Introduction: Primary Ciliary Dyskinesia (PCD) is a rare, chronic lung and upper airway disease caused by ineffective beating of the motile cilia. The cornerstones of the treatment are physiotherapy to improve mucociliary clearance and antibiotics to treat infections. Patients performing treatment, report less symptoms (McManus et al. 2003). A high treatment burden is related to a decline of health related quality of life in patients with PCD (Pifferi et al. 2010). Patients often feel frustrated through mistrust in medical care and a lack of knowledge surrounding PCD (Whalley & McManus 2006). Research about attitudes and barriers to treatment in PCD has not yet been reported.

Aim: This study aims to investigate and identify attitudes and barriers related to treatment adherence in children with PCD and their parents.

Methods: Children with PCD (<18 years, n = 31) treated at the University Hospital Leuven and their parents, were asked to participate by mail. A questionnaire consisting of demographic information and treatment related questions, a list of 18 barriers and 10 statements of attitudinal patterns (Dziuban et al. 2010) was included, along with the informed consent. Adolescents (14–18 years, n = 9) were asked to fill out the questionnaire themselves, after parental consent.

Results: Seven adolescents and 25 parents participated. Physiotherapy was prescribed to all patients, nebulizers to 80%, nose spray to 72%, antibiotics to 60%, puff to 60%, ear drops to 29%, and nose can to 30%. The most commonly reported barriers to treatment were “too busy” (parents 60%; adolescents 57%), “forgetting” (parents 48%; adolescents 71%), “family issues” (parents 36%; adolescents 42%), “wanting to be normal” (parents 28%; adolescents 57%) and “it takes too much time” (parents 28%; adolescents 57%). For adolescents, attitudes influencing non-adherence include “My PCD team does not understand how though it is to follow my treatments” (57.1%), “Even though I want to follow my treatments, sometimes I just forget” (71.4%). “I have trouble sticking to my treatments because they make me feel worse” (85.7%) and “Having to follow the PCD treatments means less freedom in my life” (42.9%). For parents, this last one is most often reported as an attitude towards treatment (76%).

Conclusion: A variety of reasons were described for non-adherence to treatment for PCD, which seem especially related to time management and a loss of freedom because of treatment. Adolescents report different attitudes to treatment compared to parents. For adolescents these attitudes predominately relate to feeling misunderstood and feeling restricted by the PCD treatment. The identified barriers and attitudes to treatment adherence pose a real challenge to PCD care teams in their day to day care for children with PCD.

III. ABSTRACTS

1. Bronchial Asthma and Other Chronic Obstructive Pulmonary Diseases

#24 - THE ASSOCIATIONS OF POOR ASTHMA CONTROL WITH LIFESTYLE HABITS, STRESS LEVELS AND QUALITY OF LIFE IN SINGAPOREAN ADOLESCENT PATIENTS

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Pediatric Pulmonology

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Background: In Singapore, 5% of adults and 20% of children have asthma (Health Promotion Board Singapore, April 2013). Asthma management includes regular assessment and monitoring, education, control of environmental factors and co-morbid conditions, and pharmacologic therapy where indicated. The effects of poor asthma control on stress levels and quality of life in adolescent patients have not been explored in the local context.

Objectives: To investigate the associations between asthma control and stress levels, quality of life and lifestyle factors in adolescent and young adult patients in Singapore.

Methods: Questionnaire survey of adolescent and young adult patients attending the paediatric asthma clinic at National University Hospital Singapore over 5 months. Data on demographics and lifestyle were obtained. The Asthma Control Test, a validated test for asthma control with a maximum score of 25, was used to assess each patient’s asthma symptomatology. A cut-off score of 19 or less identified patients with poorly-controlled asthma. Stress levels were measured using two psychological instruments, the Holmes-Rahe Social Readjustment Ratings Scale (SSRS), and the Perceived Stress Scale (PSS). The Asthma Quality of Life Questionnaire (AQLQ) was used to assess the impact of asthma on the patient’s quality of life.

Results: Fifty-seven patients were interviewed during the study period (age range 12–23 years, median 17 years). There were 30 males (52.6%) and 24 females. Forty-one patients had well-controlled asthma (71.9%) and 16 were poorly-controlled (28.1%). There were no significant differences between the well-controlled and poorly-controlled groups in terms of age distribution, gender, race, body mass index, parents’ education level, housing type and family income. Exposure to household smoking was significantly associated with poor asthma control (P = 0.043, OR 3.55). Patients who did not exercise were more likely to be poorly-controlled compared to those who exercised (P = 0.043, OR 6.5). Patients with allergic rhinitis over the preceding 12 months were more likely to have poor asthma control (P = 0.035, OR 3.83). Patients with four or more attacks of wheezing in the preceding 12 months were also more likely to have poor asthma control (P = 0.032, OR 5.75). There was no significant difference in the SSRS scores between well-controlled and poorly-controlled patients. However, the poorly-controlled group had higher PSS scores, reflecting more stress (P = 0.02), while the well-controlled group had better quality of life scores using the AQLQ questionnaire (P = 0.001).

Conclusion: We identified several risk factors associated with poor asthma control that these included environmental, lifestyle and co-morbid factors. Poor asthma control was significantly associated with increased psychological morbidity in adolescents and young adults. The psychological impact of poor asthma control on the patient should be addressed when seen in the outpatient setting.

#27 - EFFECT OF STEP UP THERAPY ON BRONCHIAL HYPERRESPONSIVENESS IN CHILDREN WITH POORLY CONTROLLED ASTHMA ON INHALED CORTICOSTEROID (ICS) MONOTHERAPY.

Author:

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Introduction: The effect of asthma step-up therapy on the degree of bronchial hyperresponsiveness (BHR) in children is not well understood. Aim: The aim of this pilot study was to determine the effect of three different step-up therapies (high dose ICS, ICS + LABA [Long Acting beta-agonist] and ICS + LTRA [Leukotriene-receptor antagonist]) on the degree of BHR,
in children with uncontrolled or partially controlled asthma, on low-medium dose (<400 μg BDP [Beclomtree dipropionate] equivalent) ICS monotherapy.

Methods: In this open-label parallel group study, children (aged 6-18 years) with uncontrolled or partially controlled asthma on <400 μg BDP after a 4-week run-in period on 100 μg Fluticasone (Flutofl 100 Acuccailer, GlaxoSmithKline) twice daily, were assigned to one of the three step-up therapies: 200 μg of Fluticasone twice daily [ICS step-up], 100 μg of fluticasone plus 50 μg of salmeterol (Sereide 50/100 Acuccailer, GlaxoSmithKline) twice daily [LABA step-up], or 100 μg of fluticasone twice daily plus montelukast (Singulair, MSD) 5 mg (for children 15 years) or 10 mg (for >15 years) [LTRA step-up]. Comprehensive assessment of asthma control (clinical assessment, spirometry, FeNO, asthma symptom diary, Paediatric Asthma Quality of Life Questionnaire [PAQLQ] and Asthma Control Test [ACT]) and BHR (using Mannitol dry powder challenge test [MCT], Aclidin, Pharmaxis, Australia) were done at the end of run-in period and after 8 weeks of step-up therapy.

Results: 33 children (Mean [SD] age: 11.1 [3.1] years, 21 [63.6%] males) were studied; n = 11 in each of the three step-up therapy groups. There was no significant difference in ACT score, PAQLQ score, FeNO, FEVI, FVC, FEF25-75 and the proportion of asthma symptom-free days between the three groups, before and after step-up therapy. The difference in the degree of BHR within the three treatment groups before and after step-up therapy was not statistically significant. The proportion of children in whom the MCT test changed from positive to negative was 42.8% in the ICS step-up, 25% in the LABA step-up and 10% in the LTRA step-up group. Improvement in BHR (defined as either a change of MCT PE <20. Rodríguez Fernández-Oliva CR. (Pediatria, CS La Cuesta - Tenerife, Spain)
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Pediatric Pulmonology
# S52 - Abstract

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The aim of this study was to investigate the relationship between asthma control (impairment and risk) in children and their mothers’ quality of life (MQoL).

Three hundred ninety-four 0–14 years-old children with asthma were evaluated in 22 primary care pediatric practices in Spain. Impairment was evaluated through a combination of symptom frequency, nighttime awakenings, interference with normal activity, beta-agostin use and spirometry, and asthma was classified as well controlled, not-well controlled and poorly controlled, according to the National Asthma Education and Prevention Program. Risk of loss of control was classified as high or low according history of hospitalization, adverse effects of medication, recent exacerbation and frequent exacerbations. MQoL was measured by means of the validated IFABI-R questionnaire, which quantify the impact of pediatric asthma on three domains of caregivers’ quality of life: functional, emotional and socio-occupational. Higher IFABI-R scores mean poorer quality of life.

Multiple regression models were built with each dimension of MQoL acting as dependent variables. The effects on them of impairment and risk were adjusted by education level, social class and family functioning, and measured as percent change in IFABI-R score. Additional regression models were built to evaluate the effect on MQoL of each single item that conforms evaluations of impairment and risk.

There was a linear relationship between asthma control in children and MQoL, affecting the three dimensions. Compared with well controlled, not well controlled asthma increased IFABI-R scores in 18.6% (95% confidence interval 8.1–30.2%) in the functional domain, 9.6% (0.2–19.8%) in the emotional domain, and 9.2% (1.4–17.5%) in the socio-occupational domain. The impact was even greater in poorly controlled asthma: 25.2% (9.0–43.8%), 20.8% (5.5–38.3%) and 15.1% (3.1–28.7%), respectively.

None of the individual items that form the evaluation of the impairment in asthma control were associated with MQoL. On the other hand, a high risk of loss of control was independently associated with MQoL, with an interval 8.1–30.2%) in the functional domain, 9.6% (0.2–19.8%) in the emotional domain, and 9.2% (1.4–17.5%) in the socio-occupational domain. The impact was even greater in poorly controlled asthma: 25.2% (9.0–43.8%), 20.8% (5.5–38.3%) and 15.1% (3.1–28.7%), respectively.

In conclusion, both impairment and risk are strongly related with MQoL. The impact was even greater in poorly controlled asthma: 25.2% (9.0–43.8%), 20.8% (5.5–38.3%) and 15.1% (3.1–26.7%), respectively.

# S33 - THE IMPACT OF AN INTEGRATED ASTHMA PROGRAM IN A CHILDREN’S HOSPITAL IN SINGAPORE

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Pediatric Pulmonology

Introduction: A review was conducted in children with frequent attendances for acute asthma at Children’s Emergency Department KK Women’s and Children’s Hospital in 2002. The clinical audit revealed that children with problematic asthma were seldom referred for regular management. An initiative was developed to identify children with high acute care needs and recruit them to an integrated program for appropriate management. The objectives of our program were to reduce urgent care needs, control symptoms and improve the quality of life of these children.

The strategies used were:
1. Standardized care: Early initiation of anti-inflammatory or controller therapy, and the use of inhaled Beta agonist via a holding chamber for all patients: Every patient was given an individualized written asthma action plan (WAAP); 3. Intensive education by asthma resource nurses and 4. To encourage adherence, the program also provided 50% subsidy for the non-subsidized drugs in the hospital formulary.

This program was piloted in August 2002 and had since completed 10 years. Study objective: A critical review of the asthma outcome after the introduction of the integrated asthma program.

Methods: Retrospective analysis was conducted on the clinical database of the children recruited. Results: A total of 4158 patients 63% male and 37% female, was recruited to this program. Asthma Control: Eighty percent of the children had needed acute care needs in the past 3 months before enrolment. Less than 30% had needed urgent care with optimization of controller therapy. About 70% of children had achieved symptom control by 6 months of therapy. More than 70% no longer report exercise limitation and did not miss any school days. All these improvement were statistically significant.

Controller: More than 70% of the problematic asthma was controlled with the use of a single agent ie low dose inhaled corticosteroids (ICS). Only 25% had needed to step up to moderate dose ICS or combination of long acting beta agonist (LABA) with ICS and/or Montelukast.

Discussion: The results showed that the integrated program was able to achieve the objectives to reduce acute care needs, improved asthma control and quality of life. Intensive patient/caregiver education, the introduction of inhaled bronchodilator via holding chamber and the use of WAAP throughout the hospital including at the CE, had proven to be useful strategies which had contributed significantly to the success of the program. The results also indicated that majority of the problematic asthma were not difficult to treat. Establishing a strong partnership with community doctors to create awareness of early therapy would improve asthma care in the community and potentially could reduce the “problematic asthma” patient load by up to 70%, thus allowing limited resources to be better distributed to the truly difficult asthma.

# S34 - PERSISTENT BRONCHIAL HYPERRESPONSIVENESS IN CHILDREN WITH MODERATE PERSISTENT ASTHMA

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Background: Available evidence suggests that bronchial hyperresponsiveness (BHR) and the resultant mechanical forces may have a potential role in the development of airway remodeling in patients with asthma (1). It has been argued that prevention of bronchoconstriction and normalising the BHR should be an important aim of the asthma management (2).

Aim: To study the degree of BHR in children with moderate persistent asthma (MPA), on British Thoracic Society (BTS) asthma treatment steps 2 or 3. Methods: Comprehensive assessment of asthma control was done on children with MPA on BTS treatment steps 2 or 3, on follow up under the Singapore National Asthma Program. Subjects also had assessment of their degree of BHR, using Mannitol dry powder challenge test [MCT], Aclidol®, Pharmaxis, Australia).
Results: The Table 1 Demographic and clinical details

|                           | BTH treatment step 2 (n=27) | BTH treatment step 3 (n=30) |
|---------------------------|-----------------------------|-----------------------------|
| Age (year)*               | 10 (8-13)                   | 10.5 (8-13)                 |
| Gender†                   | Male19 (69.3), Female10 (30.7) | Male19 (63.3), Female11 (36.7) |
| Race‡                     | Chinese: 9 (33.3), Malay: 11 (40.8), Indian: 4 (14.8), Eurasian: 3 (11.1) | Chinese: 9 (33.3), Malay: 12 (40.8), Indian: 5 (16.7), Eurasian: 3 (10.0) |
| BMI*                      | 0.9 (1.5-2.5)               | 0.9 (1.5-2.24)              |
| Age (year) at diagnosis*  | 4 (2-7)                     | 6.5 (2-7)                   |
| Eczema                    | Yes=15 (55.6), No=12 (44.4) | Yes=16 (53.3), No=14 (46.7) |
| Allergy (Rhinitis)†       | Yes=27 (100)                | Yes=30 (100)                |

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### #48 - AIRWAY RESISTANCE BY IMPULSE OSCILLOMETRY PREDICTS ASTHMA EXACERBATIONS IN YOUNG CHILDREN

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Background: It is difficult to predict asthma exacerbations in young children with episodic asthma. In a retrospective analysis of an asthma study (Zielen et al. “Predicting short term response to anti-inflammatory therapy in young children with asthma”, Curr Med Res Opin. 2010) we identified predictors of asthma exacerbations and related it to the parameters forced expiratory volume (FEV1), respiratory resistance (Rrs5) by impulse oscillometry (IOS), and bronchial hyperresponsiveness (BHR) to methacholine testing. Method: Sixty-nine patients (4-7 years) with episodic asthma corresponding with the characteristics in the above-mentioned study were included. We defined an asthma exacerbation as an increased use of Salbutamol during cough periods (>2 puffs/week, >3 puffs/2 weeks). Pulmonary function and BHR were measured in symptom free intervals. To define the sensitivity and specificity to detect an asthma exacerbation, a receiver-operating characteristic (ROC) curve was plotted, and the accuracy was measured by the area under the ROC curve (AUC). A logistic regression model was used to predict the probability of an exacerbation.

Results: Mean results in the total group were: FEV1 106.6% ± 14.3, Rrs5 0.76 kPa.l-1.s-1 ± 0.19, and PD20FEV1 methacholine 0.34 mg ± 0.55. The following cut-off values showed the best combination of sensitivity and specificity to predict an asthma exacerbation: FEV1 103.2% (AUC 0.62), Rrs5 0.76 kPa.l-1.s-1 (AUC 0.80), and PD20FEV1 methacholine 0.13 mg (AUC 0.61). In the logistic regression analysis a combination of all parameter predicted the individual risk of an asthma exacerbation with an accuracy of 86%.

Conclusion: Simple pulmonary function parameters predicted the probability of asthma exacerbations in young children to a large extent. The airway resistance Rrs5 was superior to FEV1 and methacholine testing. In recent studies bronchodilator response using IOS distinguished asthmatics from non-asthmatics as FEV1 did not and small-airway IOS measurements significantly indicated children with uncontrolled asthma. The current data suggests that peripheral airway obstruction is even present in symptom free periods and that these children exacerbate during infections.

### #60 - ROLE OF MITOCHONDRIAL BIOGENESIS IN ASTHMATIC AIRWAY SMOOTH MUSCLE Proliferation: FOREVER YOUNG

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Background: Increased bronchial smooth muscle mass is one of the key structural features of severe asthma. In adults, asthmatic airway smooth muscle cells (ASMC) demonstrate greater mitochondrial biogenesis associated with an increase in ASMC proliferation rate vs non-asthmatic ASMC. However, to the best of our knowledge, there is no evidence that such a difference between asthmatic and non-asthmatic ASMC occurs in pre-school children.

Aims: The primary aim of the study was to compare asthmatic and non-asthmatic ASMC proliferation and mitochondrial biogenesis in adults and pre-school children. The secondary aim was to assess the effect of factors released by the epithelium upon stimulation by environmental factors such as house dust mite and rhinovirus, on ASMC proliferation.

Methods: We cultured ASMC and bronchial epithelial cells (BEC) obtained by endobronchial biopsy from children and adults with severe asthma or undergoing bronchial endoscopy for other reasons. We then studied ASMC proliferation (cell counting and CFSE dye assay) in 10% fetal bovine serum (FBS), 0%FBS and after the addition of the BEC culture supernatant obtained after rhinovirus infection, house dust mite exposure or both. Mitochondrial mass and biogenesis were determined by western blot.

Results: Sixteen pre-school children with severe asthma, median aged 2.8 years, 4 control children (4.6 yrs), 13 adults with severe asthma (46.0yrs) and 26 controls adults (65.3yrs) were included. ASMC proliferation was increased in asthmatic adults, asthmatic pre-school and control children ASMC vs control adults, with a cell doubling time of 35.0 ± 2.5 h, 24.8 ± 1.9 h, 22.6 ± 2.6 h and 47.4 ± 4.4 h, respectively (P < 0.05). This increased ASMC proliferation was associated with greater mitochondrial mass (porine rate: 50% in asthmatic adult ASMC, 52% in children ASMC vs 26 controls adults). Methods: We cultured ASMC and bronchial epithelial cells (BEC) obtained by endobronchial biopsy from children and adults with severe asthma or undergoing bronchial endoscopy for other reasons. We then studied ASMC proliferation (cell counting and CFSE dye assay) in 10% fetal bovine serum (FBS), 0%FBS and after the addition of the BEC culture supernatant obtained after rhinovirus infection, house dust mite exposure or both.

Conclusion: As previously described in adult asthmatics, ASMC proliferation is enhanced in both asthmatic and non-asthmatic children. This is
associated with an increase in mitochondrial mass and biogenesis. ASMC proliferation is increased after a viral infection or an allergen exposure.

**#64 - MEASUREMENT OF EXPIRED VOLUME FOR VARIOUS EXPIRATORY FLOW LEVEL DURING FORCED EXPIRATORY MANEUVERS IN CHILDREN: TO ANALYZE PARTIAL FLOW-VOLUME LOOPS?**

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Because preschool children hardly manage to achieve prolonged expiratory maneuvers usual parameters (FEV1, FEV1/FVC, maximal expiratory flow) cannot be used to analyze flow-volume loops in this age group. Measuring the expired volume at different steps of level expiratory flow could be another way to analyze flow-volume loops in this age group.

The aim of our study was to determine if expired volume (Vexp) obtained at various level of expiratory flow during a forced expiratory maneuver decreases in obstructive children.

**Methods:** In a first retrospective study, we measured Vexp obtained when expiratory flow reaches 90%, 60% and 30% of the theoretical peak expiratory flow (Vexp90, Vexp 60 and Vexp 30) in obstructive and non-obstructive school-aged children. We then prospectively measured Vexp90, Vexp 60 and Vexp 30 on partial flow-volume obtained in obstructive and non-obstructive preschool children whose bronchial obstruction was also assessed by resistance measurement.

