

MONDAY, SEPTEMBER 3RD 2012

236. Predicting and observing paediatric allergic disease

P1931**Differences in genetic background of atopic and non-atopic asthma in children**

Vojko Berce¹, Carina Pinto Kozmus², Uros Potocnik³. ¹*Clinical Department of Pediatrics, University Medical Centre, Maribor, Slovenia;* ²*Institute for Molecular and Cell Biology, University of Porto, Portugal;* ³*Centre for Human Molecular Genetics and Pharmacogenetics, Faculty of Medicine, University of Maribor, Maribor, Slovenia*

Background: Childhood asthma has been divided into phenotypes, which differ in the age of presentation, triggers, lung function and natural history. Despite the enormous increase in the knowledge about asthma genetics, there are very few data regarding the differences in genetic background of asthma phenotypes.

Aims and objectives: To find out whether the genetic background of atopic and non-atopic asthma differs, we analyzed the association of genetic polymorphisms already associated with asthma or inflammatory diseases with different asthma phenotypes and quantitative traits.

Methods: We analyzed a case-control cohort composed of 189 Slovenian children aged between 5 and 18 years with mild or moderate persistent atopic asthma, 99 with non-atopic asthma and 273 controls. We measured numerous clinical and laboratory parameters and carried out genotyping for polymorphisms CCR5-delta32, IL4RA Q551R, IL4 C-33T, NOD2 R702W, CTLA4 CT60, MUC7 – VNTR, TNF C-1031T, TGFB1 C-509T, SLC22A4 C1672T, CD14 C-159T and IL23R rs7517847.

Results: In non-atopic asthmatics the frequency of CCR5-delta32 allele was 2.6%, which is significantly less than 9.0% in the control group (p=0.03) and the frequency of IL4RA Arg551 allele was 7.7%, which is also significantly less than 19.9% in the control group (p<0.01). We have found no association of genotype with atopic asthma. Non-atopic asthmatics homozygous for the MUC7*6 allele had a total IgE value of 263.3 IU/ml compared to 40 IU/ml in heterozygotes (p=0.02).

Conclusions: Our findings point to differences in the pathogenesis of different asthma phenotypes and contribute to understanding of asthma as a complex and heterogeneous disease on the genetic level too.

MONDAY, SEPTEMBER 3RD 2012

P1932**Maternal genetic asthma predisposition affects signaling networks in lungs of neonatal offspring**Petra Nathan¹, Stefan Dehmel¹, Rabea Imker¹, Martin Irmeler², Steffen Sass³, Nikola Müller³, Oliver Eickelberg¹, Susanne Krauss-Etschmann¹.¹Comprehensive Pneumology Center, ²Institute of Experimental Genetics,³Institute of Bioinformatics and Systems Biology, Helmholtz Zentrum München, Germany

Introduction: Exposure-induced deregulation of microRNAs (miRs) during early critical developmental periods has been proposed to contribute to the propagation of asthma risk in later life.

Aim: We asked if maternal genetic asthma predisposition is sufficient to affect pulmonary miR and also mRNA profiles in offspring that do not bear the genetic asthma risk. To address this question, we used female mice with a heterozygous deficiency for Tbx21 as they develop spontaneous airway remodeling and airway hyperreactivity (Finotto et al., Science, 2002; 295:336).

Methods: Female C57BL/6J Tbx21+/- mice were mated with wild type (wt) males. Neonatal lungs from wt pups of dams with (Tbx21+/-, n=8) and without (wt, n=8) genetic asthma predisposition were removed within 24h after birth and total mRNA including small RNAs was extracted. RNA from individual animals was subjected to microRNA (ABI, TaqMan[®] Array microRNA cards) and mRNA (Affymetrix Mouse Gene ST 1.0[®] arrays) expression profiling. Counter-regulated miRNA-mRNA pairs were further analyzed for pathway enrichment using in silico tools (GePS, IPA).

Results: After adjustment for gender differences 57 miRNAs and 2599 mRNAs were differentially regulated. Within these, 39 miRNAs paired to 1456 mRNA targets according to expression regulation. Enrichment analysis showed that developmentally important pathways (e.g. growth factor and BMP-signaling) are affected by exposure to maternal asthma predisposition even in the absence of genetic risk in the pups.

