111. Mechanisms and risk of childhood asthma and allergy

P1091

Organochlorine chemicals increase the risk of non-atopic wheeze in adolescents

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Ecologic studies have demonstrated a significant increase in hospitalization for asthma in those living near a waste site containing persistent organic pollutants (POPs), mostly polychlorinated biphenyl compounds (PCBs). POPs are lipophilic, accumulate in fat and are poorly metabolized with a half-life in the body of about 10 years. PCBs are classified by the number and position of chlorines around the biphenyl ring, with different congeners having different activities. We measured serum levels of 101 PCB congeners and 3 chlorinated pesticides [hexachloraben-

zene (HCB), DDE, the major metabolite of DDT, and Mirex] in 240 children participating in the respiratory assessment of a longitudinal birth cohort at 14 years or age. Current wheeze was reported by 63 (26.3%) and 96 (40.0%) were atopic. Levels of PCBs and pesticides were similar to those reported in American adolescents. Overall, those with higher levels of total PCBs were more likely to report current wheeze [OR 1.61 (95%CI 1.05-2.6), p=0.029]. Stratifying the analyses by atopic status revealed that the positive associations were seen in non-atopic children. In the non-atopic group associations were seen between current wheeze and total PCBs [2.59 (1.36-4.94) p=0.004], estrogenic [1.97 (1.28-3.01), p=0.002], di-ortho [2.58 (1.41-4.72) p=0.002], and tri-plus ortho [1.97 (1.20-3.23) p=0.007] congeners but not dioxin-like PCBs [1.06 (0.90-1.24) p=0.52]. Associations were also seen with HCB [2.82 (1.22-6.55) p=0.016] but not with the other pesticides. These data demonstrate that the health effects of exposure to organochlorine chemicals are dependent on the chemical structure. The lack of effect in atopic children requires clarification.

P1092

Bullying in children with asthma – What factors are associated with increased risk?

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Background: Bullying or teasing of children with any chronic medical condition is a well-recognised complication of disease. The data collected in the Room to Breathe Study, a large 6-country population survey of childhood asthma demonstrated worryingly high reports of bullying (10%). This study looks in detail at the family and child factors associated with increased bullying risk.
Methods: Parents and children >7 years with asthma were interviewed by telephone following identification using a truncated list-assisted random digit dialling sampling procedure in Canada, Greece, Hungary the Netherlands and UK. Parents and children in South Africa were interviewed face-to-face. All statistical analyses including univariate and multivariate regression were carried out using STATA v10.
Results: Detailed questionnaires including parent and child responses were available for 943 parent-child diads. Univariate analyses identified that poor GINA-defined asthma control (p=0.001), parental worry about childs' health (p=0.005), parent reported frequency of asthma attacks (p=0.002) and parental smoking (p=0.042) were associated with increased bullying risk. The childs' age and gender were not associated with risk of bullying. Children who reported bullying were significantly more likely to report feeling sad (p<0.001) and were less likely to participate in sporting activities (p=0.001).
Conculsions: Bullying or teasing is commonly reported by children with asthma and is associated with reduced particpation in sport and feelings of sadness. Modifiable child factors such as poor asthma control and parental factors such as smoking and ongoing worries about their child are associated with increased bullying risks.

P1093

The impact of gene-gene interaction on the severity of bronchial asthma in Ukrainian children

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Background: Gene-gene interaction in the development of different severity of bronchial asthma (BA) has not been investigated.
The aim of the study was to define the genetic differences among children with persistent mild and persistent moderate BA.
Methods: Comparative groups included 13 patients (aged 8,58+0,84 year) with persistent mild BA and 14 patients (aged 8,94+0,82 year) with persistent moderate BA. Sex differences among two groups were not observed. There was performed 10 genes polymorphism investigation using PCR with further RFLP. The differences in comparative groups were assessed by the two tailed Fisher test analyses. MDR program was applied for gene-gene interaction evaluation.
Results: The frequency of DD genotype in ACE gene was significantly higher among patient with persistent moderate BA (p=0,045). The patient with persistent moderate BA had also significantly increased frequency of GSTM1 gene deletion polymorphism (p=0,0004). We have observed no differences in the frequency of others genes polymorphic variants.