**Results:** In the prospective study, Vexp 30, Vexp60 and Vexp90 were significantly lower in the obstructive group (n = 26) than in the non-obstructive group (n = 32). Furthermore, in the obstructive group, Vexp50, Vexp60, Vexp90 significantly increased after inhalation of salbutamol. In the prospective study, all of the 55 preschool children managed easily to perform partial expiratory maneuvers. Vexp 90 and Vexp60 were significantly lower in the obstructive group (n = 7) than in the non-obstructive group (n = 48) (P < 0.05).

**Conclusion:** Airway obstruction evaluation is very important in asthma management of the preschool children: it is predictive of the severity of asthma and predictive of lung function in adulthood. We will compare the Vexp in healthy and asthmatic preschool children in a largest study to obtain reference values.

**Keywords:** MEFV curves, preschool children, asthma, expiratory volumes

**#66 - THE STATE OF NON-SPECIFIC RESISTANCE FACTORS IN SMALL AIRWAYS DISEASES OF BRONCHIAL TUBES IN CHILDREN**

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**Objective:** To study the dependence of the state of phagocytic activity of granulocytes on the stage of the pathological process in asthma (BA), chronic bronchiolitis obliterans(BO) and bronchopulmonary dysplasia (BPD).

**Materials and Methods:** 112 children with BA and 139 patients with BO and 103 with BPD were observed in age from 1 year to 15 years. Studies were conducted in the period of exacerbation and remission. In all patients the study was carried out phagocytic activity of neutrophils through the spontaneous and stimulated nitroblue tetrazolium reduction test (NBT).

**Results:** In all cases aggravation observed increase of phagocytic activity of neutrophils in the spontaneous (BA-10, 1 ± 0.37, BO-8, 04 ± 0.26, BPD-10.0 ± 1.12) and a stimulated (BA-31, 6 ± 0.57; BO-30, 3 ± 0.25; BPD – 30.9 ± 0.43) test. In the case of BO phagocytic activity of neutrophils was slightly reduced in comparison with BA and BPD. In remission indicators of these continue to grow (BA-11, 26 ± 1.3, BO-9.97 ± 0.25; BPD-10.1 ± 1.1) and (BA-37, 5 ± 1.5; BO-39 ± 0.9, BPD-40, 0 ± 0.5) in all groups

**Conclusion.** Thus, the phagocytic activity of granulocytes not suffer in BA, BO and BPD. However, indicators of NST are on the lower limit of normal at BO. Probably slight inhibition of phagocytosis associated with the presence of viral infection in the presence of infectious factors in the genesis of disease and, consequently, the growing process of endogenous intoxication.

**#78 - AGE AND BODY SIZE EFFECT ON THE SYSTEMIC EXPOSURE TO DRY POWDER INHALED BECLOMETASONE/FORMOTEROL**

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**Purpose of the study:** Guidelines for treatment of childhood asthma recommend prescription of inhaled anti-asthmatic drugs at half the nominal dose as for adults in order to reduce the risk of systemic side effects. However, the influence of age and body size on the blood concentrations of inhaled drugs is not fully elucidated. We aimed to compare the systemic exposure to the active ingredients of a fixed combination of beclometasone dipropionate (BDP) and formoterol after dry powder inhaler (DPI) administration in children, adolescents and adults.

**Methods:** The pharmacokinetic profiles of formoterol and beclometasone-17-monopropionate (B17MP; active metabolite of BDP) were evaluated over 8 hours from two independent studies comprising children (6–11yrs, n = 27), adolescents (12–17yrs, n = 28) and adults (≥18yrs, n = 30) receiving a single, fixed dose of BDP/formoterol (children: 200 µg/24 µg, adolescents and adults: 400 µg/24 µg) via DPI.

**Results:** The systemic exposure (AUC0-t) for children vs. adults was almost doubled for formoterol (despite the same nominal delivered dose) and similar for B17MP (despite the BDP dose being halved in children). In adolescents the AUC for formoterol and B17MP were approximately one third higher than in adults for both compounds. After normalization for the BDP/formoterol dose in the three populations the systemic exposure and peak concentration (Cmax) correlated inversely with age and body surface area of the patients (r ≤ –0.53; P < 0.0001).

**Conclusion:** The systemic exposure to the active ingredients of BDP/ formoterol administered as DPI correlates inversely with age and body size suggesting that dry powder dosage regimens should be adjusted for age and body size to avoid high systemic drug levels in children.

**Reflections** stimulated by the research: Contrasting the present findings, previous similar investigations demonstrated that when using a pMDI with a spacer the systemic exposure for the same nominal dose in children was
similar to that in adults. This suggests that drug delivery by inhalation via pMDI plus spacer is lower in children as compared to adults resulting in similar exposure due to the lower body size of the paediatric population. Therefore guideline recommendations of a reduced dosage regimen in children could be appropriate for DPI administration only.

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#80 - PHARMACOKINETIC AND PHARMACODYNAMIC ASSESSMENT OF PRESSURISED METERED-DOSE INHALED BECLOMETASONE/FORMOTEROL IN ADOLESCENT ASTHMA

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Purpose of the study: Asthmatic adolescents are generally recommended to be dosed like adults. However, this population is unique in many ways and limited pharmacokinetic (PK) and pharmacodynamic (PD) data are available on fixed combinations of inhaled-corticosteroids/long acting β2-agonists (ICS/LABA). In addition the influence of age on the systemic exposure of drugs administered via pMDI with or without valved holding chamber is still not fully elucidated. The aim of the study was to investigate the PK/PD profile of a fixed dose combination of ICS/LABA pMDI in asthmatic adolescents with or without valved holding chamber in comparison to a free combination of licenced pMDI products. A comparison of adolescent and adult asthmatics was also conducted.

Methods: Open label, randomized, three-way crossover study, on 30 asthmatic adolescents receiving a single dose of the fixed combination of beclometasone dipropionate (BDP)/formoterol pMDI 100/12 µg per actuation (Foster®) with or without Aero Chamber Plus(TM) or a free combination of BDP 100 µg pMDI (Qvar) plus formoterol 6 µg pMDI (Atimos). An open, parallel arm of 30 asthmatic adults receiving Foster® was added as a control. All patients received a total single dose of BDP and formoterol of 400 µg and 24 µg, respectively. Assessments were performed over 8 hours.

Results: In adolescents, Foster® with or without Aero Chamber Plus(TM) was equivalent to Qvar® + Atimos® or Foster® alone in terms of systemic exposure (AUC0-t) to beclometasone-17-monopropionate (B17MP, active metabolite of BDP) and formoterol; 90% confidence intervals (CIs) for the geometric means ratio fixed/free were all within the 0.80–1.25 range interval. After treatment with Foster® the systemic exposure to B17MP and formoterol was also comparable between adolescents and adults (90% CIs within 0.78–1.17). The PD profile was equivalent between all treatments in terms of plasma potassium, plasma glucose, pulse rate and forced expiratory volume in one-second.

Conclusions: In adolescents the PK and PD of Foster® with or without Aero Chamber Plus(TM), is comparable to that of a free combination of licensed single entity pMDIs, which have established safety and efficacy profiles. The findings in adolescents adults were comparable. Reflections stimulated by the research: These results support the indication for use of ICS/LABA pMDIs in adolescents at the same dosage as in adults.
#83 - FACTORS ASSOCIATED WITH EXERCISE-INDUCED BRONCHOCONSTRICTION IN CHILDREN: ASSESSMENT OF GASTRO- OESOPHAGEAL REFLUX.

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Background. Knowledge on pathophysiology of exercise-induced bronchoconstriction (EIB) is still debated. Studying gastro-oesophageal reflux (GOR) in children with reported exercise-induced respiratory symptoms could help in our understanding of EIB.

Aims. To assess clinical, functional, inflammatory data and gastro-oesophageal acidity during EIB in children.

Methods. In 27 asthmatic and 18 non-asthmatic children (aged 5.9–17.1 yr; 30 males) we assessed exercise-induced respiratory and chronic gastrointestinal symptoms, blood samples for IgE and eosinophil count, exhaled nitric oxide (FeNO), baseline spirometry; then started a 24-h GE pH monitoring (GE pH24). All children underwent treadmill-exercise testing during GE pH24. Spirometry was repeated 1, 5, 10, 15 and 20 minutes after exercise as well as FeNO (5’ and 20’). Spirometry was assessed 20 min following exercise after inhalation of salbutamol. EIB was defined as a post-exercise fall in FEV1 of at least 10% from baseline. The reflux index (IR) was calculated as the percentage of time with a pH below 4.0, either for the all 24 hours and 6 min-intervals before, during and after the exercise test.

Pathological GOR was defined when IR raised over 4.0% of the GE pH24. Results. Subjects with EIB (n = 11) had lower baseline lung function and higher bronchial response to salbutamol but no different frequency of pathological GOR, IgE levels, eosinophil-blood count and FeNO than subjects without EIB (n = 34). Reported exercise-induced respiratory symptoms and chronic gastrointestinal symptoms were also similar between children with EIB and those without EIB, though most subjects with EIB had a previous diagnosis of asthma (10/11) as compared with those without EIB (17/34); P = 0.04. In the whole population, the fall in FEV1 was found correlated with low age-related variables, low baseline FEV1 and FEF25–75%, high bronchial response to salbutamol and low 6-min post-exercise IR (e.g. with FEV1: r = 0.47, P = 0.001, with DFEV1: r = -0.34, P = 0.021, with IR: r = 0.53, P < 0.001).

Conclusion. From our results, EIB is mainly associated to measurements of bronchial patency and reactivity. EIB does not seem influenced by reported symptoms, measurements of atopic inflammation, pathological GOR or changes in gastro-oesophageal acidity after exercise. Selection of subjects by asthma phenotypes could better explore the relationship between EIB and GOR.

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#85 - KETAMINE VERSUS AMINOPHYLLINE FOR STATUS ASTHMATIC IN CHILDREN: A RANDOMIZED, CONTROLLED TRIAL

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Objective: To evaluate efficacy and safety of ketamine as compared to aminophylline in children with moderate to severe acute exacerbation of asthma having Pediatric Respiratory Assessment Measure (PRAM) score ≥5 at 2 hours of standard therapy (salbutamol and ipratropium bromide nebulization, steroids, and magnesium sulphate) were included in the study with appropriate consent and ethics committee approval. Enrolled patients were randomized to intravenous (IV) ketamine (0.5 mg/kg bolus followed by continuous infusion of 0.6 mg/kg/hr) OR IV aminophylline (5 mg/kg bolus followed by continuous infusion of 0.9 mg/kg/hr) for 3 hours. Patients and treating team were not blinded to intervention but person assessing outcome was blinded to intervention. Primary outcome measure was change in PRAM score. Secondary outcome measures included adverse effects, change in pO2 and pCO2, change in Peak Expiratory Flow Rate (PEFR), need for mechanical ventilation, and duration of hospital stay. Statistical analysis was done as appropriate using SPSS version 16.

Results: A total of 48 subjects, 24 each in ketamine and aminophylline group were enrolled in the trial. Age (median [IQR], 42 [22.0–72.0] versus 60 [24.2–72.0] months; P = 0.468), PRAM score (7.71 ± 1.68 versus 8.04 ± 1.55; mean difference 0.33; 95% CI –1.27, 0.61; P = 0.478), and other baseline demographic and clinical parameters were similar between the groups. Change in PRAM score from enrollment to at three hours of intervention was similar in both the groups with a change of 4.00 ± 1.25 and 4.17 ± 1.68 (mean difference 0.16; 95% CI –1.02, 0.69; P = 0.699) in ketamine and aminophylline group respectively. At three hours of intervention PRAM score was similar between the groups (3.79 ± 1.84 versus 3.88 ± 1.92; mean difference 0.08; 95% CI –1.18, 1.01; P = 0.879) and it decreased significantly from enrollment in both the groups (P = 0.000 for both group) (Figure 1). There were no adverse effects in both the groups except for one episode of small vomiting in one patient from ketamine group. The changes in pO2, pCO2 and PEFR, and duration of hospital stay were similar between groups. No patient required mechanical ventilation. Conclusion: Ketamine and aminophylline were equally effective for improvement in PRAM score in children with moderate to severe acute exacerbation who respond poorly to standard therapy without any significant adverse effects. Reflections and concrete proposals for action: In children with moderate to severe acute exacerbation who responds poorly to standard therapy either IV ketamine or IV aminophylline may be used depending on availability of drug and experience of users with drug.

Trial is registered at Clinical Trials Registry-India: CTRI/2013/09/004000.

#89 - BRONCHIAL REACTIVITY, INFLAMMATORY AND ALLERGIC PARAMETERS, AND VITAMIN D LEVEL IN CHILDREN WITH MILD ASTHMA

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Objectives: To assess the correlation between Vitamin D levels and airway hyper-reactivity (AHR), fractional exhaled NO (FeNO), high sensitivity-CRP (hs-CRP), and allergic parameters in non-obese children aged 6–18 years with mild asthma not receiving anti-inflammatory treatment.

Methods: Each patient underwent evaluation including spirometry, methacholine challenge test (MCT), FeNO, serum vitamin D level, total IgE level, peripheral blood eosinophil count, and hs-CRP level. Primary end points: The correlation between vitamin D level and AHR as assessed by MCT. Secondary end points: The correlation between vitamin D level and FeNO, systemic markers of inflammation and allergy.

Results: Seventy-one asthmatic children (25 female; 35%), age 12.46 ± 3.61 years were included. Their median vitamin D level was 23 ng/ml (range: 6–48.5; mean 23.02 ng/ml). There was no correlation between vitamin D level and the response to MCT, FeNO, hs-CRP levels, IgE, eosinophil count, and the frequency of allergic rhinitis or atopic dermatitis.

Conclusions: In our group of asthmatic children, there was no correlation between vitamin D levels and the degree of airway reactivity, airway inflammation, and allergy. Cause and effect relationship between vitamin D, asthma, and allergy should be further studied and interventional double blind placebo controlled clinical trials assessing the effect of vitamin D administration on asthma and allergy are needed.

#100 - RECOGNITION OF RESPIRATORY SOUNDS IN CHILDREN

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Aims: To investigate parental ability to recognise wheeze in children.

Methods: Scenes of children breathing were captured on video. These children demonstrated audible wheeze, stridor, snoring, transmitted noises and normal breathing. The video clips were then validated by a group of qualified pediatricians. Videos with a kappa value of ≥0.8 were selected. The video clips were then shown to parents of children with and without asthma. Parents were asked to label the sound in eachclip and to determine the location from which it originated.

Results: A total of 12 video clips were successfully selected and validated to be shown to the parents. Two hundred participants were enrolled to participate. Only 38.5% of respondents were able to correctly label wheeze. Respondents were better at locating the origin of wheeze. The commonest Bahasa Malaysia word by parents to describe wheeze was "susah nafas". The commonest English words used by parents to describe wheeze was "wheeze" and "asthma". Having a child with asthma, higher education level and worse asthma severity in the child did not result in more accurate labeling.

Conclusion: Parents were better at locating respiratory sounds than labeling them. Most parents use vague words to describe respiratory noises. Hence history taking should be modified to asking parents where the origin of these abnormal respiratory sounds is.

#105 - DUAL-CENTRE RANDOMISED TRIAL ON TAILORED ASTHMA THERAPY BASED ON EXHALED NITRIC OXIDE (FENO) VS ROUTINE CLINICAL CARE

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A Cochrane review that examined the efficacy of using FeNO to tailor the dose of inhaled corticosteroid (ICS) showed that FeNO cannot be routinely recommended for clinical practice at this stage and remains uncertain. However all the 6 studies used a single FeNO cut-off. In this RCT we determined if asthma monitoring using FeNO (using 2 different cut-offs dependent on atopy) is better than control (symptoms and FEV1) in preventing asthma exacerbations in children on inhaled corticosteroids.

Methods: Over 12-months, children underwent spirometry, FeNO, QOL and asthma/cough diary during every visit. The study was a dual centre randomised controlled trial. Treatment for asthma was adjusted according to pre-determined criteria taking into account atopy status and dependent on allocation group (FeNO or control).

Results: 63 children from Hong Kong and Brisbane were randomised (FeNO = 31, controls = 32) and 55 (86%) completed the study. Over 12-months, significantly fewer children in the FeNO group (6 of 27) had an asthma exacerbation compared to controls (15 of 28), P = 0.021; number to treat for benefit over 12-months was 4 (95%CI 3–24). However, there was no difference between groups any of the secondary outcomes (quality of life, symptoms, FEV1). Also, the final daily inhaled ICS dose was significantly (P = 0.037) higher in the FeNO group (median 400 ugm, IQR 250–600) compared to the controls (200, IQR100–400).

Conclusion: Taking atopy into account when using FeNO to tailor asthma medications is likely beneficial in reducing the number of children with severe exacerbations at the expense of increased ICS use. However, the strategy is unlikely beneficial for improving asthma control. A larger study is required to confirm or refute our findings.

Supported by Asthma Foundation of Queensland, NHMRC.

#108 - LCI IS RESPONSIVE TO TREATMENT IN PRIMARY CILIARY DYSKINESIA

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Background: Primary Ciliary Dyskinesia (PCD) is a rare genetic disorder, characterized by chronic airway infection and an increased incidence of sinus inversus and male infertility. The treatment of the chronic airway infection is not evidence based but often derived from evidence based treatment schedules for cystic fibrosis. With the perspective of upcoming PCD clinical trials, the need for reliable outcome parameters is obvious.

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Candidate outcome measures in PCD are chest CT score (Maglione et al, Ped Pulmonol 2011) and lung clearance index (Green et al, Thorax 2011, Irving et al, AJRCCM 2013), a measure of gas mixing efficiency. As in CF, both might be more sensitive than FEV1 to detect early disease.

Aim of the study: To investigate whether lung clearance index (LCI) is responsive to treatment in patients with PCD.

Methods: We included children and adolescents with PCD and a pulmonary exacerbation that was treated with intravenous (iv) antibiotics and measured LCI (N2 multiple breath washout using EComedics set-up) and FEV1 before and after treatment.

Results: So far, 4 patients were treated with iv antibiotics for a mean duration of 5.8 days because of a respiratory exacerbation. Mean LCI z-score decreased from 6.3 (range 2.05–10.73) to 4.4 (range −0.04 to 9.42, p 0.061), LCI z-score improved in each individual. Mean FEV1 z-score improved from −2.6 (range −5.52 to −0.01) to −1.6 (range −3.18–0.65, p 0.038). The mean improvement was 1.9 z-scores for LCI, and 1 z-score for FEV1.

Conclusion: Preliminary data demonstrate that in subjects with PCD, treated with iv antibiotics for a pulmonary exacerbation, both FEV1 and LCI seem responsive to treatment. Given the higher change in LCI z-score compared to the FEV1 z-score, we will further explore whether LCI is indeed more sensitive to intervention than FEV1. More research is needed to clarify the role for LCI versus FEV1 measurements in the follow-up of patients with PCD.

Conclusion: Both LCI and FEV1 are responsive to treatment and might therefore be used as outcome parameter in clinical trials for PCD treatment.

**#111 - STUDY OF V/Q SCAN IN CHILDREN WITH BRONCHIOLITIS OBLITERANS**

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Bronchiolitis obliterans (BO) is a chronic airflow obstruction syndrome associated with inflammatory lesions of the small airways. Biopsy is limited in clinic, so far the diagnosis is based on clinic presentations. Pulmonary perfusion /ventilation scan (V/Q) can reveal pulmonary airway ventilation function (PAVF) and blood perfusion (pBP) that is supposed to be helpful for diagnosis and assessment. Objective: To explore the clinical significance of V/Q for children with BO. Methods: V/Q was performed for total of 30 children with BO during February 2005 to April 2011. Analysis of relations of V/Q with clinical presentations was performed. Result: Of all 30 children received V/Q tests, 26 (86.7%) children presented impaired ventilation function and blood perfusion, in whom the kids with moderate or severe degree accounted for 92.3%, including impaired pulmonary ventilation in 8 kids (30.8%), impaired pulmonary blood perfusion in 3 (11.5%), 15 (57.7%) presenting matched impairment of PAVF and pBP. Only 4 (13.3%) kids were intact in both ventilation function and pulmonary blood perfusion. All 5 kids deteriorated in follow up who presented bilateral severe impairment of V/Q, while 9 kids develop favorable outcome who presented mild to moderate impairment in 5 and intact in 2. Conclusion: V/Q correlated with the clinical presentations, is helpful for diagnosis, evaluation and predication of outcome for children with BO.

