (5-114)	3.1 (0.07-24)

Data shown as medians and (ranges).

**Discussion:** The results illustrate that most Th1/Th2 cytokines in the airways can be detected in whole untreated sputum. This technique is now being applied to examine DTT treated sputum for inflammatory cytokines.

#### P2584

##### Vascular endothelial growth factor modulates matrix metalloproteinase-9 expression in asthma

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**Rationale** Vascular endothelial growth factor (VEGF) and matrix metalloproteinase-9 (MMP-9) are mediators of airway inflammation and remodeling in asthma.

**Objectives** This study investigates a potential relationship between VEGF and MMP-9, and the mechanisms by which VEGF signaling regulates MMP-9 expression in asthma.

**Methods** We evaluated whether levels of VEGF correlated with levels of MMP-9 in the sputum of asthma patients, and the effect of VEGF receptor inhibitors on MMP-9 expression in murine model of asthma.

**Results** We have found that levels of VEGF and MMP-9 are significantly higher in the sputum of asthma patients than in healthy control subjects, and a significant correlation is found between the levels of VEGF and MMP-9. This study with the ovalbumin-induced model of asthma revealed the following typical pathophysiological features of asthma in the lungs: increased numbers of inflammatory cells of the airways, airway hyperresponsiveness, increased vascular permeability, and increased levels of MMP-9 and VEGF. Administration of VEGF receptor inhibitors reduced the pathophysiological signs of asthma and decreased the increased expression of MMP-9 after ovalbumin inhalation.

**Conclusions** These results indicate that there is a close relationship between VEGF and MMP-9 expression and that inhibition of VEGF receptor down-regulates the expression of MMP-9. These findings suggest that VEGF signaling regulates MMP-9 expression and plays a critical role in initiation and maintenance of asthma.

#### P2585

##### Airway cytokine expression measured by protein array in exhaled breath condensate: correlation with physiological properties in asthmatic patients

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**(Rationale)** Exhaled breath condensate (EBC) sampling is useful to examine the inflammatory mediators in the airway. Using this technique, we have measured the cytokine expression in airways of asthmatic as well as healthy subjects. Further, we have also investigated the role of cytokines in airway obstruction and hyperresponsiveness.

**(Methods)** Ten non-smoking healthy subjects and sixteen steroid-naïve asthmatic patients were enrolled. EBC sampling, spirometry, and methacholine inhalation challenge were performed on one occasion in this cross-sectional study. The collected EBC was analyzed with protein array (Ray Biotech Inc., Norcross, USA), and the relative cytokine levels were semiquantified by chemiluminescent imaging. In addition, correlations between the relative cytokine levels and baseline lung physiological indices were analyzed.

**(Results)** The expressions of nine cytokines, such as IL-4, IL-8, IL-17, TNF- $\alpha$ , RANTES, IP-10, TGF- $\beta$ , MIP-1 $\alpha$ , and MIP-1 $\beta$  were significantly up-regulated in

asthmatic airways compared with those of healthy subjects. The relative level of RANTES was significantly correlated with the FEV1 and Rrs values. The relative levels of both TNF- $\alpha$  and TGF- $\beta$  were significantly correlated with the degree of airway responsiveness. **(Conclusion)** Inflammatory molecule analysis using EBC appeared to be useful for monitoring the asthmatic airway condition.

#### P2586

##### Association of transforming growth factor-beta with asthmatic airway remodelling: a study using induced sputum and computed tomography