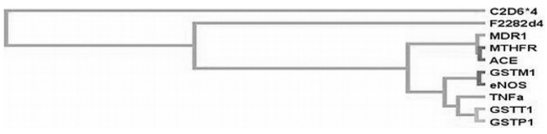

Figure 1. Interaction dendrogram for the different BA severity level.

MDR analysis has found synergy closely interaction between MTHFR (C677T) and ACE (I/D) genes and between GSTM1 and eNOS (4a/4b).
Conclusion: Gene-gene interaction defined severity of bronchial asthma in children. The further research may help to optimize BA prognosis and treatment.

P1094

Alterations in *ORMDL* expression in experimental esthma

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Introduction: A susceptibility locus on 17q21, including *ORMDL3*, has been identified in childhood asthma. We determined if expression of *ORMDL3* and the other members of the highly conserved *ORMDL* family (*ORMDL1-2*) are altered in the lungs and tissues of mice with experimental asthma.
Methods: Intraperitoneal sensitization of C57BL/6 and Balb/c mice to ovalbumin (OVA) was carried out on days 1 and 14. Sensitized and naïve mice received aerosol challenges on days 24-26. *ORMDL1-3* expression levels were analyzed in different tissues (brain, gut, heart, kidney, liver, lung, skeletal muscle, spleen, thymus) and isolated cells (lymph nodes, blood). Kinetic studies of *ORMDL* expression in lung, spleen, and thymus were performed 24h, 48h, and 72h after the last challenge. Gene expression data are described as relative fold-changes.
Results: *ORMDL1-3* expression in all tissues was shown at comparable levels for both mouse strains and mRNA levels were altered only in lung and lymphoid tissues (spleen, thymus) with a peak 48h after the last challenge. In lungs of non-sensitized/challenged (n=11) vs. sensitized/challenged (n=11) C57BL/6 mice, significant decreases were observed for *ORMDL1* (1.0 vs. 0.47, p=2.09E-07), *ORMDL2* (1.0 vs. 0.56, p=1.12E-07), and *ORMDL3* (1.0 vs. 0.50, p=2.72E-05). In parallel, significantly lower levels of *ORMDL2* (1.0 vs. 0.72, p=0.01), and *ORMDL3* (1.0 vs. 0.77, p=3.14E-05) were detected in spleen. In Balb/c mice similar significant effects were detectable, albeit to a lower degree. In contrast, *ORMDL* mRNA expression in the thymus trended upwards in sensitized and challenged mice of both strains.
Conclusion: These data demonstrate the involvement of all members of the *ORMDL* family in experimental asthma.

P1095

Remodelling of the bronchial wall in very young children at risk for developing asthma

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Remodelling of the bronchial wall in asthmatic patients includes various attributes like thickening of the basement membrane, hyperplasia of smooth muscle cells or increased vascularity of the subepithelial tissue. Although the prevalence of asthma in childhood is much higher than in adults, we still don't have much information about the onset and development of these changes. In the past, remodelling of the bronchial wall was considered to be result of a chronic inflammation going on hand in hand with the course of the disease. In this study we analyzed 30 endobronchial biopsies from very young children (average age of 18.9 months) that were taken during bronchoscopic examination done for various reasons (e.g. chronic cough, recurrent bronchitis). Thirteen children with atopic eczema or history of parental asthma were considered at risk for developing asthma and remaining seventeen children formed the control group. We found significant thickening of the basement membrane in children at risk for developing asthma compared to the controls (3.53 μm and 2.89 μm respectively). In ten of these children we analysed the proportion of laminin-positive layer in the total thickness of the basement membrane that was also significantly higher in asthma group (65.94% and 42.11% respectively). We conclude that these results may support need for early diagnosis of obstruction and subsequent preventative treatment in children in high risk for developing asthma as structural changes in the bronchial mucosa may be present with first symptoms.
Supported by GAUK 340911 and IGA MZ NT/11444.