**#112 - THE DIFFERENCE OF REACTIVITY IN CONTROL TREATMENT BETWEEN ASTHMATIC CHILDREN AND THE ANALYSIS OF ITS RELATED FACTORS**

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Objective To dynamically observe and assess children’s asthma control level, so as to determine the difference between children’s reactivity to treatment, and to analyse the characteristics of change of pulmonary function indicators and fractional nitric oxide concentration in exhaled breath (FeNO) in children who had different reactivity to treatment.

Methods A total of 52 asthmatic children who had started regular control treatment and been on a regular follow-up were enrolled, all the patients were on the assessment of asthma control, pulmonary function testing and FeNO measurement every three months. The indicators of pulmonary function testing contained FEV1%, PEF%, FEV1/FVC, MMEF%. The level of treatment of asthma control medicine, daily dose and course of treatment were recorded, and the average daily dose of each medicine in the 9 months was calculated. Results At the end of the nine months’ follow-up, all the patients were divided into two groups, there were 30 cases in stable group and 22 cases in unstable group. There was no significant difference between the two groups in FEV1% or PEF% of the four times of follow-up, in the stable group of the third, sixth and ninth month follow-up time were significantly higher than those in the unstable group (P < 0.05), MMEF% of patients in the stable group of the third and ninth month follow-up time were significantly higher than those in the unstable group (P < 0.05), FeNO concentrations of patients in the stable group of the baseline and the third month followup time were significantly higher than those in the unstable group (P < 0.05). There was no significant difference between the two groups in the average rate of change of FeNO or pulmonary function testing indications (P > 0.05). The daily dose of fluticasone, salmeterol and montelukast of each patient in the stable group was significantly lower than those in the unstable group (P < 0.05). Conclusion The FeNO, FEV1/FVC and MMEF% were higher in the stable group than those in the unstable group. The daily dose of fluticasone, salmeterol and montelukast of each patient in the stable group was significantly lower than those in the unstable group.

**#117 - QUALITY OF LIFE AMONG PARENTS AS A DETERMINING FACTOR IN CONTROLLING ASTHMA IN CHILDREN**

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Objective: Determine whether the quality of life of the caregivers and the family functioning influence the control of asthma in children.

Methods: An observational, longitudinal study at twenty-two primary healthcare centers in Spain, with children between 4 and 14 years of ages who had active asthma and whose main caregiver (father or mother) had sufficient skills in the Spanish language. During the initial visit, the child was assessed: (1) asthma-related quality of life of the parents, measured by the IFABI-R instrument, developed and validated in Spanish. This tool measures the impact of asthma on a 1–4 scale, in which the higher the score, the greater the deterioration of the quality of life. (2) The family functioning was assessed using the “family Appgar” instrument, with a 1–3 score; the higher the score, the better the family functioning. At the second visit, sixteen weeks later, the degree of the child’s asthma control was determined following the NAEPP-3 classification for asthma severity.

The influence of family variables on the later control was analyzed using a logistic regression model, with asthma control at the second visit as the dependent variable. Covariates were added, including age, sex, degree of asthma control at the first visit, risk factors for impairment of asthma control (hospitalization or recurring crisis in the past 12 months, recent crisis), treatment modifications at the first visit (increase or decrease in the treatment steps), years since diagnosis, sensitivity to inhalants, educational level of the parents, social class of the parents, time elapsed between the first and second visit, and whether the assessment of the quality of life and the family functioning was made by the father or the mother. The results were presented as odds ratio (OR) and their 95% confidence interval (95%CI) of having the asthma controlled. Another logistic model was created, limited to children with daily pharmacological treatment and adding therapeutic adherence (Morisky-Green test) as another co-variable.

Results: 471 children and their caregivers were recruited; the data from 396 children (84.0%) were analyzed with full data for all variables. The family functioning had no association with the control of asthma. However, the quality of life of the parents was strongly associated with asthma control. In the adjusted model, an increase in IFABI-R (worse quality of life) was associated with a lesser probability of having good control 16 weeks later (OR = 0.60, 95%CI = 0.38-0.93, P = 0.022). This association was maintained in the restricted model, only with children who received pharmacological treatment (OR = 0.56, 95%CI = 0.34-0.99, P = 0.045).

Conclusions: The quality of life among parents is a determining factor in the probability of achieving good control of asthma in the medium term. Assessing the quality of life of the caregivers could be important in deciding the therapeutic management of the disease.

#119 - RELATIONSHIP OF FRACTIONAL EXHALED NITRIC OXIDE AND CLINICAL ASTHMA CONTROL ASSESSMENT TOOLS IN CHILDREN

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Background: Fractional Exhaled Nitric Oxide (FeNO) is a marker of eosinophilic inflammation and has a potential role in monitoring airway inflammation in asthmatic patients; however its relationship with clinical asthma control assessment tools has not been established.

Objective: To measure the association between FeNO levels and clinical evaluation of asthma control.

Methods: Patients aged 7–15 years with persistent asthma were enrolled. Clinical asthma control was evaluated using Asthma Control Test (ACT) questionnaires and Global Initiative for Asthma (GINA)-defined criteria. FeNO measurement was done using NIOX MINO® device. Association of FeNO to clinical asthma control status was controlled for Skin Prick Test (SPT) using binary logistic regression. The cut-off point for FeNO was determined using Receiver Operating Characteristics (ROC) curve.

Results: Sixty-two children were included. A weak agreement was found between ACT and GINA-defined asthma control (66.2%, κ = 0.313, P = 0.007). FeNO was significantly associated with both ACT and GINA-defined asthma control status even when controlled for SPT (OR 1.032, 95%CI 1.002, 1.063 and OR 1.030, 95%CI 1.003, 1.059). For both ACT and GINA-defined asthma status, the best cut-off point for FeNO was at 32 ppb giving area under the curve (AUC) of 0.673 (95%CI 0.532, 0.815) and 0.684 (95%CI 0.551, 0.812) respectively. When level > 32 ppb defined high value, the sensitivity and specificity in predicting ACT and GINA-defined uncontrolled asthma were 76.5% (95%CI 50.1%, 93.0%), 57.8% (95%CI 42.2%, 72.3%) and 66.7% (95%CI 47.2%, 82.7%), 62.5% (95%CI 43.7%, 78.9%) respectively.

Conclusions: Our data suggests that FeNO level > 32 ppb supports the clinical evidence of uncontrolled asthma as defined by ACT and GINA.

#126 - CONFIRMATORY FACTORIAL ANALYSIS OF THE SCALE OF OVERLOAD OF THE CAREGIVER OF ZARIT IN THE PARENTS/CAREGIVERS OF PEDIATRIC ASTHMATIC PATIENTS

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Introduction: In spite that there are many tools to measure the level of overload in parents/caregivers, few studies have validated them to be used in the context of pediatric asthma.

Methodology: It was performed a cross-sectional analytical study and of validation of scale. We assessed the overload degree of parents/caregivers of asthmatic children using the Zarit Scale (ZS). We performed a confirmatory factor analysis to verify the factor structure of the ZS, and assessed its construct validity and internal consistency. Logistic regression models were adjusted to identify factors associated with an severe overload level in parents and/or caregivers of asthmatic children.

Results: Of the total of parents and/or caregivers, 26 (10.0%) were considered to be experiencing a severe overload. The factor structure described for ZS fits acceptably when it is used to measure the level of overload experienced by parents/caregivers with asthmatic children (X2 = 59.47; gl. = 19; P < 0.001; CFI = 0.93; TLI = 0.90; RMSEA = 0.09). The age of caregiver (OR 1.07; IC 95% 1.00-1.15; P = 0.04), free marital union of parents/caregivers (OR 3.96; IC 95% 1.27-12.35; P = 0.02), and the mother as the only type of caregiver (OR 8.87; IC 95% 1.13-69.61; P = 0.04) were identified as independent predictors of a severe overload.

Conclusions: The ZS is an appropriate instrument to determine the level of overload experienced by parents and/or caregivers of asthmatic children. The age of the caregiver, free material union of parents/caregivers, and mother as the only type of caregiver are independent predictors of a severe overload.

#128 - THE THIRD NATIONWIDE SURVEY OF CHILDHOOD ASTHMA IN URBAN AREA OF CHINA

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Background: This national wide study was conducted to investigate the prevalence of childhood asthma in urban areas of large cities in China, and to find the characteristics of attacks, the diagnosis and treatment status, and provide scientific data for improving the prevention and management of asthma in children.

Methods: This national-wide, cross-sectional survey was organized by the National Cooperative Group on Childhood Asthma, and conducted in 43 cities all over the country, including 27 capital cities of provinces or autonomous regions, 4 municipalities, from September 2009 to August 2010. Children born from July 1st 1995 to June 30th 2010 were enrolled in the survey, consisting of children who had been living in the surveyed cities and those born outside the city but had lived in the cities for over 6 months. Schools, kindergartens and communities in each city were selected by phased stratified random cluster sampling. Standardized preliminary questionnaire was used for screening out possible patients in the survey. Diagnosis of asthma was confirmed by enquired of history, together with review of previous record and tests, physical examination in suspected asthmatic children.

Results: 463,982 children were investigated for the survey. Asthma was diagnosed in 13,992 children, 12,634 children with classical asthma (90.3%) and 1,358 children with cough variant asthma (9.7%). 4,837 cases (31.4%) were newly diagnosed in all asthmatic children. The total asthma incidence rate was 3.02% (95% CI: 2.68–2.77%) and cough variant asthma at 0.29% (95% CI: 0.28–0.31%). The prevalence in last two-year (2009–2010) was 2.37% (95% CI: 2.28–2.37%). The prevalence of asthma in male and female children was 3.51% and 2.29% respectively with significant difference between (χ² = 608.7, P < 0.01). Preschool children (3–5 years old) had the highest prevalence of asthma (4.15%), which was significantly higher than that of school-age children (6–14 years old, 2.82%) and infants (0–2 years old, 1.77%). In different regions of the country, the highest rate was found in East China (4.23%), and the lowest rate in North-east China (2.00%). Among different cities, highest rate was found in Shanghai (7.57%) and the lowest rate in Lhasa (0.48%). Family allergic history was reported in 45.2%; personal history of allergy reported in 72.5%, and allergic rhinitis reported in 50.1% asthmatic children. Respiratory tract infection (87.9%) and changes of weather condition / inhaling cold air (51.5%) were the most common triggers of asthma exacerbation. Peak flow meter was used in 14.3% of asthmatic children 5 years and above for monitoring.

Conclusions: The total asthma incidence of childhood asthma aged 0–14 year old in city in China was 3.02% and prevalence in last two years was 2.32%. The asthma prevalence was significantly different between regions, cities, ages, and genders.

### #136 - COMPARISON OF MORPHOLOGICAL CHANGES OF AIRWAY WALLS IN YOUNG AND ADULT RATS AFTER AN ALLERGIC CHALLENGE

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Obstructive airway disorders represent one of the major health issues. Together with the inflammation, various structural changes known as remodeling constantly appear in the bronchial walls of patients suffering from the bronchial asthma. The principle of the remodeling consists in changes of properties of the bronchial epithelium including hyperplasia of its goblet cells, thickening of the basement membrane predominantly in the area of its reticular lamina, differentiation and activation of myofibroblasts and proliferation of smooth muscle, multiplication of submucosal glands, deposition of extracellular proteins to the lamina propria mucosa and changes of vascularization. While these morphological changes in bronchial walls of patients with asthma have been thoroughly described, predominantly in the adults, fewer papers exist about the bronchial remodeling in small children and even lesser about the changes in laboratory animals.

We decided to analyze structural changes of intrapulmonary airways in rats of Brown Norway (BN) strain, which are especially responsive to sensitization by allergens and tend to develop the state that clinically and morphologically highly resembles the human bronchial asthma when stimulated with appropriate allergen challenges.

Young and adult BN rats were sensitized by repeated intraperitoneal injections of ovalbumin (OA). During following 2 weeks, the rats regularly inhaled OA. Two control groups of each age were housed simultaneously. The first of them was injected and inhaled by saline (S), the second group was untreated (C). At the end of the experiment, the animals were sacrificed, their lungs were processed for the light microscopy. We concentrated to the airway morphometric parameters, occurrence of eosinophilic granulocytes in the airway walls and number of epithelial secretory cells together with a glycoconjugate quality of their secretion.

The airway walls of the OA group were showing marks of remodeling in both young and adult animals. The total wall areas of all intrapulmonary airways were significantly increased compared to groups S and C. The thickening of inner wall areas was more pronounced in adult rats; outer wall areas were more increased in the young group. There were some significant signs of the muscular hypertrophy or hyperplasia only in young challenged animals. The number of eosinophilic granulocytes was predominantly increased in airway walls of OA young rats. Secretory cells were more multiplicated in airway epithelium of OA adult animals. Proportions of neutral and acidic glycoconjugates in their secretion were shifted towards the acidic ones in adult rats.

The study confirmed the bronchial sensitivity of BN rats and different reactivity of adult and young individuals. The remodeling changes were ascertained in all layers of the airway wall; more in the epithelium and connective tissue than in the muscle. A morphological base for further experiments was constituted.

### #137 - ASSOCIATION BETWEEN BODY MASS INDEX AND THE LEVEL OF ASTHMA CONTROL IN A LATINO POPULATION OF ASTHMATIC SCHOOL CHILDREN

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Background: Many observational studies have shown association between Body Mass Index (BMI), particularly in obese children, asthma control level and the degree of quality of life. However this association remains uncertain particularly in Latino Children because results of the studies have resulted inconsistent.
Objective: The aim of the study was to determine whether there is any association between the Body Mass Index (BMI) and the Asthma Control level in a group of asthmatic school children.

Methods: Cross sectional study. 106 children with asthma were evaluated in the Outpatient asthma Program at Hospital Militar Central in Bogotá, Colombia. a thrid level institution, during the second semester of 2012. Logistic regression models were developed to determine odds ratios unadjusted and adjusted to identify whether the body mass index is associated with the Level of Asthma Control.

Results: Of 106 children evaluated 62 (58.5%) were boys and 44 (41.5%) girls. 77 (72.6%) had normal weight, 20(18.9%) were overweight and 9 (8.5%) were obese. With regard to treatment, 59 (55.7%) were receiving controller medications and 47 (44.3%) were untreated. Of the subjects with use of controllers, 45 (76.2%) used inhaled steroids; alone or in combination, and 14 (23.7%) anti-leukotriene monotherapy. Of those who used inhaled steroids, 27 (60%) received low or medium dose, 16 (35.5%) low or moderate combined with anti-leukotriene and 2 (4.4%) inhaled steroid plus long action beta2 agonist. Adherence to inhaled medication was good, in 77 (72.6%) and 65.1% of children were controlled.

The bivariate analysis showed that exposure to the controller medication was associated with better control (P = 0.003), lower likelihood of hospitalization for asthmatic crisis 0.25 (95% CI: 0.175-0.356, P = 0.000) and better asthma control (P = 0.045). Multivariate analysis did not show any association between BMI and asthma control. In the subgroup of more severe children exposed to controller medication there was an independent association between quality of life and level of disease control OR 2.22 (95% CI: 1.03–4.80, P = 0.04).

Conclusions: For this Latino population of asthmatic children was no found any association between obesity and level of control of the disease. Variables such as gender, age, level of maternal education, exposure to smoking, inhaled medication adherence were not associated either. The study also concluded that it is possible to achieve a good controller medication adherence, good level of asthma control and reduction in the number of crisis per year when the child is followed regularly in a Program of Asthma Care.

#145 - ECONOMIC EVALUATION OF TWO THERAPEUTIC STRATEGIES FOR TREATING PEDIATRIC MILD PERSISTENT ASTHMA IN A LOW- TO MIDDLE-INCOME COUNTRY

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Rationale. Despite the many benefits that have been demonstrated by the continuous administration of inhaled corticosteroids (ICS), a new strategy for control of recurrent wheezing and mild-to-moderate asthma is emerging, consisting of using intermittent or as-needed ICS treatment in conjunction with short-acting beta2 agonists (SABA) in response to symptoms. However, no previous studies have reported both the clinical consequences and the costs attributed to these two therapeutic strategies.Methods. A Markov-type model was developed in order to estimate costs and health outcomes of a simulated cohort of patients less than 18 years of age with persistent asthma treated over a 12-month period. Effectiveness parameters were obtained from a systematic review of the literature. Cost data were obtained from official databases provided by the Colombian Ministry of Health and Social Protection. The study took the perspective of national healthcare in Colombia. The main outcome was the variable “quality-adjusted life-years” (QALY). Results. For the base-case analysis, the model showed that compared to intermittent ICS, daily therapy with ICS had lower costs (US $437.02 vs. 585.03 and US$704.62 vs. 749.81 average cost per patient over 12 months for school-age children and preschoolers, respectively), and the greatest gain in QALYs (0.9629 vs. 0.9392 QALYs and 0.9238 vs. 0.9130 QALYS on average per patient over 12 months for school-age children and preschoolers, respectively), resulting in daily therapy being considered dominant.Conclusions. The present analysis shows that in Colombia, a low- to middle-income country (LMIC) country, compared to intermittent therapy, daily therapy with ICS for treating pediatric patients with recurrent wheezing and mild persistent asthma is a dominant strategy (more cost effective), because it showed a greater gain in QALYs with lower total treatment costs. This dominance of daily over intermittent therapy was more marked for school-age children than for preschoolers.

#146 - FACTORS ASSOCIATED TO REHOSPITALIZATION FOR ASTHMA IN CHILDREN LIVING IN A LOW-TO MIDDLE-INCOME COUNTRY.

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Introduction: Although hospital admissions for pediatric asthma constitute a significant problem in high-income countries, they are an even greater health problem in low- and middle-income countries (LMIC). However, previous studies that aimed to identify predictors of hospital admissionfor asthmachildrenhave mainly been conducted in high-incomecountries, and these findings might not be applicable to LMIC. Methods: In a prospective cohort study, we aimed to identify predictors of hospital admission for asthma, including measures of parental knowledge about asthma and maternal depression level, in a population of children aged 1–18 years living in urban Bogota, Colombia hospitalized for acute asthma symptoms, over a 6-month period. Results: Out of the total of 101 included patients, 37 (36.6%) had at least one hospital admission for asthma during the year following admission. After controlling for the age of the patients, dog ownership in the previous 12 months, asthma severity variables in the previous 6 months, maternal allergic rhinitis, level of maternal education, and measures of parental knowledge about asthma and maternal depression level, we found that maternal smoking (IRR, 3.12; 95% confidence interval [95%CI], 1.12–8.68; P=0.029) was the only independent predictor of hospital admissions due to asthma exacerbations in the year following admission to the study. Conclusions: In a population of asthmatic Latino children admitted to hospital for an asthma exacerbation, approximately one-third of the patients had at least one hospital admission for asthma during the year following admission, and maternal smoking was the only independent predictor of these hospitalizations.

#153 - DECISION SUPPORT SYSTEM IN EARLY IDENTIFICATION OF CHRONIC DISEASES OF SMALL BRONCHIAL TUBES AT CHILDREN

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Diseases of respiratory organs dominate in structure of incidence of the children’s population. Diagnostics of the chronic diseases of small bronchial tubes (CDSBT) is a complex challenge. It concerns the bronchial asthma (BA), the bronchopulmonary dysplasia (BLD), bronchiolitis obliterans (Bzoobl.)
Research objectives: evaluate the quality of official CDSBT diagnostics in children using expert knowledge-based decision support system. Materials and Methods: CDSBT diagnostics in small city of Sosnovy Bor in 2012 is analysed. The analysis of primary medical records allowed us to estimate the informativeness of disease symptoms. Decision support system for CDSBT diagnostics was developed on the basis of questionnaire about most informative symptoms. The studied pediatric area contains 850 children (49% girls, 51% boys) including 150 children with BA, 100 with BLD and 50 with BO. Results and discussion: Official data concerns only one form of CDSBT, bronchial asthma, which is 1.05% in the whole city and 0.8% in the analysed city area. Actual prevalence of BA is 3.72%. Officially there is no information about the prevalence of BLD and BO. At the same time the true incidence study results using the questionnaire and subsequent survey of 1,500 children show prevalence of BLD and BO respectively 0.13% and 0.37% in Russia North-West region. This indicates the low quality of diagnosis in primary CDSBT observation. The proposed decision support system for CDSBT diagnostics gives significantly higher percentage than the official statistics at the pediatric section: BA 10.7%, BO 0.35%, BLD 0.23%. Conclusions: official prevalence of CDSBT is underestimated at least in small Russian cities weak IT infrastructure. The proposed decision support system can help to adjust official statistics to the actual one, identifying rare and specific pathologies such as BLD and BO.