Conclusion: These data show that maternal genetic asthma predisposition affects pulmonary miR and mRNA profiles during an early developmental stage and might therefore influence lung development.

P1933**Role of maternal phenotype in asthma development in children**Liudmila Zhelenina¹, Maria Vakharlovskaya², Olga Lavrova², Tatiana Ivashchenko¹. ¹Pulmonological, St.-Petersburg State Pediatric Medical Academy, St. Petersburg, Russian Federation; ²Pulmonological, Pavlov State Medical University, St. Petersburg, Russian Federation

Children born from mothers with bronchial asthma are the most vulnerable group for development of allergic diseases.

AME of study. We have done research into data obtained from 117 pregnant women with bronchial asthma and their children. The average age of mothers was 27,7±5,2 years. Most mothers developed the disease before the age of 16 (88 mothers; 75,2%); 29 mothers got ill when they were over 16 years of age (24,8%) ("child" and "adult" bronchial asthma respectively). We have researched medical data of 117 children born from these mothers: 64 boys (54,7%) and 53 girls (45,2%). Over 70% of the children reached the age of 7-9 by the end of the observation period. Children born by caesarean section developed bronchial asthma 1.5 times more often than children born naturally. Children who had been breastfed for over 4 months had significantly lower incidence of atopic dermatitis than children fed artificially (14% and 32,7% respectively; $\chi^2=4,5042$, $p=0,033$). Children born from mothers with "child" asthma phenotype more often developed bronchial asthma by the age of 7 ($p=0,034$, $\chi^2=4,4929$). Children born from mothers with "child" asthma phenotype run a 3-fold higher risk of developing bronchial asthma than those whose mothers had "adult" asthma phenotype (OR = 3,042[CI:1,013 – 9,132]).

Conclusion: The research has confirmed the significance of hereditary load, maternal asthma phenotype, mode of child delivery, and baby feeding for development of allergic diseases in children.

P1934**A comparison of lung function and atopy between children with intrauterine growth retardation and normal birth weight in a birth cohort with documented wheeze**

Karthika Jayalal, George D'Souza, Uma Devaraj. Chest Medicine, St. John's Medical College, Bangalore, Karnataka, India

Rationale: Low birth weight and intra uterine growth retardation has been implicated in lower lung function and a higher incidence of atopy. This was tested in a birth cohort.

Aim: To compare atopic status and lung function between IUGR and normal birth weight children with documented wheeze.

Methods: Children aged 3-7 yrs from a birth cohort with documented wheezing or a parental history of child wheezing and a doctors prescription for bronchodilators were studied. IUGR was defined as birth weight of less than 2.5kg. All the children underwent spirometry and skin prick test.

Spirometry was done before and after bronchodilator according to ATS guidelines. Skin prick test was done using 10 antigens. Positive test was defined as wheal of more than 3mm of that of the negative control.

Results: A total of 92 children who were comparable were studied, out of which 36 (33%) were low birth weight and 56 (51.52%) were normal birth weight.

IUGR children had a lower FEV1/FVC ratio (FEV1/FVC 87.26±11.55) than children with normal birth weight (FEV1/FVC 93.74±7.62) p value - FEV1/FVC-0.002. They also had a lower FVC % value when compared to normal birth weight children. FVC% in IUGR -81.46±10.97 and that of normal birthweight children were -86.91±10.92 with a p value of 0.025. The skin prick test positivity in both groups were comparable (15.7% in normal birth weight and 16.7% in IUGR children, p value -0.92)

Conclusion: IUGR had lower FEV1/FVC ratio and FVC% as compared to normal birth weight children. Atopic status was comparable in both groups.

P1935**Exposure to farming environments in childhood and asthma and wheeze in rural populations: A systematic review with meta-analysis**

Jon Genuneit, Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany

Background: Particularly strong associations with asthma and allergic diseases have been described for exposure to farming environments in childhood. The aim of this systematic review was to update and extend existing narrative reviews, test for heterogeneity across studies, and conduct a meta-analysis.