P1096

Bronchial epithelial cell mediator release in children with wheeze or eczema

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Introduction: Airway epithelial cell (AEC) function is thought to be important in the regulation of airway remodelling and inflammation in health and disease. Due to the challenges in accessing paediatric airways relatively little is known about bronchial AEC function in children. Our hypothesis was that bronchial AEC mediator release will be different between children with and without a history of recent wheeze.
Methods: Children scheduled for elective operation were recruited. Bronchial AEC were removed by brushings and grown in submerged culture. Second culture

passage monolayers were stimulated for 24 hours with TNF-alpha and IL-1B. Supernatants were removed and the following mediators analysed: IL-6, IL-8, MMP-9, TIMP-1, VEGF, GCSF, RANTES and MCP-1.
Results: 32 children were recruited, mean age 6.5 years (range 1.1-16.0). 7 reported wheeze in the last year, 13 had a history of eczema including three with recent wheeze. Concentrations of MMP-9 were reduced in children with recent wheeze (geometric mean 3.4 [SEM ±1.7] pg/ml secreted from 10^4 AEC) compared to those without symptoms (11.0±14.5) p=0.021. There was a similar reduction in MMP-9 concentrations among those with eczema (3.7 ±SEM 2.1) compared to those without (11.3±5.2), p=0.037. Children with eczema also had reduced bronchial AEC release of MCP-1 (0.15±0.15) compared to those without (0.73±0.35), p=0.002. There were no differences for other mediators studied
Conclusion: Bronchial AEC release of MMP-9 is reduced in children with recent wheeze. The similar relationship seen among those with eczema but no wheeze suggests that the underlying mechanism may be related to atopy but may not be important to symptoms in this age group.

P1097
Inflammatory cytokines in serum from children with severe asthma compared to controlled asthmatics
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Introduction: Care of children with severe asthma remains a clinical challenge, partly due to the heterogeneity of the disease and the lack of definite biomarkers. In this study, we compared levels of inflammatory cytokines in serum from children with severe asthma and controlled asthma.
Methods: Children with severe therapy resistant asthma (n=34, mean age 13.3 years) and controlled asthma (n=39, mean age 13.8 years) participated in a nationwide Swedish study. The protocol included Asthma control test, exhaled nitric oxide (FE_{NO}) and blood sampling. Interleukin (IL) 4, IL5, IL12p70, tumor necrosis factor alfa (TNFα) and eotaxin were analysed from serum using multiplex technology and results presented as medians with inter quartile ranges (picogram per millilitre).
Results: Severe asthmatic children had inferior asthma control (p<0.001) in spite of high doses of inhaled steroids (> 800ug budesonide), compared to children with controlled asthma. FE_{NO} (p=0.93) and IgE (p=0.92) were comparable in these two patient groups. Children with severe asthma had increased levels of cytokines related to both Th1 inflammation (IL12p70 4.1 (0-22) vs. 0 (0-4.7), p=0.001 and TNFα 10.4 (4.6-19) vs. 4 (2.1-7.0), p< 0.001)) and to Th2 inflammation (IL4 1.6 (0-29) vs. 0 (0-1.9), p=0.02; IL5 0 (0-1.1) vs. 0 (0-0), p=0.04 and Eotaxin 97.3 (60-146) vs. 49.2 (42-68), p<0.001).
Conclusions: Severe asthmatic children have increased serum levels of cytokines related to both Th1 and Th2 inflammation compared to controlled asthmatics. These results indicate a heterogeneous pattern of inflammation, and multivariate statistical analyses to further characterize the inflammatory phenotypes are initiated.

P1098
Asymmetric dimethylarginine (ADMA) in EBC of asthmatic children
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Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide synthase (NOS). ADMA contribution to airway inflammation, oxidative stress, bronchial hyperresponsiveness and collagen deposition, suggests a role for this mediator in asthma pathogenesis (Sott JA, AJRCCM 2011). Aim of the present study was to evaluate the feasibility of ADMA measurement in exhaled breath condensate (EBC) and to compare the levels of this mediator in asthmatic and healthy children.
We recruited 60 children (5-17y) with well-controlled asthma and 64 healthy children (5-14y) who underwent spirometry and EBC collection. In a subgroup of asthmatic children serum ADMA levels and FENO levels were measured. EBC was collected using the Turbo-Deccs (Medivac, Parma, Italy). ADMA measures were performed by UPLC-MS/MS.
ADMA was measured in EBC with a good reproducibility (evaluated by analyzing 2 samples collected 24h apart in 8 subjects). ADMA EBC levels were significantly higher (p<0.001) in asthmatic children (2.2 pmol/ml [IQR 1.2 − 3.7]) than in healthy controls (1.1 pmol/ml [IQR 0.8−1.6]). In asthmatic children, no correlation was found between serum and EBC ADMA levels (p=0.45, r=0.36). No correlation was found between EBC ADMA levels and FENO values or spirometric parameters.
In the present study for the first time ADMA was measured in EBC. We found increased ADMA levels in asthmatic children, supporting a role for this mediator in asthma pathogenesis. Moreover, the lack of correlation with serum levels suggests that EBC ADMA specifically mirrors lung pathological processes. We speculate that ADMA could be a possible target for new therapeutic strategies in asthma.