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**Background:** Asthma is characterized by inflammation and remodelling of the airways. Transforming growth factor (TGF) -beta is considered to play a central role in the pathogenesis of airway remodelling, but its precise roles in asthmatic patients in vivo remain to be fully elucidated. **Materials and methods:** We studied 36 stable patients with moderate to severe asthma taking inhaled corticosteroid equivalent to beclomethasone of  $872 \pm 318$  mcg (mean  $\pm$  SD) daily and 11 healthy controls. None had ever smoked cigarettes. Helical computed tomography (CT) scans were acquired at full inspiration. Airway wall thickness of the apical segment of right upper lobe was assessed on the basis of wall area corrected by body surface area (WA/BSA) and wall thickness (T) corrected by  $\sqrt{BSA}$  according to a validated CT method (Niimi et al. AJRCCM 2000; Nakano et al. AJRCCM 2000). Induced sputum concentrations of TGF-beta 1 were examined by ELISA using a commercially available kit. Lung function was also evaluated. **Results:** FEV1 (% pred), FEV1/FVC, MEF25 (% pred) and FEF25-75 (% pred) were significantly lower in the asthmatics than in the controls. T/ $\sqrt{BSA}$ , WA/BSA and sputum levels of TGF-beta 1 were significantly higher in the asthmatics than in the controls. The TGF-beta 1 levels correlated positively with WA/BSA or T/ $\sqrt{BSA}$  and negatively with FEV1 or MEF25 for the asthmatics and control subjects analyzed together.

**Conclusions:** Sputum levels of TGF-beta 1 are increased, and associated with airflow limitation and airway wall thickening in patients with moderate to severe asthma. This indicates that TGF-beta 1 is involved in the pathogenesis of airway remodelling in asthma.

#### P2587

##### Analysis of the rheological properties of the respiratory mucus and inflammatory alterations of the airways in patients with common variable immunodeficiency associated to the bronchiectasis

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This study analyzed the physical properties of the respiratory mucus as well as the inflammatory alterations of the airways in patients with Common Variable Immunodeficiency associated to bronchiectasis, before and after therapeutic intravenous immunoglobulins. We observed a decrease in the indexes of inflammation NO ( $54.67 \pm 9.79 / 40.07 \pm 8.48$ ) and inflammatory cells ( $28.68 \pm 15.30 / 14.57 \pm 8.09$ ) and a raise of the transportability of the respiratory mucus by cough ( $42.5 \pm 18.79 / 65.0 \pm 19.7$ ) ( $p \leq 0.05$ ) after gamaglobulin administration. We concluded that the immunoglobulin administration in these patients incurred in significant improvement in the indexes of inflammation of the airways with reflex in the transportability of the respiratory mucus by the main mechanism of transport of the respiratory mucus used by this kind of patients, the cough, with clinical and pathophysiological implications to be considered.

#### P2588

##### Inflammatory markers in induced sputum of patients with allergic rhinitis in relation to exposure to pollen allergens

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We intended to verify hypothesis, that eosinophilic inflammation in lower airways during the pollen season is present not only in patients with asthma but also in patients with seasonal rhinitis without asthma symptoms.

Patients: 1<sup>st</sup> allergic rhinitis with seasonal asthma without inhaled corticosteroids, 2<sup>nd</sup> allergic rhinitis without asthma symptoms, 3<sup>rd</sup> controls.

Sputum was induced and processed by Pizzichini. We evaluated changes in cell counts (eosinophils, macrophages, neutrophils) and in humoral inflammatory marker (ECP). Cell count was evaluated by means of Hemacolor staining (DCC) and immunocytochemistry (ICC), ECP in supernatant by chemiluminescence.

Sputum ECP levels in patients with rhinitis during the pollen season were significantly elevated ( $p=0.014$ ) compared to results out of the season. ECP levels in patients with asthma were higher compared to controls, but the differences did not reach statistical significance ( $p=0.211$ ). Eosinophil counts during the pollen season in asthma and rhinitis were significantly higher ( $p=0.002$ ) compared to controls. Elevated number of sputum eosinophils in relation to exposure to pollen allergens was seen both in patients with seasonal asthma and patients with rhinitis, but the differences did not reach statistical significance ( $p=0.101$ ).

Differences in sputum ECP levels and eosinophil counts in patients with seasonal

asthma in relation to pollen season corresponds to persistent inflammation of lower airways. Elevated ECP levels (52.4 ng/ml) and eosinophils number (1.8%) in rhinitis patients during the pollen season indicate persistent inflammation in spite of absence of asthma symptoms.  
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**P2589****Features of production nitric oxide at patients with a bronchial asthma**

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**Aim:** To estimate production of nitrites in various departments of a respiratory tract in association with the immunopathologic reaginic answer in patients with bronchial asthma (BA).