Methods: Published literature was searched through PubMed including all articles added before September 1, 2011. Articles were included if they reported an epidemiological study on the exposure to a farming environment in childhood and subsequent wheeze or asthma. Heterogeneity of effect measures was evaluated using Cochran's Q and I². Effect measures were summarized by random-effects meta-analysis for various outcome definitions.

Results: In total, 357 retrieved abstracts revealed 52 articles from 39 studies with data considered for the meta-analysis. Most studies were conducted among children or on childhood onset of disease. Most data was on doctor diagnosed asthma or current wheeze. The meta-analysis showed substantial heterogeneity across studies with similar outcome definitions. Nonetheless, the combined effects were statistically significant and showed an approximate 25% lower asthma prevalence among exposed subjects compared to unexposed subjects.

Conclusions: The protective 'farm-effect' on asthma was reported in numerous studies. Its underlying factors ought to be studied and promising efforts have been already made. However, the heterogeneity of the effect across studies should also be investigated because whatever causes it is a potential threat to valid synthesis of evidence and to the detection of specific protective factors.

P1936

MONDAY, SEPTEMBER 3RD 2012

P1937**Leucotriene B4 in fractionated breath condensate: Comparison of bronchial and alveolar concentrations in children**

Christina Maria Mueller, Jordis Trischler, Stephanie K nitzer, Christiane Lex,
University Children's Hospital, Martin Luther University Halle-Wittenberg, Halle
(Saale), Germany

Background: Asthma is a chronic inflammatory disease of the airways but recent studies have shown that alveoli are also subject of pathophysiological changes.

Objectives: This study was undertaken to compare leucotriene B4 (LTB₄) concentrations in different parts of the lungs using a new technique of fractionated breath condensate sampling.

Methods: In 69 patients (10-17 years, 34 asthmatics, 35 controls) measurements of exhaled nitric oxide (FE_{NO}), lung function and LTB₄ concentrations in exhaled breath condensate (EBC) were performed. EBC was collected in two different fractions, representing mainly either the airways or the alveoli, using captopvolumetry. LTB₄ concentrations were measured using an ELISA.

Results: 44% and 49% of the LTB₄ values were below the detection limit. Concentrations of the bronchial fraction correlated significantly with those of the alveolar fraction ($r=0.73$, $p=0.000$). Differences between the fractions were not significant in a paired difference test. Subjects with obstructive lung function ($n=4$) had significantly higher LTB₄ values than subjects with normal lung function ($n=65$) ($p=0.043$, $p=0.040$, respectively). Asthmatics had significantly higher alveolar but not bronchial LTB₄ values than controls ($p=0.005$, $p=0.232$, respectively). There was no relationship between LTB₄ and FE_{NO} values.

Conclusions: Differences in LTB₄ concentrations between asthmatics and controls were only measurable in the alveolar but not in the bronchial fraction of EBC. An additional analysis of alveolar inflammation may therefore be possibly useful in asthmatics. However, lab techniques for analysing LTB₄ in EBC need to be improved and easy applicable.

P1938**High altitude stay reduces eosinophil load in airways in children with asthma**

Neeta Kulkarni¹, Vincenzo Ragazzo², Silvia Costella²,
Christopher O'Callaghan¹, Ahmad Kantar². ¹Infection, Immunity and
Inflammation, University of Leicester, United Kingdom; ²High Altitude Paediatric
Asthma Centre, Pio XII^o Institute, Misurina, Belluno, Italy

A normal sputum eosinophil count in children with asthma could result from corticosteroid treatment or reduction in eosinophil recruitment. In order to differentiate this we have described a new marker of eosinophilic inflammation (eosinophil protein content in airway macrophages)¹. At high altitude children with asthma show significant reduction in eosinophil count due to reduced exposure to allergens.

The aim was to determine the macrophage eosinophil protein content at baseline (T0) and after stay at high altitude (T1).