P1099
Sputum cells apoptosis by different asthma phenotypes in children
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Background: Reduced apoptosis is one important mechanism for cell accumulation and maintenance of airway inflammation by asthma. However the role of death factors and their receptors in the regulation of granulocyte apoptosis in childhood asthma is still unclear.
The aim was to determine the expression of apoptosis receptors in sputum cells by different asthma phenotypes in children.
Methods: Seventy eight asthma children aged 6-12 years and 25 age-matched healthy controls were assessed including skin prick testing (SPT), lung function, total and antigen specific IgE, induced sputum analysis. Expression of pro-apoptotic Apo-1/Fas and Bax and anti-apoptotic Bcl-2 antigens in sputum cells were assessed using immunocytochemistry.
Results: Among investigated children 69.2% had atopic asthma with increased total and specific IgE, positive SPT at least to one allergen. These children had mild-to-moderate asthma and sputum eosinophilia. They demonstrated decreased apoptotic ratio(AR) in sputum eosinophils that directly correlated with Apo-1/Fas and Bax expression and inversely with Bcl-2 expression and these parameters were more significant in moderate asthma than those in mild(p<0,001).
In contrast 30.8% children with non-atopic asthma had moderate-to-severe asthma and induced sputum neutrophilia. Their sputum neutrophils showed decreased Apo-1/Fas and Bax and elevated Bcl-2 expression that was more significant in severe asthma group(p<0.001).
Conclusion: Our findings indicated that sputum cell apoptosis vary in different asthma phenotypes in children.
The identification of differences in the apoptosis regulation may help to define new medicines that allow specific induction of either eosinophil or neutrophil apoptosis.

P1100
Peripheral mononuclear cell response to nonspecific antigenic stimulation in children with obese asthma phenotype
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Background: Investigation of immunopathogenetic mechanisms of obesity associated asthma may demonstrate novel therapeutic targets.
Objective: The aim of this study was to compare levels of Th1, Th2, Treg and Th17 cytokines secreted by peripheral mononuclear cell culture (PBMC) in response to nonspecific stimulation in obese and nonobese children with asthma.
Methods: Obese and nonobese children with asthma aged 5 to 16 were enrolled into this case-control study consecutively. Age at asthma diagnosis and clinical severity were recorded. Skin prick test was performed. Serum adipokine levels as well as PBMC supernatant IL-4, IL-10, IL-17, IL-23, IFNγ and TGF-β levels were measured.
Results: Mean (± standard deviation) ages of obese (n=28) and nonobese (n=39) children with asthma were 8.7±2.9 and 10.5±3.2 respectively. Asthma symptom score was higher and age at asthma diagnosis was lower in obese compared to nonobese children with asthma (p=0.03 and p=0.004 respectively). Leptin levels were significantly higher in obese than nonobese asthma group (p<0.001). IL-10 and IL-17 levels in obese group was significantly lower than nonobese group (p=0.005 and p=0.017 respectively). On the other hand, TGF-β levels were significantly higher in obese compared to nonobese children with asthma (p=0.015). IL- 4, IL-23 and IFNγ levels were not significantly different between the groups (p<0.05 for all).
Conclusion: Low IL-10 and high TGF-β levels in obese compared to nonobese children with asthma might indicate lower antiinflammatory cytokine secretion and regulatory T lymphocyte function as well as a higher remodelling process in obesity associated asthma in children.