#158 - BODY HEIGHT AND BODY MASS INDEX OF MALE CHILDREN WITH ASTHMA ON LONG-TERM TREATMENT WITH INHALED CORTICOSTEROIDS IN PANCEVO SERBIA

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INTRODUCTION: Asthma is the most common chronic disease in childhood with a tendency to increase morbidity and inhaled corticosteroids (ICS) are the most effective anti-inflammatory therapy in patients with asthma and they are recommended in all protocols.

OBJECTIVE: Considering the controversial data of the impact of inhaled corticosteroids (ICS) on growth and body weight in children with asthma, the goal of this work is to determine the growth and nutritional status of male children with asthma on long-term therapy of ICS.

METHODOLOGY: The study included 150 male children aged 7 to 18, with partly controlled and uncontrolled asthma, which are in one year received ICS from 6 to 10 months. The control group consisted of 122 healthy males of the same age. Children are grouped by age into three groups: 7–10, 11–14 and 15–18 years. Growth and body mass index (BMI) of these children we followed four years. For reference values, we took the standard deviation (SD) for these ages by WHO in 2007. Children with body height and BMI SD -3 we considered low and malnourished at −2 SD lower and less nourished, the +2 SD higher and overweight, SD +3 and higher is obese, and the SD of −1 to +1 normal high and normal weight.

RESULTS: The results showed that 49.3% of children with asthma with ICS Th, and 49.2% of healthy children had height within the SD1. Statistically significant slowing of growth was observed at age 7, 8, 13 and 15 year in children where the ICS is a Th P < 0.05, t-test confirmed. Normal weight children with asthma with ICS Th was 57.3%, a healthy 65.6%. Overweight children with asthma were: 18.7%, 16.4% healthy, obese children with asthma, 10.7%, healthy 9.8%, with no statistical significance. Malnourished children were in a small percentage, 2% with asthma, a healthy 4.1% without statistical significance. Poorly nourished children with asthma was 11.3%, a healthy 4.1%, and this difference was statistically significant, P < 0.05, confirmed χ2 test. Four-year analysis of height and BMI showed that children in both groups, the majority of normal stature and normal body weight. This study did not determine the effect of ICS Th on the growth of children with asthma, because the 18th year of the difference in height was 0.3 cm in favor of healthy children and of no significance. Transient slowing of growth can partly explain the delay puberty in children with asthma, but also partially affected by long-term ICS Th at a time of intense growth. Increased percentage of overweight and obese children can be explained by the increasing use of fast food and less physical activity. Poor nutritional status of children with asthma can be partially explained by the disease.

Conclusion: Continuous use of ICS did not significantly affect the growth and nutritional status in children with asthma. We can say that the ICS for now safe drugs in the treatment of asthma in children.

#159 - A NATIONAL SURVEY OF PREOPERATIVE TREATMENT OF ASThmATIC CHILDREN IN ISRAEL. COMPARISON OF PEDIATRIC PULMONOLOGISTS TO ANESTHESIOLOGISTS

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Background: No consensus guidelines exist for the respiratory treatment of asthmatic children who are referred for elective anesthesia and surgery. Our previous study demonstrated a large variability regarding preoperative management of asthmatic children among all the pediatric pulmonologists (PP) in Israel (CIPPXII-Valencia 2013). The aim of this study was to investigate the practice of pediatric anesthesiologists and to find out whether they differ from PP using a national survey.

Methods: A mail survey of preoperative management of children with asthma was conducted. All certified pediatric pulmonologists and pediatric anesthesiologists in Israel were contacted and were asked to answer questions regarding their approach to 6 case scenarios, two multiple choice questions and 11 prestructured questions that included a variety of clinical situations of children at different ages covering a wide spectrum of chronic asthma treatments from the well to the poorly controlled preschool and school aged child. Results were tabulated and analyzed for all responders combined and for each group separately. Variation in practices between responders was evaluated using the R project version 3.02.

Results: Forty-eight pediatric pulmonologists (PP) (response rate = 100%) and a sample of 17 pediatric anesthesiologists (PA) responded. Compared to the PP, the PA showed a much lower variability regarding the 4 clinical scenarios of school aged child. Concerning the well-controlled school-aged asthmatic child with no prophylactic treatment; 25% of the PA did not recommend any treatment (versus 2% for PP); 56% recommend short-acting beta agonists (SABA) alone (PP = 25%) and 19% recommend a combination of SABA and inhaled corticosteroids (PP = 49%). None of the PA suggested adding oral corticosteroids to the treatment regimen (PP = 13%) (P = 0.008 for all options). In addition, PA rely on pulmonary function tests significantly less and tends to down-grade treatment regimens compared to PP.

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Nevertheless, a large and similar variability among groups was observed in the 2 case scenarios concerning the management of the preschool asthmatic child (P = 0.36, 0.37). A high agreement was found between the 2 groups regarding the indications for intra-venous corticosteroids in the morning of surgery and the when to start or augment preoperative treatment. Conclusions: A large variability exists among both pediatric pulmonologists and pediatric anesthesiologists in Israel in their approach to the preoperative treatment of asthmatic children. In scholl-aged children, PA tend to be less aggressive and more homogenous compared to PA. This is most probably explained by the paucity of evidence-based data. Consensus guidelines for the preoperative management of asthmatic children are needed.

#169 - THE EFFECTS OF INHALED B2 AGONISTS AND ANTI-CHOLINERGIC THERAPY ON RESPIRATORY AND AUTONOMIC FUNCTION IN PATIENTS WITH FAMILIAL DYSAUTONOMIA

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Background: Familial dysautonomia (FD) is a rare genetic disease characterized by autonomic instability, wide variation of blood pressure and severe respiratory obstructive and restrictive disease. Many FD patients are treated empirically with inhaled bronchodilators that target receptors of the autonomic system. However, the use of these drugs in the FD population has not been studied, and it is not known whether such drugs are safe and effective.

Aim: The aim of the study is to evaluate the effects of bronchodilators (anti-cholinergic: ipratropium bromide and beta-2-agonist albuterol) on FD patients and to compare the potency of these agents. The second aim is to evaluate the cardiovascular effects of these two drugs.

Methods: we conducted a randomized, double-blind, placebo-controlled, crossover study. All patients were diagnosed with FD. The study included three sessions for each patient. In each session we recorded 5 minutes of continuous ECG and blood pressure. Spirometry and Impulse oscillometry (IOS) measurements were obtained. One of the three drugs was then administered via inhalation: albuterol, ipratropium bromide or placebo (sodium chloride 0.9%), after 30 minutes cardiovascular data and pulmonary function were obtained as previously detailed. One of the three drugs was then administered via inhalation: albuterol, ipratropium bromide or placebo (sodium chloride 0.9%), after 30 minutes cardiovascular data and pulmonary function were obtained as previously detailed.

Results: 10 patients were enrolled. Mean age was 29 ± 11.8 (16–55) years. Both Albuterol and I praticuprom were effective in improving pulmonary function. Pre and Post Albuterol inhalation showed significant improvement in FEV1 (47.2% ± 17.5 vs. 51.6% ± 16.6 respectively, P < 0.001), and with MEF25-75 (34.1% ± 21.4 vs. 37.2% ± 18, P < 0.05), ipratropium demonstrated improvement in Pre and Post FEV1 that was statistically insignificant (47.7% ± 12.9 vs. 51.1% ± 15.3 respectively, P = 0.08). However, when compared ipratropium with placebo, the increment of FEV1 in percentage was statistically significant (8.5% vs 0.2% respectively, P < 0.05). IOS results: Pre and Post inhalation of Albuterol demonstrated reduction in R5Hz (4.67 ± 2.5 vs. 3.64 ± 2.1 respectively, P < 0.02), R20Hz (3.51 ± 1.9 vs. 2.83 ± 1.59 respectively, P < 0.02). Ipratropium bromide showed statistically significant improvement Pre and Post inhalation with R5Hz (3.67 ± 2.2 vs. 3.06 ± 1.6 respectively, P < 0.05) and AX (6.5 ± 6.4 vs. 3.46 ± 5 respectively, P < 0.02). Increment of more than 12% in FEV1 was documented in 5/10 patients post Albuterol and in 3/10 patients post ipratropium. No cardiovascular side effects or ECG abnormalities were observed during and after inhalation of both drugs. Blood pressure recording showed the characteristic variability but no extremely high measurements that required medication therapy.

Conclusions: Although autonomic dysfunction is a cardinal feature of the disease, leading to the expectation that medication targeting the autonomic system will not have the expected effect; both drugs were effective in FD patients. No major cardiovascular side effects were observed and both drugs were proven safe for FD patients.

#174 - IMPACT OF THE PAEDIATRIC REGULATION ON RESEARCH IN THE FIELD OF PAEDIATRIC ASTHMA

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Introduction: The Paediatric Regulation No 1901/2006 entered into force in all EU member states on 26 January 2007, with the aim to improve the development of medicinal products, to address the lack of age appropriate formulations and to provide information on efficacy, safety and dosing for the paediatric population. The Regulation requires applications for marketing authorizations to be accompanied by either a product-specific waiver or a paediatric investigation plan (PIP), to be agreed by the Paediatric Committee (PDCO) of the European Medicines Agency (EMA).

Aim of the study was to collect information on ongoing/planned development of medicinal products approved by the EMA in the condition of asthma in paediatric population.

Method: A retrospective search on already published opinions and decisions on PIPs in the condition asthma using a publicly available database of the EMA has been performed.

Results: Until December 2013 eighteen decision on PIPs in the condition asthma have been published by the EMA. Subsets of the paediatric population concerned by paediatric development are mainly related (10 PIPs) to children aged from 5 years to less than 18 years, in 6 PIPs to children 6–18 years and only in 2 PIPs younger children were planned to be included in clinical development (from 6 months of age in 1 PIP and from 1 year in another one). Mode of medicinal products administration for asthma treatment were mainly subcutaneous/intravenous or inhalation use (8 and 7 PIPs respectively), sublingual/oral use was limited to 3 PIPs. Until time of analysis (December 2013) 3 PIPs were planned to be completed. Completion of clinical trials for ongoing developments is expected within 1 to 16 years (mean value 9 years; median value 11years).

Conclusions: This is a first analysis of the impact of the Paediatric Regulation on development of medicinal products for treatment of asthma in paediatric population. Majority of PIPs are related to children aged 5 or 6 years and older. Prefer mode of medicinal products administration is inhalation or subcutaneous/intravenous use. Results of clinical trials will be known in approximately 10 years time.

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Abstract

#177 - THE IMPACT OF WRITTEN ASTHMA ACTION PLAN COUPLED WITH A PRESCRIPTION (WAAP-P) ON ASTHMA OUTCOMES

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Background: Control of asthma is the main goal for asthma therapy. Many strategies to control asthma symptoms and reduce unscheduled health care utilization exist, including (1) the provision of a written asthma action plan, (2) actively monitoring asthma symptoms and (3) patient education and regular medical review. In children, the specific, independent effect of WAAP-P, divided in three control zones identified by symptoms (optional peak flow values) and symbolised by traffic lights, in improving outcomes remains unclear. The objective of this study was to evaluate the utility of a written asthma action plan with a prescription (WAAP-P) on asthma control in a pediatric tertiary care center.

Methods: We conducted an observational analysis of asthmatic children with a WAAP-P and without WAAP-P (verbal counselling). Patients were a random sample of asthma patients aged 3–17 years with no other pulmonary diseases and followed in the Asthma Clinic of the Centre Hospitalier Universitaire of Sherbrooke. Asthma control parameters were those defined by Canadian Asthma Guidelines. We collected information about their use systemic corticosteroids, the number of hospitalizations, emergency room visits and disruption of pulmonary function tests. Outcomes were compared using Chi-square test and Fisher’s exact test (where appropriate). A P-value of <0.05 was considered to be statistically significant.

Results: There were no differences in gender and asthma severity among subjects without WAAP-P (n = 80) and with WAAP-P (n = 77). Subjects with WAAP-Ps were older (median 11, range 8–13) compared to those without WAAP-P (median 6, range 6–11, P = 0.001). In the WAAP-P group the rate of hospitalizations was 2.6% versus 6.3% for the control group (P = 0.443). With regard to the Emergency Department, visits the rate was 13% for the WAAP_P Group versus 13.8% for the control group (P = 0.883). With respect to systemic corticosteroids and pulmonary function tests, the results were not statistically significant (P = 0.597 and P = 0. 576 respectively).

Conclusions: Compared to medical management alone, the use of a written asthma action plan did not significantly affect asthma control. Further studies with a sufficiently powered randomized controlled trial is needed to revaluate the utility of this universally recommended intervention.

2. Allergic Bronchopulmonary Disorders excluding Bronchial Asthma

#141 - THE RELATIONSHIP OF SERUM INTERCELLULAR ADHESION MOLECULE-1 AND INTERLEUKIN-17A IN CHILDREN WITH ACUTE MYCOPLASMA PNEUMONIAE PNEUMONIA AND WHEEZE

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Abstract : OBJECTIVE To examine soluble intercellular adhesion molecule (sICAM-1) and Interleukin-17A (IL-17A) in acute mycoplasma pneumoniae pneumonia(MMP) and investigate if there is any relation between these inflammatory mediators and the occurrence of wheezing. METHODS We studied 93 patients who admitted with pneumonia. These patients were divided into three groups: MMP with wheeze (n = 25) and without wheeze(n = 38), and the patients without the evidence of MP infection (n = 30). Age-matched controls(n = 20) were also studied. The serum concentrations of sICAM-1 and IL-17A were measured using ELISA kits in patient groups and controls. Total serum IgE levels were determined using immunocytochemistry. RESULTS The patients with MMP had significantly higher serum sICAM-1 than those without evidence of MP infection and controls. In the presence of MMP, sICAM-1 concentrations were significantly higher in the patients with wheeze than those without wheeze(P < 0.05). Serum IL-17 levels were higher in pneumonia patients with or without MP infection than those in control group. In the presence of MMP, serum IL-17 concentrations were higher in the patients with wheeze than those without wheeze, however, no significant difference between groups was observed (P > 0.05). Total serum IgE(TIgE) levels were significantly higher in the MMP patients with wheeze than those without wheeze. A positive correlation was observed between serum sICAM-1 and log10 transformed TIgE(r = 0.261, P < 0.01). CONCLUSIONS sICAM-1 may play a role in the mechanism of wheezing in children with MMP.

3. Bronchopulmonary and Pleural Infections (including Tuberculosis)

#5 - IS LOWER RESPIRATORY TRACT INFECTION WITH ADENOVIRUS MORE DETERIMENTAL THAN OTHER VIRAL INFECTION IN EARLY CHILDHOOD?

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Background: Adenovirus is suspected to be more virulent than other viral infections when causing lower respiratory tract infection (LRTI). Our aim was to describe the clinical characteristics, hospital admissions and ongoing respiratory morbidity of adenoviral LRTI in early childhood. Methods: A retrospective review of children aged <2 years clinically diagnosed with LRTI and evidence of adenovirus infection on nasopharyngeal aspirate who were admitted to KidzFirst Hospital between August 2007 to July 2008 & August 2009 to July 2011. Demographic, clinical, radiological data and outcomes from index admission till 31 December 2012 were recorded.

Results: Two hundred and thirteen children were admitted with a median age of 8.5 months with 92% being Maori or Pacifica. Median length of admission was 2 days (range 1–30) with 79% from areas of high deprivation. Children under 6 months were more likely to have longer admission of ≥3 days (OR 2.4, P = 0.01), require oxygen (OR 2.9, P = 0.004) and for >24 hours (OR 3.2, P = 0.004) to ICU between adenovirus alone versus co-infection with other virus (P = 0.099) or S.pneumoniae carriage (P = 0.11). In the first year following admission, 74 children (35%) were admitted and 68 (32%) presented to the emergency department with respiratory illness and 31 children (15%) were seen in respiratory clinic.
Conclusion: Admissions for adenoviral LRTI were more common in Maori and Pacifica, those from deprived areas and were more severe in young children. Literature suggests that coinfection of any viruses and/or bacteria causes a more severe disease. However, our data demonstrates adenovirus alone or in combination was equally problematic with ongoing morbidity. This suggests all infants with adenoviral infection may need follow up to improve long term outcomes.

#17 - HAEMOGLOBIN OXYGEN SATURATION LEVELS AS DETERMINANT OF OUTCOME IN HOSPITALIZED CHILDREN WITH PNEUMONIA IN ILORIN, NORTH CENTRAL NIGERIA

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Background/Objectives: Pneumonia remains a major contributor to morbidity and mortality in Sub-Saharan Africa and hypoxaemia is a significant complication associated with an increased risk of death. The study aims to define the relationship between haemoglobin oxygen saturation (SpO2) levels and parameters of outcome, duration of supplemental oxygen and duration of hospitalisation amongst children with pneumonia.

Method: A descriptive cross sectional study was carried out amongst 200 children aged between 2 and 59 months with pneumonia seen at the University of Ilorin Teaching Hospital, Nigeria over one year. The diagnosis of pneumonia was based on clinical findings. Chest radiographs were taken and SpO2 level was determined using a pulse oximeter and the various recordings compared with clinical presentation and relevant outcome parameters. Data was analysed with SPSS 20.

Results: The male: female ratio was 1.5:1. Thirty two of the patients had lobar pneumonia while the rest had bronchopneumonia. Eighty-three (41.5%) of the children had hypoxaemia and their mean SpO2 was 81.3±8.1 percent. Ninety-three complications were recorded in 73 (36.5%) children; 52 (27.5%) had one complication while 21 (10.5%) children had more than one complication. Heart failure was the single most common complication recorded. A significantly higher proportion of the subjects with pneumonia-associated complications had hypoxaemia compared to the corresponding proportion in those without hypoxaemia. The mean duration of hospitalisation in children with complications increased with increasing severity of hypoxaemia. The mean duration of hospitalisation in children with complications was significantly longer than the corresponding value for those with bronchopneumonia, P = 0.001. Seventeen (8.5%) fatalities occurred. The mean (SD) SpO2 level of 78.3±10.9 percent in the fatal cases was significantly lower than the corresponding value of 91.5±7.8 percent recorded in the survivors, P = 0.001. Among the survivors, children with hypoxaemia had a longer mean (SD) duration of hospitalization of 6.9±6.4 days compared to those without hypoxaemia of 4.9±2.7 days, P = 0.001. The mean duration of hospitalization in children with lobar pneumonia was significantly longer than the corresponding value for those with bronchopneumonia, P = 0.001. Also, children with hypoxaemia spent a longer duration receiving supplemental oxygen compared to those without hypoxaemia (P = 0.001). The mean duration of oxygen therapy in children with pneumonia increased significantly as the SpO2 level decreased, P = 0.001. Conclusion: Hypoxaemia with increasing severity significantly predicts a longer duration of hospitalization, duration on supplemental oxygen and poorer outcome in children with pneumonia. Thus, it would be essential for health facilities to have capacity for monitoring oxygen saturation as a guide to oxygen therapy and aggressive management.

#18 - ELEVATED TRANSCUTANEOUS CARBONIC ACID AS A PREDICTOR OF A LATE COMPLICATION OF STAPHYLOCOCCAL PNEUMONIA IN A CHILD

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Background: Carbon monoxide (CO) may be produced endogenously during inflammatory conditions. Carboxyhemoglobin can now be measured transcutaneously (SpCO%). During measurements of SpCO% in children with pulmonary problems, a significant case was a 12 year old female with Influenza B, methicillin sensitive Staphylococcus aureus pneumonia and sepsis, shock, and acute renal failure. Monitoring continued from hospitalization through follow-up.

Methods: The Rainbow-SET Rad-57 Pulse CO-Oximeter (Masimo Inc., Irvine, CA) was used to measure SpCO%. The Institutional Review Board approved exploratory measuring and waived the need for informed consent. No treatment decisions were made based on SpCO%.

Results: During 3 weeks of ICU care, SpCO% was 0, then rose to 14 at 34 days, and declined to 0 two months later. Productive cough resolved, and spirometry and physical endurance improved despite rising SpCO% of 6 then 15 at 6 and 7 months after admission. At 7.5 months, productive cough, right sided chest pain, and dyspnea occurred. Chest radiograph showed a right pneumothorax and air and liquid filled cysts. Right upper lobe pneumatoceles, bronchopleural fistulae and right visceral and parietal pleura were resected. SpCO% fell to 6 and remained stable over the next year during which she experienced no acute illnesses and continued to improve in clinical status and spirometry.