**Material and methods:** Surveyed a representative sample from 30 persons suffering BA (criterion GINA), and 15 volunteers comparable on age and a sex (the informed consent). The contents of serum levels IgE and Il-4 determined an ELISA. NO concentration in condensate of expired air (CEA) and a bronchoalveolar lavage (BAL) estimated under the maintenance nitrite-anion spectrophotometrically.

**Results:** The highest contents NO in CEA has been marked at patients with a severe BA, it has made 8,13±2,15 µmol/l against 2,64±0,46 µmol/l and 4,45±1,06 µmol/l (r<0,001) at patients with mild and moderate BA respectively. At all patients, without dependence from severities of disease, contents NO in BAL was significantly above, than in control group (1,36±0,34 µmol/l at mild, 1,89±0,37 µmol/l - moderate and 1,82±0,15 µmol/l at a severe BA against 0,39±0,09 µmol/l at healthy persons). And increased level NO in BAL correlated with number of neutrophils and a level Il-4 (r=0,81; r=0,70; p<0,01 respectively). The level of reaginic antibodies at a severe BA was significantly lower (104,02±65,72 ME/ml), than at an mild and moderate BA (524,10±109,98 ME/ml and 446,65±165,28 ME/ml, r<0,01 respectively).

**Conclusion:** The introduced data confirm, that level NO in the upper respiratory tract is higher than those in the inferior respiratory pathes. Presence of a close functional linkage between a level nitric oxide, severities of BA and atopic markers of the inflammation, confirming anti- and proinflammatory potential NO in development of BA fixed.

**P2590****Iron in serum and induced sputum of patients with allergic rhinitis and allergic asthma**

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**Background:** Iron is a transition metal which can increase production of reactive oxygen species through Fenton reaction. On the other hand, iron-binding proteins ferritin, transferrin, lactoferrin act as antioxidants. Our aim was to measure iron level in serum and induced sputum of patients with allergic rhinitis and allergic asthma.

**Methods:** We have measured concentration of iron in serum and in supernatant of induced sputum in 21 patients with allergic asthma, in 13 patients with allergic rhinitis and in 10 control subjects.

**Results:** There was no statistically significant difference between levels of iron in serum, as well as in induced sputum in patients with allergic rhinitis, allergic asthma and control subjects. We have also found positive linear correlation between concentration of iron in serum and in induced sputum in control subjects and in patients with asthma.

**Conclusion:** Although iron may play a role in pathophysiology of allergic respiratory diseases, we did not find difference of iron level in serum and induced sputum between asthmatics, rhinitics and healthy subjects.

**P2591****Expression of adamalysin proteases (A Disintegrin And Metalloprotease) and their inhibitors in sputum from asthmatics**

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**Background:** ADAMs (A Disintegrin And Metalloprotease) are a family of cell surface proteins containing disintegrin and metalloprotease domains which associate features of adhesion molecules and proteases. ADAMTSs (A Disintegrin And Metalloprotease with Thrombospondin motifs) bear thrombospondin type I motifs in C-terminal extremity and are for most of them secreted proteins.

**The aim of the present work** was to study mRNA expression profile of several ADAM(TS) proteases in asthma and to investigate the relationship between

expression of these proteases and asthma-associated inflammation and airway obstruction.

**Methods:** mRNA expression profile of ADAM(TS) proteinases (ADAM-8, -9, -10, -12, -15, -17, -33, ADAMTS-1, -TS-2, -TS-15, -TS-16, -TS-17, -TS-18, -TS-19), their physiological inhibitors TIMPs-1, -3 and RECK, a membrane-anchored MMP activity regulator was obtained by RT-PCR analysis performed on cells collected by sputum induction from 21 asthmatic patients and 17 healthy individuals.