P1101

The overwhelming inflammation type in school children with asthma in the region "South Banat" obtained induced sputum cytology

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Introduction: Induced sputum is a noninvasive method for direct measurement of inflammation in asthma and we use it to distinguish eosinophilic asthma from other types, as well as therapy guide.
Objective: The aim of this study was to determine which type of inflammatory cells dominated in school children with asthma in the region "South Banat" and is that different in children in Pancevo with the air pollution and children from surrounding villages with relatively clean air.
Methodology and results: We did cytological analysis of induced sputum in 109 school children in the mild and moderate acute asthma, aged 6 to 17 years (average 10.6). From Pancevo was 53, and from a surrounding villages was 56 children. In 98 (89.91%) children we received an adequate sample for sputum analysis, from Pancevo 48, and from surrounding villages 50 children. Neutrophils has 37 (37.75%), Eosinophils 31 (31.63%) children. In Pancevo, eosinophilic type of inflammation has 23 (47.92%), in the surrounding villages 8 (16%) children, and this difference was highly statistically significant, $\chi^2 = 11.535$, $p < 0.0006$. Neutrophilic type of inflammation in the surrounding villages has 24 (48%), in Pancevo 13 (27.08%) children and this difference was statistically significant, $\chi^2 = 4.559$, $p < 0.03$. Mixed asthma type have 3 children, all from surrounding villages.
Conclusion: The results showed that in the region, "South Banat" is equally represented eosinophilic and neutrophilic inflammation type. Further analysis showed that there were significant differences in the type of inflammation in children from Pancevo and surrounding villages, which can be attributed to environmental conditions.

P1102

Outcome in preschool age after hospitalization for wheeze in infancy

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Background: Risk factors for the progression from early infant wheeze to the development of later bronchial obstructive symptoms are not fully known.
Aim: To investigate if the development of bronchial obstructive symptoms during preschool years was influenced by time of the first hospitalization in infancy for acute respiratory distress with wheeze.
Subjects: 150 infants younger than 18 months were hospitalized for the first time at Borås hospital with the diagnoses acute bronchitis, bronchiolitis or asthma during one calendar year. For 110 infants it was the first episode ever. 144 children (85 males) were followed up (96%), ages: < 6 months, 67 infants, 6-<12 months, 57 infants, and 12-<18 months, 20 infants.
Methods: All hospital records were analysed. Structured telephone interviews were made with the families of the 144 children, at mean age 4.5 years (range 3.5 – 5.6 years). Data from medical records of all the children with reported remaining respiratory symptoms were analysed.
Results: 71 children (49%) still had current wheeze requiring medication periodically (60 children) or continuously (11 children). Episodic (viral) wheeze was reported in 46 and multiple-trigger wheeze in 25 individual with a similar distribution in the three age groups (21/67, 21/57, 4/20 and 11/67, 9/57, 5/20 respectively). Suspected or diagnosed allergy to inhaled allergens was reported in 15 of the 71 symptomatic children (21%) and in one child without wheeze.
Conclusions: Almost half of infants with hospitalization due to early wheeze had current wheezing symptoms, needing medication at mean age 4.5 years. In this heterogeneous group of children age at the first hospitalization did not seem to influence the outcome.

P1103

Wheezing childhood phenotypes from birth to 7 years using latent class analysis

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Introduction: Childhood asthma prevention is hampered by the heterogeneity of childhood wheeze.
Aim: To refine childhood wheeze phenotypes (0 to 7 years) using latent class analysis (LCA).
Methods: A high risk birth cohort (n=620) recorded: current wheeze 18 times to age 2 years; yearly (ages 3 to 7), and at 12; eczema by age 6 months; food allergen sensitization aged 1 year; aeroallergens at 2 years; lower respiratory tract infection (LRT) by 1 year, and parental asthma. LCA of wheeze at 23 times defined the optimal number of wheezing classes from model fit parameters.
Results: Five latent classes were identified. (Non-wheezers, n= 264 (42.7%)). All wheezing classes except early transient had greater risk of wheeze aged 12. Also: early transient wheeze (27.5%) was associated with LRT (OR 3.0; 95%CI 1.6, 5.7); early persistent wheeze (5.7%) with LRT (OR 6.8; 2.8, 16.7) and aeroallergen sensitization (OR 5.0; 1.8, 13.9); intermediate onset wheeze (20.7%) was associated with both these factors and eczema (OR 2.6; 1.7, 4.7), food sensitization (OR 2.7; 1.5, 4.7) and parental asthma (OR 2.2; 1.0, 4.5); late onset wheeze (3.5%) had no associations.