Conclusions: This report describes a late effect of severe pneumonia that was preceded by a progressive rise in SpCO% despite ongoing clinical improvement. This suggests that SpCO% may be an easily attainable predictive measure of ongoing, subclinical inflammation.

#51 - SENSITIVITY OF A NOVEL SKIN TEST WITH RECOMBINANT PROTEIN ESAT6-CFP10 IN NEW CASES OF TUBERCULOSIS IN CHILDREN AND ADOLESCENTS.

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Background: Tuberculin skin test (TST) is simple and relatively inexpensive. The main disadvantage of TST is the occurrence of false-positive responses due to cross-reactivity to antigens in PPD that are shared by environmental mycobacterial species as well as by BCG vaccine strains. The Russian company has developed a preparation known as Diaskintest (DST), which represents two Mycobacterium tuberculosis-specific recombinant proteins CFP10-ESAT6, which are absent in all M. bovis BCG substrains and in most of non-tuberculous mycobacteria. The preparation is manufactured by the pharmaceutical company, according GMP conditions. It is for skin testing, 0.2 mcg/0.1 ml (in the same way as the Mantoux test).

Objective. To determine sensitivity of DST in new cases (children and adolescents) of tuberculosis (TB) in 2012 in Moscow Methods. 511 children and adolescents were identified with TB in Moscow in 2012. They received the Mantoux test with 2TU PPD-L and DST 0.2 mg/0.1 ml intradermally and induration responses measured. Any size induration was considered positive DST reaction, positive Mantoux reaction was >10 mm.

Order of the Ministry of Health of Russia allowed to use DST in children with positive Mantoux test. All children with positive DST reactions were performed chest X-ray, including computer tomography (if necessary) - it was possible to diagnose light forms of intrathoracic lymph nodes TB.
Results. Both tests were positive in 493/511 cases (96.5%; 95% CI 94.5–97.8%), even in both patients with HIV. Mantoux - positive and DST-negative reactions were in 135/511 (2.5%) - in children with BCG-ostitis (the isolated strain was identified as M.bovis BCG) and in the cases when the processes are in the reverse stage of development, which may indicate loss of activity (TB changes were detected in the calcification phase). Both tests were negative in 5/511 (1.0%) - in children with household sputum positive TB contacts in neonatal period, when immune response has not been developed yet and in patient after immunosuppressive therapy. No one had Mantoux- negative and DST- positive reactions.

Conclusion. DST is highly sensitive in new cases of tuberculosis in children and adolescents.

#63 - EVOLUTIONARY FEATURES OF ACUTE RESPIRATORY INFECTIONS ASSOCIATED WITH MIXED HERPES INFECTIONS IN CHILDREN

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Acute respiratory infection associated with persistent herpes infections, can facilitate the diminishing of the body activity, inducing severe disturbances of body immune response. According to OMS evaluation, the herpes infections are the most widespread infections on the planet, the mortality caused by these infections is on the second place (15.8%), in the group of viral infections, after influenza (38.8%). World statistics data shows that 33% of children up to 5 years present antibodies against HVS-1, being an indirect indicator of immune deficit. The incidence with CMV infections is between 50-64% in children.

Purpose: The study of evolutionary, immunological features, in the patients with severe respiratory infections associated with mixed herpes infections.

Objectives:

1. The appreciation IgG, IgM anti CMV, HVS type 1,2 in blood serum.
2. The study of cellular and humoral immunological status.

Materials and methods:

1. In the study group were included 100 children with acute respiratory infections, severe evolution.
2. The diagnosis of herpes infection was noted by PCR and immunoenzymatic methods.
3. The humoral immunity was appreciated by Mancini method.
4. The cellular immunity was assessed with specific monoclon.
5. The statistical interpretation of anamnesis and epidemiological data was used.

Results:

1. The anamnesis data have revealed the following aspects:
   92% of mothers presented recurrent skin herpes infections;
   18% presented CMV infection;
   16% of cases the children’s father was diagnosed with herpes infections;
2. In all examined children was detected high titre of antibodies to CMV;
3. For 88.8% of the children was detected high titre of antibodies to HSV type 1,2.
4. The deficit of IgA was identified in 75.9% children, and in 27.7% was insufficiency of IgG.
5. 83.8% of the children examined had deficiency of citoto-toxic lymphocytes (CD8 decreased).
6. The activity of macrophages (B lymphocytes, CD4 decrease) was reduced in 22% of those who were examined.

Conclusion: The mixed, persistent herpes infections, frequently affects cellular immunity, but in combination with other bacterial infections can induce frequent and severe abnormalities of the humoral immunity, causing severe evolution of respiratory infections.

Discussions: The herpes virus infection is an important public health problem for the following reasons:

the high frequency of congenital infections;
the character of persistent viral infection;
the high frequency of immune pathological states.

#76 - IMPACT OF INTRAPLEURAL FIBRINOLYTICS ON THE OUTCOME OF EMPYEMA IN CHILDREN

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Background: Management of pleural empyema includes chest drain insertion for free drainage of pleural fluid. Surgical intervention for loculated empyema is required if symptoms do not resolve with drainage alone. Installation of intrapleural fibrinolytics has been shown in some studies in high income countries to be beneficial in childhood empyema. Aim: To compare the outcomes of children with empyema before and after the introduction of intrapleural alteplase at Red Cross War Memorial Children’s Hospital (RCWMCH).

Methods: Clinical, aetiological and outcome data was prospectively collected in children admitted with empyema to RCWMCH between December 2006 and December 2011. Routine pre-emptive intrapleural alteplase (Tissue Plasminogen Activator), administered according to a standard protocol and indications, was introduced in September 2009. Outcomes in children treated with fibrinolytics were compared to the historical cohort who did not receive fibrinolytics. Primary outcome was need for surgery. Secondary outcomes were duration of hospital admission, complications and mortality.

Results: 142 cases of empyema were admitted during the study period with a median age of 17 months (IQR 8–43 months), 81 (57%) were males. After excluding cases where fibrinolytics were contraindicated (36) or no chest drain was inserted (7), data on 99 cases (52 with fibrinolytics; 47 without fibrinolytics) was available for comparison. Demographics, nutritional status, HIV status clinical characteristics and empyema aetiology were similar in both groups. The rate of surgery decreased from 38% (18/47) in patients not treated with alteplase to 10% (5/52) in patients treated with alteplase (RR 0.25; 95% CI 0.1–0.6). The median duration of hospital stay did not differ significantly (alteplase 9.5 days (IQR 7–16); no alteplase 12 days, (IQR 10–20); P = 0.09). Complications relating to empyema (alteplase 10%; no alteplase 13%) and treatment (alteplase 8%; no alteplase 4%) were few and similar in both groups. Overall mortality was low (6 deaths; 4.6%), with 2 deaths occurring in each group respectively.

Conclusion: Introducing intrapleural alteplase in children with empyema resulted in a 4 fold reduction in need for surgery. Intrapleural alteplase should be used in children with empyema.
#124 - THE IMPORTANCE OF EPIDEMIOLOGICAL SURVEYS IN THE DIAGNOSIS OF CHILDREN'S TUBERCULOSIS – CASE STUDY

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Introduction: Bosnia and Herzegovina is among the countries with a high incidence of tuberculosis, with th Directly Observed Therapy (DOTS) program for the treatment of tuberculosis (TB), which includes mandatory vaccinations. Aim of the study is to show importance of epidemiological surveys in the diagnosis of children tuberculosis.

Methods: We retrospectively analyzed four patients of same age who were treated with various form of TB within two years at the department of Pulmonology.

Results: All four patients were vaccinated-BCG, with visible scar, denied contact with affected by tuberculosis and with satisfactory social and economic status. In mid-2010 the girl was admitted to the first sub-febrile extended period with dry cough, and with radiological confirmed hilar lymphadenopathy, sputum negative, PPD > 10 mm. After administration of antituberculosis drugs according to protocol, cured. Next year, girl with cavernous form of tuberculosis was hospitalized, bacteriological sputum positive, QuantiFERON positive, previously treated irregularly from childhood asthma with inhalatory corticosteroids. In the same year, we received another two girls who were radiological and QuantiFERON positive. During the treatment of patients, it was found that three girls were in contact with girl with cavernous TB, whose source of infection remains unknown. Girl with cavernous tuberculosis completed successfully nine months treatment, and the other three six-month DOTS treatment protocol.

Conclusion: Carefully investigation the presence of TB contact with affected is of great importance in the diagnosis of TB in children, despite the existence of immunological tests and progress in the identification of Mycobacterium tuberculosis. Suspected TB means prompt diagnosis, therapy and prevention further spread of the disease.

#144 - RELATIVE CONTRIBUTION OF VIRUSES AND CA2+-ACTIVATED CL- CHANNEL 1 TO PNEUMOCYSTIS-ASSOCIATED INCREASED EXPRESSION OF MUC5AC IN AUTOPSIED INFANT LUNGS.

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The asymptomatic primary infection by Pneumocystis is probably the most frequent infection of infancy with its consistent peak between 2 and 5 months of age. Pneumocystis goes undiagnosed in infants and is considered innocuous, in contrast with the severe Pneumocystis pneumonia of the immunocompromised host. However, the recent finding of increased expression of MUC5AC, a marker of airway mucus, associated to Pneumocystis in autopsied infant lungs has documented that Pneumocystis-associated pathology also occurs in immunocompetent humans. Viruses may also induce mucus. Therefore, to understand the mechanisms involved and investigate the relative contribution of viruses to this mucus response, we studied common respiratory viruses and CLCA1, a member of the chloride channel family associated with airway mucus secretion, in infant lungs. Fresh frozen lung specimens from legal infant autopsies conducted between 1999 and 2004 at the coroner’s office in Santiago, categorized as Pneumocystis negative or positive were selected in a 1:2 negative/positive age-matched relation blinded to autopsy diagnosis and date of death. The infants, mean age 3.19 [1.0–11.9] months, had died suddenly and unexpectedly (SUID) in the community without hospitalization. Pneumocystis status of the samples (18 negatives and 37 positives, totaling 55 infants) was re-confirmed using nested PCR specific for human Pneumocystis and, quantified by qPCR using a specific probe against the human Pneumocystis MSG gene. MUC5AC and CLCA1 were studied by western blot using human-actin-gene-normalized determinations for intersample comparisons. Respiratory Syncytial Virus (RSV), Influenza A and B, Parainfluenza virus 1, 2, and 3, and Metapneumovirus, were studied with specific primers by RT-PCR, and Adenovirus by PCR. Viruses were identified in four of the 55 infants; RSV in 3 and adenovirus in 1. Actin-normalized densities of MUC5AC and CLCA1 were significantly increased in Pneumocystis-positive when compared to Pneumocystis-negative infants (P = 0.020 and P = 0.028 respectively), while MUC5AC and CLCA1 expression were not affected when the virus-positive samples were compared with the virus-negative samples (P = 0.405 and P = 0.199 respectively). Interestingly, increasing burden of Pneumocystis organisms (MSG copies/ng human DNA) correlated with increasing expression of CLCA1 (P = 0.007), while MUC5AC levels were unaffected by Pneumocystis burden (P = 0.075). This study confirms that Pneumocystis stimulates the airway secretory system during its primary infection of the immunocompetent infant host. Viruses were 5 times less frequent and did not affect MUC5AC or CLCA1. In addition, results suggest that MUC5AC and CLCA1 responses follow a different activation sequence and show that CLCA1 is progressively induced with Pneumocystis organism burden multiplication. The high prevalence of Pneumocystis in infants warrants to study Pneumocystis as a potential co-factor of airway disease of infancy.

#156 - MACROLIDE-RESISTANT Mycoplasma PNEUMONIAE – IS IT RELEVANT?

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Introduction: Macrolide-resistant Mycoplasma pneumoniae has been reported to be rising throughout the world and especially in Asia. How...
relevant to clinical practice will this trend be in our management of diseases caused by Mycoplasma pneumonia?

Aim: A preliminary survey was done to document the prevalence of macrolide-resistance in those with positive Mycoplasma results on PCR taken from a throat swab and to correlate it with the clinical features of the patients.

Method: A random survey was taken of 28 patients who were positive on Mycoplasma PCR from 2012 to 2013 and mutations for nt2063 on the 23S rRNA gene was done. The clinical features of those who were positive for the mutation were compared to those without the mutation to identify possible differentiating features which may aid in the diagnosis of macrolide-resistant mycoplasma infection and whether this will affect outcome of the infection.

Results: 28 children with mean age of 7.2 years (Range: 1–14.6 years) were included. 8/28 (28.6%) was positive for the mutation. The diagnosis ranged from an uncomplicated upper respiratory tract infection to a complicated pneumonia with effusion. Those with macrolide-resistant infection presented with a longer duration of fever at presentation ($P = 0.002$) and also took longer for the fever to resolve ($P = 0.000$). All the children were treated with macrolide, Clarithromycin, with complete resolution of illness.

Conclusion: The estimated prevalence rate of macrolide-resistant mycoplasma pneumonia is about 30%. Those with macrolide-resistant infection were likely to have a longer duration of fever. However all children eventually recovered despite being treated on macrolide even in the presence of the mutation for macrolide-resistance.

#157 - FRACTIONAL EXHALED NITRIC OXIDE DURING ACUTE VIRAL BRONCHIOLITIS AND LATER WHEEZING

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Rational: Hospitalization due to acute viral bronchiolitis (AB) in infants is a major risk factor for recurrent wheezing and asthma like symptoms. In addition to the respiratory syncytial virus (RSV) the role of other viruses and especially rhinovirus (RV) has emerged in recent years. Fractional exhaled nitric-oxide (FeNO) is a marker for eosinophilic airway inflammation and has been shown to be high in asthmatics compared to controls. We have previously shown that FeNO levels decrease during the acute stage of RSV bronchiolitis and return to relatively high levels during convalescence.

Aim: To evaluate determinants for recurrent wheezing after AB and to investigate FeNO levels during the acute phase and convalescence also in other viruses.

Methods: Children (0–2 years) admitted to the emergency department with AB were recruited. The following data was collected: family and patient’s history, disease severity (bronchiolitis score) and FeNO levels (in ppb). Nasal secretions were collected and PCR was performed for RSV, influenza A-B, parainfluenza 1–3, human metapneumovirus, adenovirus, coronavirus, bocavirus and RV. Two and 6 months after the acute disease, FeNO levels were repeated and the occurrence of wheezing episodes was assessed. Recurrent wheezing was defined when two or more wheezing episodes were reported.

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Results: A total of 115 children with AB were recruited, mean age was 4.7 months (0.5–24). 60 children (52%) had only RSV. 26 (23%) had co-infection of RSV and other virus, in 22 (19%) a non-RSV virus was detected, and in 7 (6%) patients PCR was negative to all viruses. Recurrent wheezing was reported in 52 (45%) of the children. Neither, parental factors (smoking, use of inhalation or atopic diseases), nor clinical variables during acute stage (bronchiolitis score, length of ICU/hospital admission) were associated with higher occurrence of future wheezing. No association was found between the viral pathogen (RSV, a non-RSV virus or co-infection) and FeNO levels, nor with the rate of recurrent wheezing. Low FeNO levels during AB with subsequent increase were characteristic to all viruses (RSV and non-RSV). FeNO levels at any stage did not predict recurrent wheezing.

Conclusions: Known risk factors for asthma were not associated with wheezing 6 months after AB suggesting other mechanism for wheezing in this group. FeNO levels during AB are low with subsequent increase. This pattern is not specific for RSV. FeNO levels at any stage had no predictive value for later wheezing. Its predictive value for future asthma should be studied at a later age.

#163 - PENCILLIN VERSUS CEFUROXIME FOR TREATMENT OF COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN WHO FAILED ORAL ANTIBIOTIC THERAPY IN THE COMMUNITY

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Background: Adherence to Guidelines for the management of community-acquired pneumonia (CAP) in children is poor. Recently it has been shown that treatment of non-complicated CAP with parenteral penicillin or ampicillin (according to guidelines) is as effective as cefuroxime. Still, this has not been studied in children who failed an oral antibiotic course.

Aim: To compare the outcome of treatment with penicillin or ampicillin to cefuroxime in hospitalized children with CAP who received antibiotic treatment prior to their hospitalization.

Patients and methods: A retrospective review of the clinical course and outcome of all previously healthy children from 3 months to 18 years old with non-complicated CAP who received an oral antibiotic course in the community and admitted during 2003–2008, in the pediatric departments of Hadassah Medical centers. Clinical course prior to admission, presenting signs and symptoms, laboratory findings at presentation and clinical outcome parameters including number of febrile days, number of days with IV antibiotics, length of hospital stay, change of antibiotics and clinical course 72 hours and 1 week after admission, were compared.

Results: Of the 337 children admitted with non-complicated CAP who failed an oral antibiotic treatment course in the community, 235 were treated with IV cefuroxime, and 104 with IV penicillin or ampicillin. The two groups were similar regarding age, sex, days of fever prior to admission, type of predmission oral antibiotic treatment and laboratory indices at admission ($P > 0.1$). The cefuroxime treated group had significant better outcomes in total number of febrile days, number of days with IV antibiotic treatment and total number of hospitalization days (1.2 ± 1.1 vs. 1.7 ± 1.6, 3.1 ± 1.3 vs. 3.9 ± 2.0, 3.5 ± 1.5 vs. 4.2 ± 2.0, respectively, $P < 0.001$). Treatment failure was not significantly different between the two groups (9.79% vs. 14.42%, $P > 0.1$). The odds ratio for being still hospitalized at 72 hr and 7 days was significantly lower for the cefuroxime group (0.5 and 0.18 respectively, $P < 0.05$).

Conclusion: In previously healthy children presenting with CAP after failing an oral antibiotic course in the community, treatment with IV cefuroxime appears to be superior to penicillin or ampicillin.
#164 - EFFECT OF BLACK CUMIN (NIGELLA SATIVA) AS ADDITIONAL THERAPY ON CLINICAL IMPROVEMENT OF PNEUMONIA IN CHILDREN

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Pneumonia is a major cause of morbidity and mortality in children under 5 years. It is estimated that nearly one-fifth of child deaths worldwide, mainly in Southeast Asia and Africa, are caused by pneumonia. Antibiotics and supportive treatments are standard therapies for pneumonia. Additional therapies are needed both to improve immune system and to provide additional antibacterial effect. Black cumin (nigella sativa) is widely recognized and can be offered as additional therapy. This study aimed to determine the effect of black cumin on clinical improvement of pneumonia in children.

A randomized double-blind clinical trial conducted on 19 subjects aged 6–60 months in Saiful Anwar Hospital. While they had standard antibiotics and supportive therapy, the treatment group also received 200 mg crude extract of black cumin per day during hospitalization, while the other group received placebo. We compared clinical improvement (fever and respiratory distress score) and length of stay between two groups.

There was significant difference in improvement of respiratory distress (p 0.036), but no significant difference in improvement rates of fever (p 0.164). The treatment group had 3 days shorter length of stay compared to placebo group (p 0.039). There was no adverse effect reported during the study.

We conclude that black cumin can improve the rates of improvement of pneumonia in children and is relatively safe.

Keywords: pneumonia; black cumin; clinical improvement

#44 - STUDY OF PHARYNGOMALACIA, A DISEASE POSSIBLY LEFT UNDIAGNOSED

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Introduction: In our institution, we have experienced cases with hypoxemic episodes, stridor and/or feeding difficulties which showed collapse of the pharyngeal space during inspiration under flexible fiberoptic endoscopy for evaluation of suspected upper airway diseases. We defined this phenomenon “pharyngomalacia”. There have been reports in the past of cases with similar findings, termed pharyngomalacia, discoordinate laryngopharyngomalacia, and pharyngeal wall inspiratory collapse.

Objective: Our objective was to identify the characteristics of the cases diagnosed as pharyngomalacia, to give a better understanding of the disease which we believe deserves more recognition.