Sputum induction was performed at T0 ($n=54$) and T1 in children attending High Altitude Children's Asthma Center in Misurina. Differential count was obtained by counting 400 non-squamous cells (eosinophilic asthma defined as $\geq 3\%$). One hundred macrophages were imaged at high-resolution using digital camera. The percentage of macrophage cytoplasm with red hue was determined by image analysis. The groups were compared using Mann-Whitney and Wilcoxon t tests. There was no significant difference ($p=0.39$) between median airway macrophages (AM) red hue percentage in eosinophilic ($n=30$) [median (range)] [5.9(0.6-57.6)] and non-eosinophilic asthma ($n=24$) [8.7(0.34-71.2)]. Children at T1 had significantly lower i) eosinophil count Median (range) [$p=0.001$, 1(0-30) vs 3(0-52)] ii) AM red hue percentage [$p=0.005$, 3.82(0.41-59.82) vs 7.04(0.72-71.23)] than at T0.

The high AM red hue in non-eosinophilic asthma on arrival suggests ongoing eosinophilia in the absence of sputum eosinophilia. The reduction in eosinophil count after stay at high altitude is due to reduction in eosinophil recruitment in airways.

¹ Kulkarni NS et al. JACI 2010; 126(1):61-9.

P1939**Airway macrophage phagocytosis after high altitude residence in children with asthma**

Neeta Kulkarni¹, Vincenzo Ragazzo², Silvia Costella², Ahmad Kantar²,
Christopher O'Callaghan¹. ¹Infection, Immunity and Inflammation, University of
Leicester, United Kingdom; ²High Altitude Paediatric Asthma Centre, Pio XII^o
Institute, Misurina, Belluno, Italy

Airway macrophages (AM) perform crucial function of clearing pathogens and presenting antigens. AM phagocytosis in adults with mild asthma is enhanced compared to healthy individuals and possibly related to higher level of activation

of macrophages¹. At high altitude there is reduced exposure to allergens. However it is not known what effect this has on the macrophage phagocytosis.

The aim was to determine the phagocytic function of airway macrophages at baseline (T0) and after stay at high altitude (T1).

Sputum induction was performed at T0 and T1 in children with mild to moderate asthma attending High Altitude Children's Asthma Center in Misurina. Differential count was obtained by counting 400 non-squamous cells (eosinophilic asthma $\geq 3\%$). AM were isolated by adherence and cultured with FITC labelled heat killed staph aureus in the ratio of 1:10 (AM: bacteria). One hundred macrophages were imaged using confocal microscope. The median bacterial count/AM was calculated using Image J and Cell profiler software. The groups were compared using paired and unpaired t-tests.

There was no significant difference ($p=0.3$) between median bacterial count in eosinophilic ($n=16$) [Mean (SD)] [77.56(36.6)] and non-eosinophilic asthma ($n=8$) [68.22(11.5)] at T0. Children at T1 ($n=19$ pairs) had significantly lower i) median bacterial count [Mean (SD)] [$p=0.006$, 39.55(4.51) vs 73.26 (39.42)] than at T0.

The sputum macrophages in children with mild to moderate asthma are equally phagocytic in eosinophilic or non-eosinophilic groups. After stay at high altitude macrophages were less phagocytic (possibly due to return to normal level of activation).

Reference:

[1] Lay JC et al Thorax 2009; 64:313-320.

P1940**The impact of sublingual immunotherapy (SLIT) of asthma on Th1 cells susceptibility to apoptosis**

Olga Ciepiela¹, Anna Zawadzka-Krajewska², Iwona Kotula¹, Urszula Demkow¹.

¹Department of Laboratory Diagnostics and Clinical Immunology of
Developmental Age, Medical University of Warsaw, Poland; ²Department of
Pediatric Pneumology and Allergology, Medical University of Warsaw, Poland

Asthma is a chronic inflammatory disease of the airways. Allergen-specific immunotherapy is the unique disease modifying treatment of atopic diseases. SLIT is effective treatment associated with low incidence of systemic reactions. A disturbed T cells apoptosis plays a crucial role in the development of airway inflammation in the course of asthma. Nevertheless, the effect of sublingual immunotherapy on T cell apoptosis has not been elucidated. The aim of present study was to evaluate the influence of one year allergen-specific immunotherapy in asthmatic children on the frequency of Th1 Bcl-2 positive cells in peripheral blood.