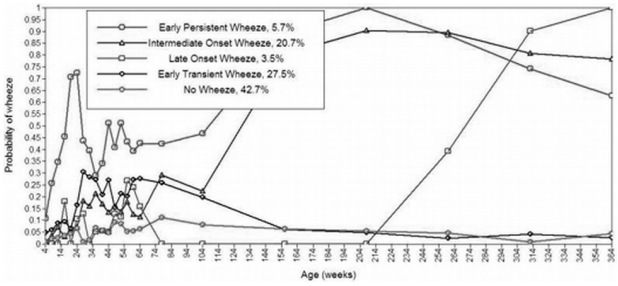

Figure 1. LCA of wheeze.

Conclusion: LCA on wheeze in a high risk cohort yielded 5 classes up to age 7. In contrast to previous studies, food sensitization and early eczema were only related to the intermediate class suggesting this may be the group where atopic march is most relevant.

P1104

Day care attendance, recurrent infections, wheezing and eczema

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Background: The majority of studies of recurrent infections, wheezing and eczema are seeking for genetic background, possible immunodeficiency, and atopy. Exposure to pathogens, particularly viruses seems to be very important for aberrations in the development of the immune system that may lead to chronic conditions later in life.
Methods: In order to determine the importance of day care attendance in the pathogenesis of recurrent infections, wheezing and eczema, children aged one to two years, with recurrent infections, wheezing or/and eczema and attending day care were analyzed. The parents from all children were advised to withdraw from day care attendance. On the criterion of the acceptance of withdrawing patients were divided in two groups: I that accepted (53) and II that did not accept such advice (32). Both groups were followed up next 12 months, for the incidence of infections, wheezing and eczema episodes. The excluding criteria for the study were: intolerance/allergy to cow milk and other nutritional allergens, treatment with steroids and antyleukotriens.
Results: During one year follow up in the group that was withdrawn from day care attendance the symptom scores related to respiratory infections reduced by 76%, wheezing by 36% and eczema by 29%.
Conclusion: Our results indicate that withdrawing from day care attendance reduces the symptom scores related to recurrent infections, wheezing and eczema episodes. This suggests that viral infections, the most frequent infections in this age are important for inappropriate development of the immune system and may be a pathogenetic factor in chronic inflammation, asthma and eczema development.

P1105

The effect of 1,25-$(OH)_2D_3$ supplementation on the expression of vitamin D receptor (VDR) on the lung of baby rats with asthma

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Aim: To investigate the effect of different doses of 1,25-$(OH)_2D_3$ supplementation on the expression of vitamin D receptor in the lung of baby rats with asthma.
Methods: Thirty two Wistar rats were randomly divided into four group and were given different doses of 1,25-$(OH)_2D_3$ except for the control group receiving normal saline. Then we chose eight weaned baby rats to establish asthma model. Expression of VDR was measured by immunochemistry and RT-PCR.
Results: Light microscope showed that inflammation was less serious in medium and low dose group, but more seriously in high group.
Immunohistochemistry indicated that the expression of VDR decreased in low and medium dose group, but increased in the high group($p<0.01$).
RT-PCR were consistent with immunohistochemistry.

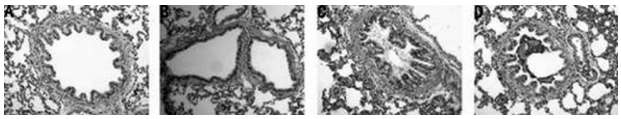

Table 1. The VDR expression in the lung of asmatic rat of different groups

Groups	n	VDR (IOD) value
Control group	8	9.29±2.84
Low dose group	8	8.10±2.01
Medium dose group	8	6.89±3.22
High dose group	8	13.33±4.49
F value		11.017
P		<0.001

Table 2. The VDR mRNA expression in the lung of asmatic rats of different groups

Groups	n	VDR mRNA
Contol group	8	1
Low dose group	8	0.6094±0.19129
Medium dose group	8	0.5092±0.18242
High dose group	8	7.8635±2.21018

Conclusions: Appropriately 1,25-$(OH)_2D_3$ supplementation decrease VDR expression and alleviate airway inflammation in baby rats with asthma, while overdosage supplementation might play deterimental effect.