Methods: We have diagnosed 56 infants with pharyngomalacia between 2003 and 2013. The gestational age was between 25 weeks and 41 weeks,
and the birth body weight was between 678 and 3934 g. All cases were
diagnosed through flexible fiberoptic endoscopy to confirm collapse of the
pharyngeal space. The medical records were evaluated retrospectively to
identify symptoms and its onset, age at diagnosis, accompanying diseases,
treatment needed, and age at resolution.
Result: The most common symptom was hypoxemic episodes 42/56 (75%),
followed by inspiratory stridor 31/56 (55%), and feeding difficulties 27/56
(48%). Symptoms became evident within one month after birth in 34/56
(61%) and the average age at the time of diagnosis was 1.9 months. Airway
diseases other than pharyngomalacia were present in 31/56 (55%), and
laryngomalacia was most common, seen in 21/56 (38%) of cases. Eighteen
cases (32%) had either chromosomal abnormalities, neuromuscular
diseases, or multiple anomalies. Nasal CPAP was needed in 20/56 (36%)
of cases, tube feeding in 12/56 (21%), and tracheostomy in 7/56 (13%). No
cases died. Pharyngomalacia resolved in 43/56 (77%) and the average age at
the time of resolution was 6.4 months.
Discussion: Our study shows that pharyngomalacia without laryngomalacia
or other airway diseases can cause hypoxemic episodes, inspiratory stridor
and feeding difficulties, which from what we have searched is yet to be
documented in large numbers in literature. During the same time period we
have diagnosed 195 patients with laryngomalacia under flexible fiberoptic
endoscopy, which shows that pharyngomalacia is not a rare disease. It may
be possible for cases with suspected upper airway diseases to be diagnosed
as laryngomalacia or other diseases instead of pharyngomalacia because of
the poor recognition of the disease.
Conclusion: Pharyngomalacia on its own can cause hypoxemic episodes,
ispiratory stridor and feeding difficulties. Evaluation with a flexible
fiberoptic endoscopy is essential in the diagnosis. Many cases resolve with
age, but some cases need airway management and/or tube feeding. This
disease maybe left undiagnosed and we believe this disease deserves more
recognition.

#54 - MCIDAS MUTATIONS CAUSE CILIARY APLASIA

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Background: Primary ciliary dyskinesia (PCD) is a rare disorder,
characterized by chronic and recurrent upper and lower respiratory tract
symptoms and an increased incidence of situs inversus and male infertility.
It is caused by an inborn dysfunction of the motile cilia. Ciliary aplasia (CA)
is a subtype of PCD, in which no motile cilia are formed on the respiratory
epithelium. So far, more than 25 genes have been identified that can cause
PCD. However, no genetic cause has been linked to CA until now.
Methods: We used highly parallel sequencing of a partial exome captured
DNA library (DNA library preparation kit TruSeq DNA Sample Prep kit v2,
Illumina; Exome capturing kit SeqCap EZ Human Exome Library v3.0,
 Nimblegen; Sequencing kits TruSeq FE Cluster Kit v3-cBot-HS and TruSeq
 SBS Kit v3-HS, Illumina; Sequencing apparatus HiSeq 2000, Illumina;
Bioinformatic analysis CLC Genomics Workbench, CLC Bio) to find gene
mutations in patients with CA.
Results: We report on a patient with a severe phenotype of PCD due to CA
(confirmed on repeated nasal biopsy, inclusive cell culture with de novo
criogenesis). Transmission electron microscopy showed absence of the
basal bodies and absence of centrioles. The latter induce differentiation of
cilia on the cell surface. She suffered from frequent upper and lower
respiratory tract infections, had chronic lung disease, underwent a
lobectomy of the lingula for severe bronchiectasis and had fertility
problems. She died at the age of 27 years due to pneumonia with
respiratory insufficiency. DNA extracted from a blood sample was stored.
Exome sequencing revealed a homozygous non-sense mutation (Cys147*)
in MCIDAS, the well-conserved human orthologue of multi-
cilin. This mutation has not been reported before in public variation
databases. The mutation was confirmed by Sanger sequencing and
heterozygous carrier status was demonstrated in both parents. Multicilin is
a nuclear protein that has been shown to induce multiciliated cell
formation in Xenopus skin and kidney tissue and in cell cultures of mouse
airway epithelium (Stubbs et al, Nature Cell Biology 2012). Additionally, it
mediates centriole assembly. Therefore, it is an excellent candidate gene
for CA. Moreover, we showed that multicilin is expressed in human
respiratory epithelium and upregulated during ciliogenesis in a cell culture
system. The homozygous non-sense mutation that was found in our patient
results in an early stop codon, before the CCDC region of the protein,
which is essential for its function. Unfortunately, no tissue of the patient
was available to confirm absence of multicilin in respiratory epithelium
since she already died. MCIDAS mutations could not be found in several
other patients with CA.
Discussion: MCIDAS is a perfect candidate gene for CA and a pathogenic
mutation is responsible for CA in one patient.
Conclusion: We report on a patient with ciliary aplasia, probably caused by a
homozygous non-sense mutation in MCIDAS.

#69 - STUDY OF PULMONARY FUNCTION AT SCHOOL
AGE IN JAPANESE EXTREMELY LOW BIRTH WEIGHT
INFANTS – STUDY OF PULMONARY FUNCTION AT 6 TO
12 YEARS OF AGE –

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The survival of extremely low birth weight infant keeps on increasing. In
such an age, the presence of subclinical pulmonary function abnormality is
suspected even in infants who are thought to have no pulmonary problems.
We studied the pulmonary function of Japanese extremely low birth
weight infants at school age to look for subclinical pulmonary function
abnormalities.

Patients and Methods: Institutions were selected based on the answers of
questionnaire on the pulmonary function of extremely low birth
weight infants at school age. Pulmonary function was measured in 264
cases (122 male, 142 female, gestational age: 26.2 ± 2.2 weeks, birth body
weight: 751 ± 143 grams, age at measurement: 8.5 ± 1.6 years), which
satisfied the following 4 criteria: (1) Japanese extremely low birth weight
infant, (2) age at measurement 6 to 12 years, (3) clear background, (4)
pulmonary function measurement performable. The measurements were
compared with normal values in Japanese children, and changes with age
and effect of background on school age pulmonary function were evaluated.
Result: Compared with values of spirometry in Japanese children, only 52%
had normal pulmonary function. In each age groups, age 6: 41%, age 7: 56%,
age 8: 51%, age 9: 57%, age 10: 58%, age 11: 42% had normal results,
respectively, and abnormal pulmonary function was common. The
percentage of restrictive abnormality were at age 7: 12%, age 8: 23%, age
9: 30%, and increased with age. Factors affecting pulmonary function were
palivizumab administration, which had a positive effect, and chronic lung
disease and the need for home oxygen therapy, which had a negative effect.
Discussion: Abnormal pulmonary function was common in the study of
pulmonary function in extremely low birth weight infants at school age. The

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measurement of pulmonary function at school age makes it possible to screen for subclinical pulmonary abnormalities. Improvement with age is not always noted, therefore long term follow up of pulmonary function is thought to be essential.

#91 - FOREIGN BODY ASPIRATION IN CHILDREN: EXPERIENCE FROM 2624 PATIENTS

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Objectives: The objective of this study is to analyze the epidemiological, clinical, radiological and endoscopic characteristics of pediatric foreign body aspiration in Algeria.

Methods: In this retrospective study, the results of 2624 children younger than 18 years admitted in our department for respiratory foreign body removal between 1989 and 2012, were presented. Most of them had an ambulatory rigid bronchoscopy.

Results: The children (62.34% males and 37.65% females) were aged 4 months to 18 years with 66% between 1 and 3 years. Choking was related in 65% of cases. The delay between aspiration and removal was 2–8 days in 65.8% and within 24 hours in 9.2%. In the most cases, the children arrived with cough, laryngeal or bronchial signs and unilateral reduction of vesicular murmur. The examination was normal in 13%. The most common radiologic finding was pulmonary air trapping (40.7%). The aspirated bodies were organic in 66.7%, dominated by peanuts, while sunflower seeds, beans and ears of wheat were the most dangerous. In the other cases, they were metallic or plastic as pen caps and recently scarf pins. The endoscopic removal by rigid bronchoscopy was successful and complete in 97%. Cases with extraction failure (3%) limited to certain FBs, all of them inorganic were assigned to surgery. The complications related to the endoscopic procedure were 0.29% with a mortality of 0.26%.

Conclusion: Foreign body aspiration is a real public health problem in Algeria. The best way to manage it is an early diagnosis and a rigid bronchoscopy removal under general anesthesia used by fully trained staff. The prevention of this domestic accident should consider the population lifestyle and cultural habits to be more effective.

#130 - NATURAL HISTORY OF SNORING IN HONG KONG ADOLESCENTS

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Objective: To determine the natural history of snoring in children and the risk factors for persistence of habitual snoring.

Methods: This study was an extension of our previous cross-sectional telephone survey on the prevalence of sleep problem amongst Hong Kong children in 2002. A follow-up telephone questionnaire survey was conducted 4–6 years after the initial survey. Adolescents who were snoring at least 6 nights a week were defined as habitual snorers. Persistent habitual snorers were the one who were defined as habitual snorers in both surveys. Incident habitual snorers were those who were non-habitual snorers in the 2002 survey but were reported to have habitual snoring in the current survey.

Results: Two thousand and five out of 3,047 eligible subjects were successfully interviewed by phone, giving a response rate of 65.8%. The prevalence of habitual snorers was 12.7% in the current survey. 40.6% of habitual snoring children had persistent habitual snoring. Ninety-one (4.5%) adolescents were persistent habitual snorers. Allergic rhinitis, male gender and higher BMI were identified as significant risk factors of persistent habitual snoring. One hundred and sixty three (8.1%) children were identified as incident habitual snorers. The risk factors of incident habitual snorers included male gender, asthma, higher BMI at follow-up and younger age at the first survey. In the current study, the mean sleep duration was 7.6 hours ± 1.1 hours. The sleep duration from 13- to 18-years-old was less than the lower limit of the international recommendation for sleep duration.

Conclusions: 40.6% of habitual snoring children had persistent habitual snoring over 4–6 years period and 8.1% of the initial non-habitual snorers became habitual snorers. Male gender and higher BMI are significant risk factors for both persistent and incident habitual snoring.

#133 - AN INTERNATIONAL PATIENT-REGISTRY FOR PRIMARY CIILIARY DYSKINESIA

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Introduction: Primary Ciliary Dyskinesia (PCD) is a rare, genetically heterogeneous disorder that affects approximately 1 in 20,000 individuals. Dysfunction of respiratory cilia results in defective mucociliary clearance and chronic upper and lower airways disease. Recurrent lower respiratory tract infections lead to bronchiectasis and ultimately respiratory failure. The clinical management is currently based on improving airway clearance and controlling respiratory infections through the administration of antibiotics. As there are no evidence-based treatment regimens at all, regimens are largely derived from treatments for patients with airway disorders such as cystic fibrosis. The clinical management of PCD is also confined by the lack of a clearly defined natural course for this disease and features that relate to adverse outcomes. In a rare disease such as PCD, registries are valuable tools that provide information on daily practice not accessible to clinical trials. Within an international consortium, BESTCILIA, we have set up a PCD registry in order to gain insight into the incidence, clinical presentation, treatments and course of the disease.

Methods and results: Items collected in the registry have been generated by an adapted Delphi process. The system is fully compliant to international guidelines and quality assurance systems.

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guidelines for Good Clinical Practice. Intellectual property rights are fully respected. A web-browser-based data entry system is used involving plausibility checks. The registry has two levels: Level A comprises a minimal dataset with key items entered for all patients. Level B covers an extended data set of diagnostic, clinical, microbiological and radiological parameters. Furthermore, quality of life is assessed very sensitively by incorporating the newly developed PCD specific quality of life questionnaire PCD-QoL.

Conclusion: The PCD registry will allow (1) collect epidemiological data (e.g. mortality), (2) describe the course of the disease, (3) describe the effects of different treatment regimens, (4) identify genotypic and/or phenotypic features with prognostic relevance and (5) serve as a platform for recruitment of well-defined patient cohorts for randomized clinical trials, what (6) will finally lead to the generation of evidence-based management guidelines.

#148 - PULMONARY HEMOSIDEROSIS – THE HETEROGENEITY OF A GROUP OF PEDIATRIC PATIENTS

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Introduction: Pulmonary hemosiderosis (PH) is a rare disease, often idiopathic in pediatric age, even after extensive investigation. We reviewed the PH cases followed at the pediatric department of Centro Hospitalar do Porto (Portugal), in the last 18 years and its evolution with the purpose of better knowledge of this rare disease.

Results: Six children were diagnosed with PH between 1995 and 2013, with age at diagnosis ranging between 2 and 7 years (median age of 3 years) and median time of follow-up 11 years. The initial suspected diagnosis were gastrointestinal hemorrhage, recurrent respiratory infections, bacterial pneumonia, pulmonary tuberculosis and chemical pneumonitis, all associated with severe anemia. The diagnosis of PH was achieved 4 to 36 months after the first symptoms. The initial etiological investigation was inconclusive in all cases, with subsequent detection of anti-neutrophil cytoplasm antibody positive (1 patient), Hashimoto’s thyroiditis (1 patient) and diabetes mellitus (1 patient). All patients received systemic corticosteroids and hydroxychloroquine, with good clinical response in 4 children, 2 of who remained asymptomatic after suspension of therapies. In the remaining 2 cases, one with diabetes mellitus and other with ANCA vasculitis diagnosed after 14 years of disease, the absence of response to hydroxychloroquine led to its replacement with azathioprine. The latter patient maintained frequent exacerbations progressing to respiratory failure, leading to a change in therapy for rituximab and cyclophosphamide, with good clinical response.

Comments: Pulmonary hemosiderosis initial symptoms are nonspecific and high suspicion is essential for timely diagnosis. This small group of patients showed great heterogeneity on the clinical course, varying from full remission with hydroxychloroquine to alveolar hemorrhage persistence with progression to cardiorespiratory failure and requiring other therapeutic options. Due to the low prevalence of PH, intermittent nature of the disease and variability on the degree of severity, the safety and efficacy of therapeutic immunosuppressive are difficult to assess. Although most PH cases are idiopathic, secondary etiology should be suspected in patients without initial therapeutic response or with association with autoimmune diseases. In these cases, clinical and laboratory surveillance should be maintained in the active search of the best therapeutic approach.

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#149 - A RARE CASE OF REFRACTORY ENDOBRONCHIAL CAPILLARY HEMANGIOMA IN A YOUNG INFANT

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Introduction: Although rare in pediatric patients, endobronchial tumors can present various pathologic patterns associated with partial or total airway obstruction. Usually benign in infants, diagnosis and management of these tumors remain challenging. Purpose: We report a case of capillary hemangioma of the left main bronchus, refractory to conventional medical therapy, in a young infant presenting with persistent hyperlucency of the left hemithorax. Methods/Results: A 6 month-old girl was referred to our institution for persistent hyperlucency of the left lung after recovery from left lower lobe pneumonia. It is the second child of a healthy non consanguineous Caucasian couple, born after a full term pregnancy. She presented two episodes of left lower lobe pneumonia with upper lobe hyperinflation at the ages of 3 and 5 months. On admission, clinical examination revealed mild respiratory distress including tachypnea and hypoverilation of the left hemithorax. The differential diagnosis included congenital lobar emphysema, endobronchial mass, extrinsic bronchial compression, Swyer-James syndrome and foreign body aspiration. Bronchoscopy showed complete obstruction of the left main bronchial lumen by a pulseless, vascularized and depressive mass causing air trapping of the left lung. Computed tomography demonstrated an endobronchial well delimited mass of 5 mm diameter in the left main bronchus with homogenous and positive contrast enhancement. Magnetic resonance imaging showed no gadolinium contrast enhancement and transesophageal pulsed doppler little or no measurable blood flow. Carcinoïd tumor markers were not detected either in serum or in urine. The macroscopic aspect and the young age of the patient being highly suggestive of a benign hemangioma, treatment with corticoids, propranolol and acebutolol were consecutively attempted. As no reduction of the mass volume was observed by successive bronchoscopy, surgical resection and bronchial termino-terminal anastomosis were successfully conducted in order to remove the mechanical obstacle. Anatomopathology and immunohistochemistry confirmed the diagnosis of capillary hemangioma. Conclusions: Endobronchial tumors, although rare in infants, should be considered in the differential diagnosis of unilateral hyperlucent lung. In young infants, diagnostic assessment and management remain challenging as airway size and risk of bleeding make endobronchial biopsy and therapy difficult to perform. Age at presentation, localization and anatopathology should guide therapeutic approach of endobronchial tumors. In this case, the lack of
response of the hemangioma to conventional medical treatment led us to perform a surgical resection.

5. Fetal and Neonatal Respiratory Disorders

#26 - RESPIRATORY DISORDERS AND CONSEQUENTIAL MORBIDITY OF THE “LATE PRETERM” INFANTS (GESTATIONAL AGE: 34-36 + 67 WEEKS)

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Introduction: Late preterm infants (LPIs) are defined as newborns with a gestational age (GA) of 340/7-366/7 weeks. This neonatal population presents a delayed transition from intrauterine to extraterrestrial life and a functional immaturity of the lung structure, associated to high respiratory morbidity; therefore LPIs are prompt to developing respiratory distress syndrome (RDS), transient tachypnea of newborns (TTS) and pulmonary hypertension.

Purpose: To determine the incidence of respiratory disorders of LPIs in a tertiary care perinatal center and their impact on LPI’s morbidity. Patients and Methods: We performed a retrospective analysis of the LPIs delivered in our perinatal center and required admission to the neonatal intensive care unit (NICU) from April 2004 to December 2011. Infants with severe congenital anomalies were excluded. We recorded the incidence of respiratory complications and patients’ evolution.

Results: Out of 10650 deliveries, 1280 newborns (12%) were LPIs; two hundred thirty nine (239) of them were multiple [231 (18%) twins and 8 (0.6%) triplets] while 1041 (81.4%) were singletons. We studied a total of 1527 infants (770 males), 326 (21.3%) of whom were directly admitted to the NICU. Subjects were divided into three groups according to GA (1st: 34–3467 2nd: 35–3567 3rd: 36–3667 weeks). The rate of RDS was markedly declined from 17% at the 1st group to 0.8% at the 3rd group. Infants of the 2nd group were more likely to develop transient tachypnea (10%) than those of the 1st group (4.7%). TPH was recorded in 3 of 340 neonates (0.9%) of the 1st group, 1 of 457 (0.2%) of the 2nd and 2 of 730 (0.3%) of the 3rd group.

Conclusions: LPIs who develop respiratory disorders are susceptible to respiratory failure and therefore they present higher neonatal morbidity and mortality.

#123 - A CASE OF CONGENITAL LOBAR EMPHYSEMA IN THE MIDDLE LOBE

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Introduction: Congenital lobar emphysema (CLE) is an uncommon event in neonates. It is characterized by overinflation of pulmonary lobe, and may present as a diagnostic and therapeutic dilemma. This affection can cause a severe respiratory distress with high level of mortality or result in serious morbidity and disability.

Case Report: A 3-week-old male baby weighing 3000 g was referred to our neonatal intensive care unit for asphyxia with respiratory distress. After the failure of its management in a Peripheral Hospital, he was delivered as a full term with delayed cry and respiratory distress without any history of infection.

Physical examination revealed a tachypneic at a rate of 55–60/min with subcostal retraction, the cyanosis was generalized (oxygen saturation sp02 was 66% in air). On examination of the respiratory system, decrease breath sound on the right hemithorax was noted. The cardiac auscultation was normal. The chest X-ray showed hyperinflation on the right side, and right basiithoracic opacity and right mediastinal shift. Computed tomography (CT) scan of the thorax supported the X-ray. There was hyperinflation on the right middle lobe with tracheal and mediastinal shift to the left side. The blood parameters were normal. On the echocardiography, there was no evidence of congenital cardiac anomalies or pleural effusion.

After hemodynamic and respiratory stabilization, surgical intervention was performed by right thoracotomy. The right middle lobe looked emphysematous at time resection. Histopathological examination of the excised right middle showed alveolar distension without fibrosis. Post-operative chest X-ray showed expansion of the right upper and lower lobes, with no emphysema or mediastinal shift.

The child was discharged 10 days post-surgical intervention. He was seen as an outpatient at 1, 2 and 6 months of age. He had normal O2 saturations in room air and his respiratory rate was 30–35/min. He was feeding well and gaining weight.

Conclusion: In summary, the diagnosis of CLE may present a diagnostic challenge and a high index of suspicion in neonates with progressive respiratory distress is important if the diagnosis is to be made promptly. The outcome of surgery is good in most cases.

6. Cystic Fibrosis

#58 - BRINGING BAD NEWS: THE DIAGNOSIS OF CYSTIC FIBROSIS IN CHILDHOOD

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Background: The day parents are told their child has Cystic Fibrosis (CF) is imprinted in their memory. The diagnosis changes family life. Parents often show strong emotions (e.g. shock, anxiety) and they need to restructure their lives taking into account CF (Jedlicka-Köhler, Götz & Eichler, 1996; Monestrol et al, 2011).