Twenty-five children, suffering from bronchial asthma and allergic rhinitis were enrolled to the study. Children were shortlisted for sublingual specific immunotherapy with solution containing specific allergen (grass pollen or house dust mite) extracts. The frequency of Th1 cells and the intracellular expression of Bcl-2 were evaluated using flow cytometry before and after 12 months of treatment. The frequency of Th1 cells after immunotherapy was significantly increased (13,22 [10,34; 18,95]% before versus 19,86 [16,37; 24,52]% after SLIT, $p=0.01$), moreover significant increase of Bcl-2 positive Th1 cells was found after treatment. At a baseline 58,34 (31,23; 76,28) % of Th1 cells showed expression of Bcl-2 protein, whereas 73,61 (68,47; 82,43) % Th1 cells expressed Bcl-2 after one year of SLIT, $p=0.0465$.

The increase of Th1 cells frequency secondary to SLIT might be associated with enhanced resistance to apoptotic signals. However, further studies are needed to clarify the role of T cell apoptosis in resolution of allergic airway inflammation.

P1941**A relationship between exercise-induced bronchoconstriction and allergic rhinitis in Japanese children**

Yoko Murakami¹, Satoru Honjo¹, Hiroshi Odajima¹, Yuichi Adachi²,
Koichi Yoshida³, Yukihiro Ohya⁴, Akira Akasawa³. ¹Paediatrics, National
Hospital Organization, Fukuoka National Hospital, Fukuoka, Japan;
²Paediatrics, Toyama University, Toyama, Japan; ³Allergy, Tokyo Metropolitan
Children's Medical Center, Tokyo, Japan; ⁴Allergy, National Centre for Child
Health and Development, Tokyo, Japan

Introduction: A relationship between allergic rhinitis (AR) and Exercise-induced bronchoconstriction (EIB) has not been fully studied.

Aims: The aim of this study was to examine the relationship between EIB and AR among children aged 6-17 in Japan.

Methods: EIB and AR were ascertained by International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire among randomly selected schools across the nation. Number of the subjects were 43,813 of 6-7 year old attending the elementary schools, 48,641 of 13-14 year-old attending the junior high schools and 54,138 of 16-17 year old attending the high schools. We examined relationship between having AR and risk of EIB, and severe EIB in current asthmatics in a case-control design using logistic regression model. We also investigated an association of degree of life disturbed by AR with risk for EIB, and severe EIB. And the risk for having EIB due to sex, school grade and severity of asthma was examined among current asthmatics with mutual adjustment for these covariates using multiple logistic regression analysis.

Results: Response rates were 83.4%. Odds ratio (OR) of having EIB due to current AR was 1.47 (95% confidence interval (CI) = 1.34 - 1.60, $p<0.01$), and OR of severe EIB was 1.13 (0.99 - 1.30, $p=0.076$), respectively. Risk of EIB and that

MONDAY, SEPTEMBER 3RD 2012

of severe EIB were elevated with increasing severity of life disturbed by AR, respectively (p for trend <0.01 and <0.01).

Conclusions: Risk of EIB was increased among children with AR as compared to those without AR. Degree of life disturbed by AR was related to increasing risk of EIA, and severe EIA.

P1942

Physical activity: Children with asthma and without asthma

Andrey Sousa, Celso Carvalho, Milton Martins, Anna Cabral. *College Medicine of University of São Paulo, University of São Paulo, SP, Brazil Pediatric Clinic, Darcy Vargas Children's Hospital, São Paulo, SP, Brazil*

Background: It is well known that regular physical activity has health benefits, reducing obesity, morbidity and mortality. Currently, the practice of physical activity in asthmatic patients shows a significant improvement of disease symptoms, however, there is disagreement in the literature whether asthmatic children are more sedentary than children without asthma.

Objective: To compare level of daily physical activity in children with and without asthma.

Method: We studied 121 children (79 asthmatics) of both genders among 7-12 years. Were selected for the study asthmatic patients with controlled disease. The level of daily physical activity was monitored by use of the accelerometer for six days (four weeks on and two on the weekend).