**Results:** mRNA levels of ADAM-8, ADAM-9, ADAM-12, TIMP-1 and TIMP-3 were significantly increased while mRNA levels coding for ADAMTS-1, ADAMTS-15 and RECK were significantly decreased in asthmatics as compared to control patients. ADAM-8 expression was negatively correlated with FEV<sub>1</sub> (r=-0.57, p<0.01) while ADAMTS-1 and RECK expression was positively correlated to FEV<sub>1</sub> (r=0.45, p<0.05 and r=0.55, p=0.01, respectively).

**Conclusion:** We conclude that expression of ADAM(TS)s and their inhibitors is modulated in airways from asthmatics and that these molecules may play a role in the pathogenesis of asthma.

**P2592****Assessment of bronchoprovocation test positivity and response to montelukast therapy in chronic urticaria patients**

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In this study, assessment of bronchoprovocation test (BPT) positivity and effect of treatment with montelukast in chronic urticaria patients with positive methacholine challenge test (MPT) were investigated.

The inclusion criteria to study were disease duration more than 1 year, no chronic urticaria exacerbation in two months, no history of long acting antihistaminic and corticosteroid usage in a month. The patients with asthma and pulmonary symptoms, disease causing positive BPT, contraindication to the MPT, and abnormal pulmonary function test were excluded.

156 patients with chronic urticaria were included to the study. Pulmonary function test and MPT were performed to the all patients with chronic urticaria. Montelukast 10 mg/day was given to patients with positive challenge test during 8 weeks. After 8 weeks, MPT was performed again. At the beginning, MPT positivity was detected in 41 (26,3%) patients. There was no significant difference between patients with MPT (+) and MPT (-) according to demographic findings. Mean dose of MPT was 2,64±3,36 mg/dl and it was increased to 4,57±4,87 mg/dl after treatment with montelukast in MPT (+) patients. The provocation dose was increased in 30 patients (73,2%) and found same in 11 patients (26,8%). Decrease in provocation dose was not observed in any patients.

As a result, BPT can be positive in chronic urticaria patients without pulmonary symptoms and the provocation dose can be changed with the medication against to the leukotrienes which play an important role in pathogenesis of chronic urticaria.

**P2593****Sputum inflammatory biomarkers and exhaled nitric oxide (FE<sub>NO</sub>) in varying severity asthmatics**

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Airway inflammation is a major characteristic of asthma with eosinophilic predominating as its hallmark. Exhaled nitric oxide (FE<sub>NO</sub>) and sputum eosinophil counts are both non-invasive biomarkers of inflammation in asthma. Furthermore, apoptotic eosinophil clearance is considered important in the resolution of inflammation. Presence of eosinophils and a reduction in their apoptotic induced removal can be indicative of unresolved inflammation. The aim of this study was to evaluate the association between sputum inflammatory biomarkers and FE<sub>NO</sub>. Altogether, 39 varying severity asthmatics and 13 non-asthmatic controls (19-65 years) underwent FE<sub>NO</sub> and sputum induction using nebulised hypertonic saline solution. Sputum was processed and cytopins prepared for light microscopy to determine normal and apoptotic eosinophils. Subjects also underwent spirometry, phlebotomy and both current disease control and symptom score questionnaires. Significant correlations were found between FE<sub>NO</sub> and differential sputum eosinophil counts (Rs = 0.505, p = 0.008) but not with FE<sub>NO</sub> and eosinophil apoptotic ratio (AR) (Rs = 0.330, p = 0.100). Furthermore, significant correlations were demonstrated between sputum eosinophils and FEV<sub>1</sub> (Rs = -0.456, p = 0.017). This study suggests that FE<sub>NO</sub> can be used as an alternative investigative technique to induced sputum to monitor eosinophilic inflammation in asthma. In addition, the lack of significant association between FE<sub>NO</sub> and AR suggests that eosinophil apoptosis is not the most important process in the resolution of airway eosinophilia in asthma and suggests that other factors are important in determining airway eosinophil load.