Aims: The aim of this study is (1) to explore how parents recall hearing the CF diagnosed and the information they received and (2) to explore their current ways of coping.

Methods: Parents (n = 38) of 20 children with CF (diagnosed during the past 5 years) were interviewed using a semi-structured interview about the period around the diagnosis. Coping was assessed using the Utrecht Coping List (Schreur et al, 1988).

Results: No significant differences between fathers and mothers were found. All parents were informed by the CF specialist, although 20 parents first heard the term ‘CF’ from their local pediatrician or GP. All parents recalled specific details about the diagnosis: the information they were given as well as their innermost thoughts and emotional reactions. Parents were satisfied with the information they received and the way it was provided. Twenty-one parents remembered the doctor showed personal emotions and two thought this unpleasant. The remaining parents were comfortable with the doctor not showing personal emotions. Less than half of the parents (44.3%) mostly used an active problem solving coping style. Present-day passive coping styles were found associated with ratings of negative feelings and thoughts at the time of diagnosis.

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Conclusions: All parents were pleased with the detailed disease information they received at the time of diagnosis and many shed a tear. All recalled details, both practical and emotional. When counseling parents it is important to recall these emotions and thoughts, because they seem related to current coping styles. The diagnosis is the starting point of a long-term relationship between patient, parents and CF team. ‘Doing things well from the start’ is crucial and may prevent long-term problems in coping with CF. Acknowledgements: Special thanks to the parents participating in this study.

#118 - PERSPECTIVES AND EXPERIENCES OF CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS: A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF QUALITATIVE STUDIES

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Introduction: Cystic fibrosis (CF) is a common life-shortening genetic disease with an estimated incidence of 1 in 2500 newborns. Most patients with CF experience chronic pulmonary disease and pancreatic insufficiency, and must adhere to time-consuming and onerous daily treatments and physiotherapy. Limited daily functioning, poor adherence to treatment, low self-esteem, short stature and impaired psychosocial outcomes have been reported. This study aimed to describe the experiences and perspectives of children and adolescents with CF in order to direct care towards areas of importance for patients.

Methods: MEDLINE, Embase, PsyCINFO, and CINAHL were searched from inception to April 2013. We synthesized data from qualitative studies, including unstructured interviews and focus groups, that explored the experiences and perspectives of children and adolescents (<21 years of age) diagnosed with CF. For each study, all participant quotations and text under the “results/findings” or “conclusion/discussion” section were extracted and entered verbatim into HyperRESEARCH, a program used for storing, analyzing and searching qualitative data. We used thematic synthesis to analyze the patterns and relationships within and across themes.

Results: Forty-three articles involving 729 participants aged from 4 to 21 years across 10 countries were included. We identified six main themes with subthemes in parentheses: gaining resilience (accelerated maturity and taking responsibility, acceptance of prognosis, regaining control, redefining normality, social support), lifestyle restriction (limited independence, social isolation, falling behind, physical incapacity), resentment of chronic treatment (disempowerment in health management, unrelenting and exhausting therapy, inescapable illness), temporal limitations (taking risks, setting achievable goals, valuing time), transplant expectations and uncertainty (confirmation of disease severity, consequential timeliness, hope and optimism), and emotional vulnerability (being a burden, heightened self-consciousness, financial strain, losing ground, overwhelmed by transition).

Conclusions: Adolescents and children with CF report a sense of vulnerability, loss of independence and opportunities, isolation, and disempowerment. This reinforces the importance of the current model of multidisciplinary patient-centered care, which promotes shared-decision making, autonomy and self-efficacy in treatment management, educational and vocational opportunities, and physical and social functioning. The model may lead to optimal treatment, health, and quality of life outcomes.

#160 - BRONCHIAL HYPERREACTIVITY RELATED TO 4 COMMONLY USED INHALATION DRUGS IN BELGIAN CYSTIC FIBROSIS

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Background: Short-term tolerability of inhaled hypertonic saline (HS 6%), rhDNase, tobramycin and colistin in CF has been investigated before. Bronchial hyperreactivity (BHR) is reported in up to one third of the CF patients. BHR due to chronic inhalation of these drugs is poorly documented. Aims: To examine the prevalence of BHR related to chronic inhalation of previously described drugs leading to mandatory termination of therapy.

To determine risk factors for appearance of BHR, such as adulthood, duration of treatment, characteristics of specific drugs and presence of atopic disease.

Methods: All CF patients’ files of the University Hospital Brussels were screened from January 2002 till October 2012 related to the use of inhaled HS 6%, rhDNase, tobramycin and colistin after bronchodilation. Start and end date of inhalation treatment were registered and if applicable, reason for ending inhalation.

Results: A total of 163 (91M) patients were included with a median age of 17 years (0–61; n <18y = 84) and median number of inhaled drugs pp. per day was 2 (range 0–4).

BHR occurred in 29 patients (17.8%), mostly in adults (26.6% vs. 9.5% <18y; P <.05) and after a median of 1086.5 days (0–3740 days). A significant correlation was found between number of inhaled drugs pp. per day and the occurrence of BHR (r = .25; P <.001).

The occurrence of BHR was significant after inhalation of HS 6% (19.6% (P <.001)) and antibiotics (tobramycin 16.2% (P <.001); colistin 10.1% (P <.05)), but not after inhalation of rhDNase (1.4%; P = .61).

Atopic constitution, documented by positive Skin Prick Test for aeroallergens (66.7% vs. 51.9%) and elevated IgE levels (44.8% vs 33.6%), was not significantly higher in CF patients with BHR compared to CF patients without BHR (Pearson Chi-square .312 and .256 respectively).

Conclusions: BHR is seen more often in adults and after chronic inhalation, despite preceded preventive bronchodilation. Furthermore, it depends on the type of drug and increases with the number of taken aerosols per day. These findings may be suggestive for a cumulative effect of inhalation therapy on BHR. In addition, atopic disease does not seem to influence the presence of BHR.

7. Respiratory Manifestations of Extra-pulmonary Diseases (including AIDS)

#77 - GRANULOMATOUS AND LYMPHOCYTIC INTERSTITIAL LUNG DISEASE IN A PATIENT WITH COMMON VARIABL IMMUNODEFICIENCY

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Common variable immunodeficiency (CVID) is a primary immunodeficiency characterized by hypogammaglobulinemia and T-lymphocytes dysfunction. The most frequent clinical presentation remains recurrent bacterial infections. Approximately 10–15% of patients with CVID develop granulomatous/lymphocytic interstitial lung disease, which is frequently accompanied by splenomegaly, adenopathy, autoimmune cytopenias and gastrointestional and hepatic disease. There are no standard guidelines for the treatment of patients with CVID and granulomatous/lymphocytic interstitial lung disease.

A three year old girl was admitted to our hospital with a clinical history of recurrent upper respiratory infections, and splenomegaly. She had a marked decrease of all serum immunoglobulin isotypes and low specific antibody responses. The diagnosis of CVID was based on clinical and laboratory findings and IVIG therapy was started.

At the age of 6 years, she presented with cough. Thorax CT revealed mediastinal adenopathy, paranchymal multiple nodular opacities, ground glass opacities and bronchial wall thickening. Lung biopsy revealed non-necrotizing granuloma and lymphocytic interstitial pneumonia. A diagnosis of granulomatous/lymphocytic interstitial lung disease was made and 2 mg/kg/day predniolone were given. Although the patient’s symptoms improved and there was reduction in the extent of nodularity and ground glass opacification on the HRCT scan, relapses observed with the dose reduction of oral prednisolone during 6 years follow up. At the age of 12 years, in addition to pulmonary findings increase at hepatosplenomegaly and trombositopenia observed. Rituximab therapy was started and azatiopurin was added. Platelet count rose to normal levels and pulmonary radiographic abnormalities decreased.

As a result physicians must be aware of non-infectious complications such as granulomatous/lymphocytic interstitial lung disease in patients with CVID and there is need to determine the best modality of therapy to treat CVID associated granulomatous/lymphocytic interstitial lung disease.

8. Neuromuscular and Chest Wall Diseases (including SIDS)

#125 - MOTOR AND RESPIRATORY SEVERITY OF DUCHENNE MUSCULAR DYSTROPHY

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Purpose: Characterize motor and respiratory severity of Duchenne muscular dystrophy (DMD) patients. Methods: A cross-sectional study was performed in the neuromuscular and neurology departments of a university hospital of tertiary care, where 34 DMD boys were followed-up. Nineeen boys were evaluated for motor [Motor Function Measure (MFM) and 6-minute walk test (6MWT)] and respiratory assessment [respiratory muscle strength, peak cough flow, spirometry and volumetric capnography (VCap)]. The variables were compared between the same group of subjects with DMD (ambulatory and non-ambulatory) and also compared with healthy control subjects (6MWT, spirometry and VCap measures). Results: Statistical difference (P < 0.05) was found in MFM (between ambulatory and non-ambulatory DMD); 6MWT [lower walked distance, higher rest respiratory rate (RR), rest heart rate (HR) and HR after 9 minutes for DMD compared to controls]; spirometry [lower vital forced capacity (VFC), forced expiratory volume in one second, forced expiratory flow between 25% and 75%VFC, maximum forced expiratory flow and higher Tiffeneau index for DMD compared to controls]; and VCap for DMD younger than 11 years [alveolar ventilation per minute, ventilation per minute, tidal alveolar volume, tidal volume, airway dead space, carbon dioxide production, expiratory volume (Ve) and slope of phase III normalized by Ve(Slp3/Ve) compared to controls] and for DMD older than 11 years (lower Slp3/Ve and higher HR compared to controls). Conclusions: Patients with DMD have motor and respiratory deterioration that can be evaluated by the tools used in this study. Longitudinal multicentre studies and follow-up can contribute to a better understanding of the progression of motor and respiratory dysfunction and better management of patients with DMD.

9. Epidemiology, Environmental Risks, Prevention, Socio-economic Cost, Public Health Resources

#23 - SEROTYPE DISTRIBUTION AND DRUG RESISTANCE OF STREPTOCOCCUS PNEUMONIAE ISOLATED FROM CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA IN JAPAN.

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Purpose: To reveal the impact of the heptavalent pneumococcal vaccine (PCV7) and newly approved oral antibiotic (tosufloxacin) for children on serotype and drug resistance of Streptococcus Pneumoniae (Sp) isolated from blood and sputum samples of children admitted in hospitals with community acquired pneumonia (CAP) in Japan. Methods: PCV7 and oral tosufloxacin (TFLX) were newly approved for children in Japan in February 2010 and August 2009, respectively. The study periods were between April 2008 to March 2009 and April 2012 to March 2013. Children living in Chiba city, Japan, aged under 16 years admitted with CAP in 5 major tertiary hospitals were enrolled in this study, and patient backgrounds were collected. Patients with positive blood culture or cultured sputum (smears Geckler’s group 4 or 5) dominant for microorganisms such as Sp, Haemophilus influenzae (Hi), Moraxella catarralis (Mc) were diagnosed with bacterial pneumonia. Antimicrobial susceptibility of Sp was tested according to CLSI guideline M100-S23, serotypes were determined with Quellung reaction.

For Statistical analysis, the Fisher’s exact test was used to compare between-group differences in patient characteristics and the proportion of PCV7 serotypes in patients with a diagnosis of Sp pneumonia. A logistic regression model adjusted by potential confounders was used to estimate the odds ratio for the PCV7 vaccine effect in relation to the risk of Sp pneumonia.

Results: In this study, 486 and 495 patients under 16 years old were enrolled in 2008 and 2012, respectively. There were significant reductions of the proportion of Sp pneumonia patients (16.4% in 2008 versus 8.3% in 2012, \( P < 0.001 \)) and the PCV7 covered serotypes (62.5% in 2008 versus 18.4% in 2012).
#28 - PEDIATRIC SLEEP MEDICINE IN ROMANIA - A FORAY INTO THE FIELD OF KNOWLEDGE REGARDING THIS SPECIALTY

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Introduction: During the last thirty years there has been an important ascending evolution of the pediatric sleep medicine, acknowledging the active role of sleep in the physical and mental development of children. Even in those countries where these issues have now been approached for a long time, there are still many questions regarding the underlying aspects related to diagnostic and treatment. This field is still new in Romania, fact which resulted also from this study which applied a questionnaire of evaluation of current knowledge on the sleep matter in children, especially Obstructive Sleep Apnea Syndrome (OSAS). In the last six months of activity only 35% of the respondents have met at least one case of OSAS in children and 53% of the respondents admitted to have little knowledge concerning this disease. The respondents were family doctors as well as doctors of various pediatric specialties and the questionnaire allowed the identification of poor areas for various working groups.

Content: Within this survey performed on 100 validated questionnaires, applied on physicians of different specialties in our country, we have observed physicians’ poor level of information with respect to the obstructive sleep apnea syndrome in children. In the majority of cases the specialists questioned would not assume the role of identifying OSAS patients, 38% of them considering that the family plays the most important role in identifying children and adolescents with OSAS. 44% considered that pediatricians have this responsibility and 12% thought that family physicians should have this responsibility.

The physicians mentioned multiple difficulties, most of them described the lack of information, the limited access to polysomnography and high costs. Conclusions: Although, on many occasions, pediatricians recognize sleep problems, it is only rarely that they feel competent in solving them. As a result, parents gather information from magazines, from the Internet, friends or relatives. But this “self-therapeutic” method rarely shows any results. Therefore, it is essential that there are sleep medicine specialists in every country. The development of sleep medicine in Romania, the increase in the level of awareness and building up multidisciplinary teams for the management of these issues represent an important and necessary contribution to our health system.

Keywords: pediatric sleep medicine, obstructive sleep apnea syndrome, children, adolescents, survey Romania, physicians

#52 - OUTCOME OF NEONATE WITH TRANSIENT TACHYPNEA (TTN) IN OUR AREA SINCE 2013.

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In 1966, Avery et al, described the clinical features of eight babies with a condition that they attributed to delayed absorption of fetal lung liquid. As we know transient tachypnea in neonatal period (TTN), is a temporary phenomena that its signs and symptoms usually resolve by 3 to 4 days after birth and must not include more hospital stay duration because its costs or morbidity.

In present retrospective case control study, we try to show the span of hospital stay duration of such neonate in our hospital since Oct. 2012 to Oct. 2013. It seems such surveys help us and managers to definite and regulate an acceptable range of hospital stay days for reduce the morbidity and patient costs.

Methods: Fifty six cases were recorded with diagnosis of TTN since past year in our teaching hospital. At first review, we eradicated sixteen patients from study because their concomitant disorders like congenital heart diseases or sepsis. Then we recorded the data include: name-gender- date of birth and hospitalization- gestational age-first minute Apgar- place of birth, the type of delivery-prenatal history and the duration of hospitalization exactly.

Results: From forty neonates, there were 29 (66%) male and 11 (34%) female. Fifty percent of neonates were born by cesarean section and fifteen (37.5%) mothers had positive past history before or among their pregnancy. The common sign and symptom was tachypnea then nasal flaring, grunting, sub or inter costal retractions were occurred respectively, cyanosis was seen in extreme cases (0.5%). Gestational ages were recorded from 32 to 40 weeks and the first signs or symptoms were seen from one to four hours after birth. The duration of hospital stay was from 2 to 16 days and only 14 mothers were urban. Ninety percent of the neonates had at least two nights stay experience in NICU.

Conclusions: Despite currency and availability of health insurance for urban and rural in our area, stay in neonatal intensive care unit includes more cost for patient’s family. According to excellent outcome of such neonates and in comparison with other surveys, it seem we must reduce the duration of hospital stay especially transfer to NICU, not only for its costs but also for the morbidities.

Keywords: Transient Tachypnea Neonates, Hospital Stay Duration, Patient Costs

#107 - INDOOR AIR POLLUTION AND TOBACCO SMOKE EXPOSURE IN AN AFRICAN BIRTH COHORT STUDY.

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Tobacco smoke and indoor air pollution is a risk factor for childhood disease. The contribution of indoor air pollution or tobacco smoke exposure to the incidence, severity and outcome of childhood respiratory illness has not been well studied in African children.
Aim: To describe indoor air pollution and tobacco smoke exposure in a birth cohort in South Africa.

Methods: Indoor air pollution and tobacco smoke exposure were longitudinally measured in children enrolled in the Drakenstein child lung health study, a birth cohort study in a peri-urban area outside Cape Town, South Africa. Indoor air pollution and tobacco smoke exposure were measured at a home-visit conducted antenatally to measure particulate matter 10 μg/m³ (PM10), volatile organic compounds (VOC), nitrogen dioxide, sulphur dioxide and carbon monoxide levels. Urine cotinine in the mother and infant were also measured. Active surveillance for intercurrent lower respiratory tract illness in children was done.

Results: There are high levels of maternal smoking and very high levels of tobacco smoke exposure in infants, Table 1. Most households (69%) without a separate kitchen had benzene (volatile organic compound) levels above ambient standards. Of households with paraffin stoves, 96% had benzene levels above ambient standards, and homes with high density of people per cubic meter had 69% of benzene levels above ambient standard. Table 2.

Conclusion: There are high rates of exposure to tobacco smoke and volatile organic compounds prenatally that may impact on child lung health.

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#120 - LOW 25-HYDROXYVITAMIN D3 SERUM LEVELS ARE ASSOCIATED WITH PNEUMONIA IN CHILDREN: A CASE-CONTROL STUDY

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Background: Pneumonia kills an estimated 1.2 million of children under age five every year. The role of vitamin D in respiratory infections including pneumonia is unclear; therefore, we aimed to determine if low serum 25-hydroxyvitamin D3 is associated with an increased risk of pneumonia in children.

Methods: We performed a case–control study of children ages 3–60 months from the Guatemala City metropolitan area hospitalized with community–acquired pneumonia between September and December 2012. Controls were selected from the well–baby/care immunization clinic serving the population from which cases emerged. We analyzed serum 25-hydroxyvitamin D3 levels and conducted parental interviews to assess subject age, height, weight, sex, race, feeding type, vitamin D supplementation, frequency of sun exposure, and maternal education. Complete information was available for 70 (83%) of 84 eligible cases and 68 (60%) of 113 eligible controls.

Results: The median (IQR) serum 25-hydroxyvitamin D3 concentration for cases was 23.2 ng/mL (14.4–29.9) compared to 27.5 ng/mL (21.4–32.3) in controls ($P = 0.006$). On multiple regression analysis using an a priori cut–point for vitamin D of <20ng/mL, children with pneumonia were more likely to have low 25-hydroxyvitamin D3 levels than controls (adjusted odds ratio [aOR] 2.4, 95% confidence interval [CI] 1.1–5.2, $P = 0.02$).

Conclusions: Low 25-hydroxyvitamin D3 levels are associated with an increased risk of pneumonia in children. However, it’s possible that the marker 25-hydroxyvitamin D3 is simply a marker for nutritional insufficiency.

10. Investigation and Diagnostic Tests

#22 - ADENOSINE 5’-MONOPHOSPHATE CHALLENGE AS A TOOL FOR ASTHMA DIAGNOSIS AND TREATMENT IN PRESCHOOL CHILDREN

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Background: Challenge test with auscultation to breathing sounds is one of the tools for diagnosis of asthma in young children.

Purpose: To test the hypothesis that adenosine challenge test in young children - can assist the physician to diagnose and treat early childhood asthma.

Methods: The study is a retrospective cohort study and included 159 children (26–131 months, mean 54.5 months) with recurrent respiratory complaints, which undertook the challenge test in the Lung Institute, Hadassah Ein - Karem Jerusalem, between the years 2004–2010.
Srikanta JT. (Department of Paediatrics, National University Hospital - Singapore, Singapore)

Results: 73 tests were negative, 86 tests were positive, of which 51.2% had severe score, 17.4% moderate and 31.4% had mild score on the challenge test. Predictability of adenosine challenge test for asthma 3 years after the challenge ranged between 73.3% and 88.9% according to the different ages at the time of the challenge. Significant correlation was found between the severity score of the challenge and a positive diagnosis of asthma 3 years after the challenge ($P < 0.018$) and a positive diagnosis of asthma at school age ($P = 0.018$). Significant correlation was found between the severity score of the challenge and emergency visit to the emergency departments and hospitalizations after the challenge ($P = 0.05$). Positive challenge test reduced the number of visits to emergency departments and hospitalizations in the period of three years after challenge ($P = 0.016$). Positive challenge test influenced toward escalating the asthma treatment ($P = 0.03$) in general and the preventive asthma treatment as lone ($P = 0.01$). Negative challenge test influenced toward reduction in preventive treatment ($P = 0.023$). It was shown that there is a significant correlation ($P = 0.022$) between the levels of IgE antibodies and the diagnosis of asthma three years after challenge.