Results: Total number of steps, steps and time in moderate physical activity between genders of the asthma and control groups were similar.

Total number of steps, steps and time in moderate physical active during weekdays

	Boys		Girls	
	Asthmatic	Controls	Asthmatic	Controls
Total steps	15346	14245	12150	11264
Moderate steps	6934	6457	5524	5368
Moderate time	54,4	50,7	42,8	39,5

All findings are presented as mean. P value $>0,05$.

Percentage of children classified as active by steps and time are similar.

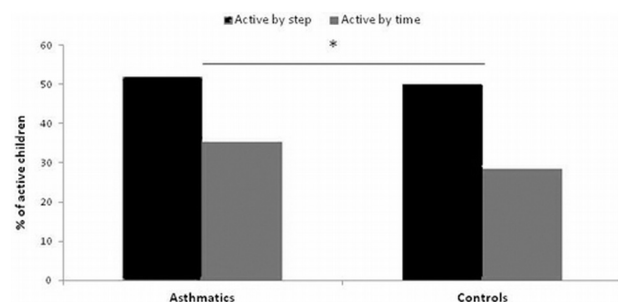


Figure 1: Active children by steps and time are presented in percentage. Children were considered active by steps when boys reached steps total ≥ 15000 and girls ≥ 12000 , while children were considered active as time when average reach time in moderate physical activity ≥ 60 minutes. $p > 0,05$

Conclusion: Characteristics related to asthma do not seem to affect the physical activity in children with controlled disease, making the practice of daily physical activity similar to that of children without asthma.

P1943

Obesity and asthma symptoms in children

Francisco-Javier Gonzalez-Barcala¹, Sonia Pérezga², Juan Sánchez Lastres³, Miguel Angel San José Gonzalez³, Luis Bamonde³, Luciano Gamelo³, Teresa Pérez Castro⁴, Manuel Sampedro³, Luis Valdes¹, José-Manuel Alvarez-Dobaño¹, Lucía Ferreira¹, Angel López Silvarrey⁵.

¹Respiratory, Clinic University Hospital, Santiago de Compostela, Spain;

²Clinical Epidemiology and Biostatistics Unit, Clinic University Hospital, A

Coruña, Spain; ³Pediatrics, Galician Health Service, Santiago de Compostela,

Spain; ⁴University College of Health Sciences, University of A Coruña, Spain;

⁵Pediatrics, Maria Jose Jove Foundation., A Coruña, Spain

Introduction: The relationship between obesity and asthma show inconsistent results. The purpose of our study was to evaluate the prevalence of asthma according to obesity in a large sample of the child population in our region (total population 2795422).

Methods: A cross-sectional study, following the ISAAC study methodology, was conducted on randomly selected 6-7 year old children.

The asthma symptoms, demographic characteristics, and other potential risk factors were determined from the questionnaire. Overweight and obesity were defined based on the body mass index.

Multiple logistic regression were used to obtain adjusted prevalence odds ratios (OR) and 95% confidence intervals (95% CI) between asthma symptoms and obesity.

Results: Finally, 7485 children were included (50.8% female). Our results showed that 23.4% of our children were overweight, and 9.6% were obese.

The prevalence of wheezing ever was 39.0%, that of current asthma 13.5%, severe asthma 4.9%, and exercise induced asthma 6.4%.

Obesity was associated with an increase in the probability of wheezing ever (OR: 1.35) and exercise induced asthma (OR: 1.62).

Odds ratio for prevalence of asthma symptoms according to obesity and overweight in children

	Wheezing ever OR (95% CI)	Current asthma OR (95% CI)	Exercise induced asthma OR (95% CI)	Severe asthma OR (95% CI)
Normal weight	1	1	1	1
Overweight	1.07 (0.92-1.25)	1.10 (0.88-1.36)	1.10 (0.80-1.52)	0.96 (0.66-1.41)
Obesity	1.35 (1.10-1.66)	1.31 (0.98-1.74)	1.62 (1.10-2.36)	1.20 (0.74-1.94)

OR: Odds Ratio. CI: Confidence interval. Adjusted by gender, cat and dog keeping, maternal education, parental asthma and parental smoking.