P1106

Respiratory symptoms during double blind placebo controlled food challenges in children in a general paediatric clinic

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Although double blind placebo controlled food challenges (DBPCFC) are the gold standard for the diagnosis of food allergy, a risk factor for severe asthma, studies examining respiratory symptoms during DBPCFC have come from children with severe eczema in specialized allergy centres. We examined the occurrence of respiratory symptoms during DBPCFC in children referred for evaluation of food allergy to a paediatric department in a general teaching hospital.
Between 2006 and 2011, we performed 234 DBPCFCs to cow's milk, hen's egg, peanut, hazelnut, and soy in children 2 months-17 years of age (median 22 months). 85 tests were positive (36.3%). The symptoms on which food allergy suspicion was based included respiratory symptoms in 55 cases (23.5%), and were accompanied by symptoms from other organs in 54. Respiratory symptoms were seen on the placebo day in 8 patients (3.4%) and on the verum day in 23 patients (9.9%, p<0.001): rhinitis in 11, stridor in 3, wheeze in 6, and dyspnoea and cough in 16. None of these 23 patients had respiratory symptoms on the placebo day; 22 also had symptoms of other organ systems. The only patient with only respiratory symptoms (dyspnoea without wheeze) on the verum day had a negative DBPCFC to cow's milk, because his symptoms on the verum day did not match the symptoms at referral (erythema, vomiting, diarrhoea). Only 4 patients required bronchodilator treatment.
In a general paediatric clinic, respiratory symptoms rarely occur in DBPCFC, and respiratory symptoms are never the only manifestation of food allergy in children.

P1107

Peanut allergy and asthma: A dangerous liaison?

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Objectives: Peanut allergy (diagnosed by sensitization to peanut) has been associated with increased risk of severe asthma and anaphylaxis in tertiary care centres. We determined the association between (the severity of) asthma and peanut allergy diagnosed by standardized food history and food challenges in children from primary and secondary care.
Methods: We conducted a prospective cohort study among 280 peanut-sensitized children (0-18 yrs of age), referred for sensitization testing by general practitioners and paediatricians between 2003 and 2010. Diagnosis of peanut allergy was made or rejected in a stepwise fashion. Children who reported ingestion of peanut and no symptoms in a food allergy quality of life questionnaire or detailed food history were considered to be peanut tolerant. All others were invited for open or double-blind peanut challenges. Children who consistently reported wheeze or shock after peanut exposure were classified as anaphylaxis. Asthma was assessed by ISAAC and asthma control questionnaires, and spirometry.
Results: Levels of peanut-specific IgE were not significantly different between the 139 children with and 141 children without asthma (p=0.456). Asthma was more likely in children with peanut allergy (n=32, 61.5%) than in those without (n=85, 44.7%, p=0.032), but children with asthma were no more likely to have anaphylaxis than those without (p=0.242). Most cases of asthma were well controlled (ACQ <7, 74%); there was no association between asthma control, peanut allergy and peanut sensitization.
Conclusion: In this cohort of children from primary and secondary care, peanut allergy is associated with an increased risk of asthma, but not with poor asthma control or an increased risk of anaphylaxis.

P1108

Proximal and distal airway contributions of nitric oxide in atopic asthmatic and healthy children. Estimates from two series of multiple exhalation flows