Conclusion: In our population, obesity was associated with a higher prevalence of asthma in young children.

P1944

Prevalence of asthma and rhinitis in school-age children in Fortaleza, northeast Brazil

Daniela Chiesa¹, Maria de Fatima Luna², Gilberto Fischer², Marcelo Gurgel Silva³, João Rafael Luna⁴. ¹Internal Medicine, Universidade de Fortaleza, Ceara, Brazil; ²Pulmonology Post Graduate Program, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil; ³Medicine, Universidade Estadual do Ceara, Fortaleza, CE, Brazil; ⁴Medicine, Universidade Federal do Ceara, Fortaleza, CE, Brazil

Introduction: In Brazil, the mean prevalence of asthma symptoms is 13.3%. Fortaleza is the fifth largest city of Brazil and there is no recent official data from asthma prevalence in children.

Objective: The aim was to evaluate the prevalence of asthma and rhinitis symptoms in 6/7 years old children in Fortaleza.

Method: The protocol of the International Study of Asthma and Allergies in Childhood (ISAAC) was used. Random sample were taken from 3000 students from public and private schools in 2010. The surveys were sending with their homework for the parents to fill it and returning to the school in the next day.

Results: The prevalence of wheezing was 52.6% and wheeze in the last 12 months, 28.3%, while diagnosed asthma was 12.4%. For symptoms associated with severity, the rate of wheezing with speech impairment was 4.1%, four or more wheezing attacks in the last year, 3.9% and sleep disturbance by wheezing in one or more nights a week, 6.7%. The rate of wheezing after exercise was 7.2% and dry nocturnal cough was 39.7%. Mother's smoking ($p < 0.001$), father's smoking ($p = 0.011$) and contact with pets ($p = 0.007$) were associated with asthma symptoms. Mother's smoking ($p = 0.011$) and the use of antibiotics ($p = 0.011$) in the first year of the child's life were associated with severe asthma. The prevalence of rhinitis symptoms was 50.9%, rhinitis in the last 12 months, 42%, rhinoconjunctivitis, 15.4% and diagnosed rhinitis, 28.1%. Impaired daily activities by rhinitis was 19.6% (little), 3.8% (moderate) and 1.9% (high).

Conclusions: The prevalence of asthma and rhinitis in 6/7 years old children in Fortaleza were similar to Brazilian national mean rate. Asthma and rhinitis are underdiagnosed among children in Fortaleza.

P1945

Dynamics of asthma prevalence in children in the Novosibirsk (preliminary results)

Elena Kondiurina, Tatiana Elkina, Natalia Gulevskaia, Maria Shably, Andrei Likhonov. *Department of Pediatrics, State Medical University, Novosibirsk, Russian Federation*

Background: The study of the asthma epidemiology according to the ISAAC program (Phase Three) was over in 2002. Afterwards the studies with the use of standardized methods have not been carried out in the world.

Aim: To study the dynamics of asthma prevalence among the 6-7 years old children in the Novosibirsk.

Methods: According to the ISAAC 3249 children were examined in 2002 and about 3000 children aged 6-7 years old were examined in the years of 2011-12. This abstract introduce the preliminary results based on the questioning of 970 parents in the years of 2011-12.

Results: There decreased the prevalence of wheezing from 24.1% to 17.3% ($p < 0.0001$), the prevalence of current asthma symptoms from 10.8% to 6.3% ($p < 0.0001$), the number of exacerbations over 12 times a year from 0.5% to 0.2% ($p = 0.001$). The prevalence of nocturnal asthma symptoms decreased from 4.3% to 2.2% ($p = 0.001$), the number of symptoms limiting speech decreased from 0.9% to 0.1% ($p = 0.012$). The diagnose of asthma was established in 2.4% of children in 2002. In 2011-12 this percentage increased up to 3.4% ($p = 0.07$), this indicates the improvement in the diagnostics and the better level of knowledge of physicians about the asthma. The prevalence of asthma symptoms associated with the physical exertion was not significantly changed (3.6% in 2002 and 3.3% in 2011-12, $p = 0.4$). The registration of nocturnal cough not associated with the infection of the respiratory tract decreased from 8.6% to 7.6% ($p = 0.2$).

MONDAY, SEPTEMBER 3RD 2012

Conclusion: The obvious trend in the first decade of the XXI century is the decrease in the prevalence of the asthma symptoms among 6-7 years old children in the Novosibirsk with some improvement in the disease diagnostics.

P1946

Bronchodilator responsiveness following methacholine-induced bronchoconstriction in children with clinically highly suspected asthma

Tae Won Song, Pediatrics, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Republic of Korea

Rationale: Patients who were clinically highly suspected asthma occasionally showed negative results in methacholine challenge test (MCT), but showed higher bronchodilator responsiveness (BDR) after methacholine induced bronchoconstriction. The aim of this study was to assess the usefulness of BDR following methacholine-induced bronchoconstriction as a tool for the therapeutic plan in clinically suspected asthmatic patients with negative results in MCT.

Methods: MCT was performed in 530 children for evaluation of asthma. Immediately after MCT, patients were asked to inhale short-acting beta2 agonists to evaluate BDR. BDR was measured as the percent increase in FEV1 after treatment. Total serum IgE levels, total eosinophil counts, and specific IgE levels were measured in most children. Schedule visits at 1-month to 6-month intervals were done for 3 months to 4 years.

Results: Among 530 children, 219 patients showed negative results ($PC_{20} > 25\text{mg/mL}$) in MCT. Out of children with negative MCT, 37 patients expressed over 12% increase (high BDR) and 182 patients expressed under 12% increase (low BDR) in FEV1 after bronchodilator following methacholine induced bronchoconstriction. Among patients with high BDR and negative MCT, 37.8% patients were required inhaled corticosteroid therapy for control of their symptoms. But, among patients with low BDR and negative MCT, only 10.8% patients were required inhaled corticosteroid.

Conclusion: In clinically highly suspected asthmatic children with negative MCT, BDR following methacholine-induced bronchoconstriction seems to play a considerable role for the decision of treatment with inhaled corticosteroid.

P1947

Relationship between phenotypic characteristics of children with sickle cell disease and airway nitric oxide levels

Glenda Bendjak, Dimas Mateos-Corral, Anwar Sallam, Hartmut Grasemann. Division of Respiratory Medicine, Department of Pediatrics, Hospital for Sick Children, Toronto, ON, Canada

Background: Children with sickle cell disease (SCD) have evidence of airflow limitation on spirometry, and evidence for increased airway nitric oxide (NO) levels.

Objective: To determine the relationship between phenotypic characteristics (atopy, asthma, acute chest syndrome (ACS), pulmonary function test abnormalities) and airway NO levels in children with SCD.

Methods: Children with SCD were recruited during visits for routine annual pulmonary function testing. Subjects completed ISAAC/medical questionnaires, skin prick testing for aeroallergen sensitization, and pulmonary function testing. Nasal (NNO) and the fraction of exhaled NO (FENO) were measured. Subjects were classified by phenotypic characteristics, and NNO and FENO compared between groups, using Mann-Whitney tests.

Results: 154 children participated. Seventy-six (49%) were male. Mean(\pm SD) age was 12.6 ± 3.3 years. Hemoglobin levels were 96.0 ± 18.3 g/L. FVC, FEV1, and FEF₂₅₋₇₅ were 86.7 ± 14.0 , 84.7 ± 15.0 , and 84.4 ± 30.0 percent predicted, respectively. NNO and FENO were 890 ± 387 and 17.9 ± 15.9 ppb.

Eighty (52%) subjects were atopic. Thirteen (8%) subjects taking asthma medication, and 38 (25%) with an asthma diagnosis or wheezing, were classified as asthmatic. Twenty (13%) subjects had a significant bronchodilator response ($\geq 12\%$) in FEV1 or FVC. Seventy-three (47%) subjects reported previous ACS or pneumonia. No significant differences were seen in NNO or FENO between any groups compared.

Conclusions: Airway NO measurements did not correlate with any of the phenotypic characteristics evaluated in this cohort of children with SCD, and therefore may not be a meaningful tool in the assessment of SCD lung disease.