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Background: Partitioned contributions of nitric oxide (NO) are being studied to assess atopic airway inflammation in asthma. Selection of flow rates could influence data on disease or atopy.
Aims: To compare partitioned airway NO concentrations in asthmatic and healthy children using two different series of exhalation flows.
Methods: In 30 asthmatic and 21 healthy children aged 11.2±2.5 yr, 35 males, we measured the fractional NO concentration (FENO) at multiple exhalation flows: 50, 100, 150 and 350 ml/s. From two series of either 3 (50-150) and 4 (50-350 ml/s) flow rates, the alveolar NO concentration (CaNO3, CaNO4) and the maximum airway NO flux (J'awNO3, J'awNO4) were calculated. Spirometry and skin-prick testing for common allergens were assessed.
Results: Asthmatic children had lower lung function and higher median (IQR) FENO, CaNO3, J'awNO3 and J'awNO4 but no different CaNO4 than healthy children [J'awNO3:1140.0 (2105.8) nl/s *vs* 506.6 (585.8) nl/s, p=0.001]. Patients using inhaled corticosteroids, ICs (n=11) had lower CaNO3 than those steroid-naive (n=19): 2.99 (6.82) *vs* 8.84 (8.38) ppb, p=0.001. All NO-related variables but CaNO4 correlated with house dust mites (Dpt, Dpf) and cat fur (e.g. with Dpt, CaNO3: r=0.57, J'awNO4: r=0.50, p<0.01). In healthy children, CaNO4 correlated with FEF_{25-75}% (r=0.81, p=0.000).
Conclusion: Estimates of partitioned airway NO concentrations from exhalation flows 50-150 ml/s help to evaluate atopic airway inflammation; CaNO3 is suitable to assess ICs therapy in asthmatic children. A further exhalation flow 350 ml/s, do not improve peripheral NO estimates and probably induces airway collapse.

P1109

Methacholine airway hyperresponsiveness is associated with fraction of nitric oxide irrespective of asthma

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Background: Augmented levels of fractional exhaled nitric oxide (FeNO) reflect airway inflammation and associated airway hyperresponsiveness (AHR) in asthma patient. There are many children who had no asthma but increased level of FeNO. We sought to evaluate the correlation between FeNO and AHR in children.
Methods: Two hundred fourteen children, who had controlled asthma without controller, aged 8 to 16 years were included. Forty seven children without asthma were recruited from community school. Children were evaluated using FeNO measurements, skin prick test, spirometry, and methacholine challenge tests.
Results: AHR was diagnosed in 153 (71.5%) children with asthma and 27 (57.4%) children without asthma. Geometric mean (GM) of FeNO was significantly higher in children with AHR compared children without AHR in both group (all, p <0.001). FeNO and PC_{20} were negatively correlated for both children with asthma and children without asthma (r=-0.364, p<0.001; r=-0.603, p<0.001). The sensitivity, specificity, and positive (PPV) and negative predictive values (NPV) of FeNO measurements in children with asthma for the diagnosis of AHR at the best cut-off value of 22 ppb were 58.2%, 86.9%, 91.8%, and 45.3%, respectively. In the children without asthma, the cutoff value of FeNO 10 parts per billion (ppb) was associated with the highest combination of sensitivity (96.3%) and specificity (74.3%). At a cut-off value of 27 ppb, specificity and PPV of diagnosis of AHR were above 90% (95.0% and 92.9%).
Conclusions: Airway hyperresponsiveness is associated with level of FeNO irrespective asthma. These findings shows that inflammation of airway is associated with asymptomatic AHR.

P1110

Neonatal lungs are characterized by the presence of high numbers of CD11b+Ly6Chigh myeloid derived suppressor cells that potentiate rather than suppress sensitization to house dust mite

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Allergic asthma most often develops during childhood, when both the immune and the respiratory system are still in an immature state. In this study we investigate immune cell development and the immune reactions to house dust mite (HDM) in lungs of neonatal mice. We find high percentages of granulocytic CD11b+Ly6G+ and monocytic CD11b+Ly6G-Ly6Chigh cells (20 and 10% of alive cells at day +1 resp) in the spleen and lungs of neonatal mice. Both cell types start entering

the lungs a few hours before birth, a process that continues until two weeks after birth. The homing process to the lungs is independent of GM-CSF or TLR4. Upon entering the lung neonatal CD11b+Ly6Chigh, but not CD11b+Ly6G+ cells gain suppressive capacity. This suppressive capacity, as measured by suppression of T cell proliferation in vitro, is arginase-1 dependent. Neonatal lung CD11b+Ly6Chigh cells can therefore be classified as myeloid derived suppressor cells. The cells do not proliferate locally, but keep entering the growing lungs until the age of two weeks. Within the first week the Ly6G+ cells become apoptotic and the Ly6Chigh cells differentiate into dendritic cells and M1 and M2 macrophages. M2-macrophages, consequently peak in numbers between 7 and 14 days after birth. The high frequency of suppressive CD11b+Ly6Chigh cells in the neonatal lung do not suppress but rather potentiate sensitization to house dust mite by differentiating into ST2 expressing CD11b+ dendritic cells.