Conclusions: Adenosine challenge test is an effective tool for the physician to care for young children who are suspected for the diagnosis of asthma. Challenge test results help the physician to adjust the medication and as a direct result - positively affect the prognosis of these patients. Adenosine challenge test in pre-school children can predict in a good manner which children will suffer from asthma at school age.

#43 - EVALUATION OF PNEUMOCOCCAL TITERS AND RESPONSE TO 23-VALENT PNEUMOCOCCAL POLYSACCHARIDE VACCINE IN CHILDREN WITH COUGH

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PURPOSE: To examine the prevalence and clinical significance of low pneumococcal titers, pre and post 23-valent pneumococcal polysaccharide vaccine (PPSV-23), in pediatric patients ≥2 years presenting with cough.

METHODS: We reviewed 826 charts of children ≥2 years presenting to Ochsner Pediatric Pulmonology Clinic from 2006 to 2012 with a diagnosis of cough. We determined the prevalence of low pneumococcal titers pre and 4–6 weeks post PPSV-23. Low pneumococcal titers were defined as ≤1.2 mcg/mL in ≥50% of the 14 serotypes tested. Adequate response was defined as doubling of the pre-immunization titer or titer ≥1.2 mcg/mL in at least 50%. Clinical significance was evaluated by examining whether patients with adequate titers post PPSV-23 had clinical improvement in cough, and by determining whether various clinical characteristics were associated with low pneumococcal titers either pre or post PPSV-23. These characteristics included wet cough, duration of cough, abnormal chest X-rays & CT’s, abnormal BAL, history of asthma, tobacco smoke exposure, prior antibiotics for cough, IV antibiotics for infection, and previous diagnoses of pneumonia, otitis media, and sinusitis. STATA was used for statistical analysis. Fisher’s exact test was used to determine statistical significance.

RESULTS: Pneumococcal titers were measured in 276 patients. Abnormal titers were found in 73.2%. Adequate response to PPSV-23 occurred in 77.5%. Inadequate response occurred in 6.3% and 16.2% did not have repeat titers measured. Clinical improvement in cough was documented in 53.5% of patients with adequate response to PPSV-23. There were no statistically significant associations between any of the clinical characteristics and low initial pneumococcal titers, except for environmental tobacco smoke (ETS) exposure. Low titers were found in 80% of these patients. None of the clinical characteristics evaluated demonstrated a significant association with poor response to PPSV-23.

CONCLUSION: Our pediatric patients with cough often had low pneumococcal titers, with good response to PPSV-23. Response to PPSV-23 correlated with clinical improvement in cough in >50% of these patients, suggesting that PPSV-23 may be beneficial in treating pediatric cough regardless of infection history. ETS exposure was associated with low initial titers. ETS exposure has been shown to have a variety of effects on the immune system including alterations in antigen presentation. Our finding suggests poor pneumococcal antibody production may contribute to cough in children with ETS exposure. These children in particular may benefit from evaluation of pneumococcal titers and immunization with PPSV-23. Further studies investigating the role of ETS exposure on immune system function are needed. Larger, prospective studies would also be helpful in predicting which children with cough are likely to benefit from PPSV-23, and which children may have specific antibody deficiency with cough as a presenting symptom.

#62 - PULMONARY FUNCTION TEST PARAMETERS FOLLOWING BONE MARROW TRANSPLANT IN PEDIATRIC PATIENTS

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INTRODUCTION: Children undergoing bone marrow transplants are well known to have pulmonary complications. These account for a sizeable proportion of post-transplant morbidity and mortality. The majority of data available on post-transplant pulmonary function come from adult studies, although several small pediatric case series have been described. This study was undertaken to evaluate long-term pulmonary function changes in patients who underwent bone marrow transplantation in our pediatric unit.

METHODS: This was a retrospective review of serial pulmonary function tests (PFTs) results in child and adolescent patients who underwent bone marrow transplantation (BMT) for hematopoietic disorders at National University Hospital Singapore over a thirteen year period (2001-2013). PFT values before and after BMT were analysed, including forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and total lung capacity (TLC). Mean PFT values were plotted against time and statistical analysis was performed using IBM SPSS Statistics v20 (IBM Corp, NY).

RESULTS: Sixty-seven patients had 174 PFTs performed during the study period. Age range at the time of bone marrow transplant was 2 years 5 months to 20 years 8 months (median age 12 years 6 months). There was a considerable decline three months post-BMT in mean FEV1 (15% fall), mean FVC (19% fall), and mean TLC (21% fall) compared to pre-BMT baseline values. Pulmonary function test values remained low at six months post-BMT (compared to pre-BMT baseline, FEV1 fell by 13%, FVC by 14% and TLC by 4%). The mean FEV1, FVC, and TLC values improved by 8%, 12%, and 17% respectively during six months and two years post-BMT but remained below pre-transplant levels. Twenty children had follow-up

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PFTs done at five years. There was little change in mean FEV1/FVC ratio in the first five years post-BMT (92% predicted at baseline compared to 93% predicted at five years post-BMT). However, there was an overall decline in PFT values at five years post-BMT compared to values at two years (which were already below pre-transplant levels) with regards to FEV1, FVC and TLC values. This was suggestive of a restrictive pattern in lung function several years after BMT, with a decline in FVC (11% fall from two years to five years post-BMT), FEV1 (12% fall) and TLC (3% fall). CONCLUSION: Our results suggest that, in children undergoing bone marrow transplant, a fall in pulmonary function test values occur three to six months post-transplant, with a partial recovery at one to two years. However, pulmonary function test values were overall reduced at five years compared to values at two years. Our findings emphasise the need for longitudinal respiratory monitoring and follow-up to detect any deterioration in lung function in the years following bone marrow transplant.

#68 - QUANTITATIVE EVALUATION OF THE VENTILATORY RESPONSE TO CO2 IN PRETERM INFANTS.

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Background: The incidence of apnea in preterm infants is higher than in term infants because of the immature respiratory center. However, there are few reports evaluating the respiratory center in preterm infants. We have evaluated the respiratory center quantitatively by measuring the Ventilatory Response to CO2 (VR CO2) and reported the normal values in term infants and the VR CO2 in several diseases including Congenital Central Hypoventilation Syndrome. The VR CO2 is a value obtained from the relationship between apnea, progression of respiratory distress, nose bleeding and agitation were defined as outcome variables of pressure support failure.

Method: We performed a retrospective study of preterm infants whose VR CO2 was measured before 37 weeks corrected gestational age (CGA) between January 2010 and November 2013. The VR CO2 was measured using a pulmonary function measuring system made by Aivision Co. (Tokyo, Japan) and Read’s rebreathing technique in which a mixture of 95% O2 and 5% CO2 was inhaled in a closed circuit. We compared the VR CO2 in preterm infants with term infants and 29 weeks to 33 weeks CGA (29W-33W CGA) with 34 weeks to 36 weeks CGA (34W-36W CGA). Correlation between the VR CO2 and CGA, and changes in VR CO2 with theophylline administration was also considered. The t test and Wilcoxon signed rank test were used for statistical analysis.

Result: This study included 33 preterm infants, 13 male, 20 female, with a mean gestational age of 31.1 ± 3.0 weeks and birth body weight of 1470 ± 524 grams. The mean age of measurement was day 14 and CGA was 33.1 ± 2.1 weeks. 23 cases were measured at 29W-33W CGA and 10 cases at 34W-36W CGA. The mean VR CO2 of the 33 preterm infants was significantly lower than that of the term infants measured in our institution (23.95 ± 10.0 ml/min/kg/mmHg, 40.4 ± 14.8, respectively: P = 0.001). The VR CO2 of 29W-33W CGA was not significantly different from that of 34W-36W CGA (24.1 ± 2.1, 23.6 ± 3.3, respectively: P = 0.902) and there was no correlation between the VR CO2 of preterm infants and CGA (R = 0.197). Nine preterm infants were examined before and after administration of theophylline. The VR CO2 improved significantly after administration (17.6 ± 8.3, 27.7 ± 11.1, respectively: P = 0.026).

Conclusion: The VR CO2 is useful in evaluating the respiratory center in preterm infants. It is shown quantitatively that the respiratory center of preterm infants is physiologically premature than that of term infants which may play a role in the high incidence of apnea in preterm infants. The VR CO2 of preterm infants does not increase until 36 weeks CGA, on the other hand the administration of theophylline increases the VR CO2. Therefore regular administration of theophylline is effective in preterm infants with apnea. In the future, the VR CO2 in preterm infants after 37 weeks CGA should be evaluated in order to investigate how the respiratory center matures.

11. Therapeutic Procedures

#15 - COMPARISON OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) AND CPAP WITH INTERMITTENT PRESSURE IN PRETERM NEWBORNS

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Objective: To describe differences in clinical indicators and in the failure of two noninvasive pressure systems in preterm newborns.

Methods: Cross-sectional, prospective, analytical and observational cohort study. The study included 80 infants, who received noninvasive ventilation. The infants were randomly divided into two groups: 40 infants used nasal continuous positive airway pressure (cpap) and 40 used cpap with intermittent positive pressure. The infants were observed over the first 48 hours. Respiratory rate, heart rate, and oxygen saturation were recorded. Apnea, progression of respiratory distress, nose bleeding and agitation were defined as outcome variables of pressure support failure.

Results: The infants were classified as very low weight (1.337 ± 0.242 g and 30.3 ± 2.4 weeks), 55% were males. no significant difference in birth characteristics was observed between groups. Pressure support failure was observed in 55% children receiving cpap and in 30% receiving cpap with intermittent pressure, indicating an association between noninvasive ventilation failure and cpap without intermittent pressure (p=0.01, odds ratio 2.2). apnea was the main consequence of cpap failure. The clinical variables did not differ significantly between treatment modalities.

Conclusion: No difference in clinical indicators was observed between the two noninvasive positive pressure modalities. However, a higher frequency of pressure support failure was significantly associated with the use of cpap without intermittent pressure.

12. Cellular and Molecular Biology

#1 - B-TYPE NATRIURETIC PEPTIDE INHIBITS ANGIOTENSIN II-INDUCED Proliferation AND Migration OF PULMONARY ArTERIAL SMOOTH MUSCLE CELLS

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Pediatric Pulmonology
BACKGROUND: Pulmonary vascular remodelling, characterized by disordered proliferation and migration of pulmonary arterial smooth muscle cells (PASMCs), is a pathognomonic feature of pulmonary arterial hypertension (PAH). Pharmacologic strategy targeting on anti-proliferation and anti-migration of PASMCs may have therapeutic role for PAH, but is still lacking. The aims of the present study were to investigate the effects and underlying mechanisms of B-type natriuretic peptide (BNP) on angiotensin II (Ang II)-induced proliferation and migration of PASMCs.

METHODS: Vascular smooth muscle cells isolated from rat pulmonary artery were cultured and used at passages 3–5. Proliferation and migration of PASMC were induced by Ang II and evaluated by MTT test and Boyden chamber assay, respectively. PASMCs were incubated with Ang II, with or without BNP pretreatment to determine its effects on proliferation and migration. In addition, potential underlying mechanisms including Ca2+ influx, oxidative stress, MAPK and Akt signaling and the cGMP/PKG pathway were also examined.

RESULTS: BNP inhibited Ang II-induced PASMC proliferation and migration dose dependently. In addition, BNP attenuated intracellular calcium overload caused by Ang II. Moreover, Ang II-induced ROS production was mitigated by BNP, with associated down-regulation of NADPH oxidase 1 (NOX1) and reduced mitochondrial ROS production. Finally, downstream signal transduction including ERK1/2 and Akt activated by Ang II were also counteracted by BNP. Of note, these effects of BNP were all inhibited by Rp-8-Br-PET cGMPS, a PKG inhibitor.

CONCLUSIONS: BNP inhibits Ang II-induced PASMC proliferation and migration. These effects are potentially mediated by decreased calcium influx and reduced ROS production by NOX1 and mitochondria, through the cGMP/PKG pathway. Therefore, BNP may have a valuable role in the prevention of pulmonary vascular remodelling.

#2 - EFFECTS OF PNEUMONIA AND MALNUTRITION ON THE FREQUENCY OF MICRONUCLEI IN PEDIATRIC PATIENTS

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The aim of this study was to evaluate the effects of bacterial pneumonia and malnutrition on the frequency of micronuclei (MN) in peripheral blood of pediatric patients through flow cytometric analysis. Patients and Methods: The study was an analytical case-control study involving 100 pediatric patients through flow cytometric analysis. The patients were divided into two groups: Group 1 included 50 children with pneumonia and severe malnutrition, while Group 2 included 50 age-matched healthy children. Results: The frequency of micronucleated reticulocytes (MN-RETs) and MN-RBCs was higher in children with severe pneumonia and malnutrition compared to healthy children. Conclusion: The results of this study showed an increased frequency of micronuclei in children with pneumonia and malnutrition, which may be due to the effects of bacterial infection and poor nutrition on the integrity of the cell cycle and DNA repair mechanisms.

#6 - DECREASED AMBIENT OXYGEN TENSION ALTERS THE EXPRESSION OF ENDOTHELIN-1 IN ALVEOLAR MACROPHAGE

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Abstract: Endothelin-1 (ET-1) is a potent vasoconstrictive peptide that plays a crucial role in the pathogenesis of pulmonary hypertension, particularly in children. Decreased ambient oxygen tension (O2) is a common feature in children with respiratory distress syndrome (RDS) and may alter the expression of ET-1 in alveolar macrophages. The aim of this study was to investigate the effects of decreased ambient O2 on ET-1 expression in alveolar macrophages.

Materials and Methods: Rat alveolar macrophages were cultured at different O2 levels (10%, 5%, and 1%). The expression of ET-1 was measured using RT-qPCR and Western blot. The results showed a significant increase in ET-1 expression in low O2 conditions compared to normoxic conditions.

Conclusion: Decreased ambient O2 tension alters the expression of ET-1 in alveolar macrophages, which may have implications for the development of pulmonary hypertension in children with RDS. Further studies are needed to elucidate the underlying mechanisms and potential therapeutic targets.
the induction of hBD2 and IL-8 gene expression in A549 cell by S. pneumoniae. SIRT1 may play a key role in host immune and defense response in A549.

#168 - THE EFFECT OF IMMUNOTHERAPY, PROBIOTICS AND NIGELLA SATIVA IN THE NUMBER OF CD4+ IL-4+ CELL, TOTAL IGE LEVEL AND ASTHMA CONTROL TEST (ACT) SCORE

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Asthma is a chronic inflammatory disorder of the airways dominated by Th2. Immunotherapy has benefits for asthmatic patients. Its long duration of treatment is often caused drop out of treatment. Probiotics and Nigella sativa as immunomodulator for asthma expectancy could increase the efficacy of immunotherapy. The aims of this study was to evaluate the therapeutic efficacy of immunotherapy combined with probiotics and Nigella sativa in the number of CD4+ IL-4+ cells, Total IgE level and Asthma Scoring Test. A total of 31 children with mild asthma were evaluated and then randomized to receive immunotherapy or immunotherapy plus Nigella sativa or immunotherapy plus probiotic or immunotherapy plus Nigella sativa plus probiotic openly for 14 weeks. We used subcutaneous HDM immunotherapy (build up phase), 2 × 10^9 mixed live bacteria Lactobacillus acidophilus and Bifidobacterium lactis and 15 mg/kg BW/day Nigella sativa. Number of CD4+ IL-4+ cells was evaluated using flowcytometry of PBMC isolated from peripheral blood and analyzed using BD Cell quest Pro software. Total IgE level was measured using Enzyme Chemiluminescence Immunoassay by Roche Elecsys 2010. The children were accompanied by their parents while they answer ACT questions.

There was no significant difference in the pre and post test mean number of CD4+ IL-4+ cells in all three treatment group. The Total IgE level was decreased significantly in the immunotherapy+ probiotic+ Nigella sativa group (p 0.022). The ACT score were increased in the immunotherapy+ Nigella sativa group (p 0.001), in the immunotherapy + probiotics group (p 0.004), and immunotherapy+ Nigella sativa+ probiotics group (p 0.000). Correlation test found a significant association between the number of CD4+ IL-4+ cells, Total IgE level and ACT score in all groups. The combination of immunotherapy, Nigella sativa and probiotics could decrease the Total IgE level thus improve the clinical symptoms.

13. Pediatric Pulmonology in Developing Countries

#16 - ROLE OF ZINC IN SEVERE PNEUMONIA: A RANDOMIZED DOUBLE BIND PLACEBO CONTROLLED STUDY

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Background: Pneumonia is a leading cause of morbidity and mortality in children. Objective: The aim of study was to evaluate the efficacy of Zinc supplementation in treatment of severe pneumonia in hospitalized children. Design/Methods: A double blind randomized, placebo- controlled clinical trial conducted at a tertiary care centre of a teaching hospital. Children with diagnosis of severe pneumonia were randomly assigned to receive supplementation with either elemental zinc or placebo by mouth at the time of enrollment. From day 2, they received 10 mg of their assigned treatment by mouth twice a day for 7 days along with standard antimicrobial therapy. Results: The baseline characteristics like age, sex, weight, weight Z score, height, height Z score, weight for height Z score and hemoglobin were comparable in both study groups. The respiratory rate, chest indrawing, cyanosis, stridor, nasal flaring, wheeze and fever in both groups recorded at enrollment and parameters did not differ significantly between the two groups. The outcome measures like time taken for resolution of severe pneumonia, pneumonia duration of hospital stay, nil per oral, intravenous fluid, oxygen use, treatment requiring 2nd line of drug and 3rd line drug were evaluated and found to be same. Conclusion: The present study did not show a statistically significant reduction in duration of severe pneumonia, or reduction in hospital stay for children given daily zinc supplementation along with standard antimicrobial therapy. Therefore, zinc supplementation given during the acute episode does not help in short term clinical recovery from severe pneumonia.

Keywords: Pneumonia, Children, Zinc

#20 - ROLE OF METHYLPR EDNISOLONE TREATMENT IN SEVERE MYCOPLASMA PNEUMONIAE PNEUMONIA IN CHILDREN

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Objective: To investigate the therapeutic effects of methylprednisolone on severe MPP. Methods: Sixty-two children with severe MPP were enrolled to receive azithromycin combined with methylprednisolone (treatment group, n = 26) or receive azithromycin alone (control group, n = 36). Clinical symptom changes (defervescence time), hospitalization time, C-reactive protein (CRP) levels, and pulmonary radiographic images were assessed at the end of the study. Results: Patients in the treatment group experienced defervescence from 4 to 16 h after enrollment, whereas no defervescence was observed among patients in the control group. Atelectasis rate was 2/26 in the treatment group and 11/36 in the control group (P < 0.05). The mean defervescence time was 8.8 ± 3.8 h in the treatment group and 32.9 ± 16.2 h in the control group (P < 0.01). The mean hospitalization time was 7.5 ± 1.4 d in the treatment group and 11.3 ± 3.5 d in the control group (P < 0.01). Within three months of follow-up, 23/26 patients in the treatment group showed complete pulmonary infiltration absorption, and 23/36 patients in the control group showed the same result (P < 0.05). No significant difference in the mean fever duration prior to admission and the CRP mean value (P > 0.05) between the treatment group and the control group was observed. Conclusions: Early methylprednisolone therapy with adequate macrolide content is helpful in the treatment and quick recovery of children with severe MPP.

Keywords: Children; Mycoplasma pneumoniae; methylprednisolone; Pneumonia; pulse; severe

#103 - FACTORS INFLUENCING OUTCOME OF VENTILATED NEONATES IN INTENSIVE CARE UNIT IN A DEVELOPING COUNTRY

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Pediatric Pulmonology
Abstract

Background: Large number of neonates in NICU require mechanical ventilation with a high fatality.

Objective: To find out the factors influencing outcome of ventilated neonates in ICU.

Materials and methods: This study was conducted from March 2006 to December 2009 in the ICU of Dhaka Shishu (Children) Hospital, Bangladesh. Neonates consecutively put on mechanical ventilator during the study period were enrolled. For each ventilated neonate, information included age, sex, admission weight, gestational age and primary diagnosis. Observations at the time of initiation of ventilation included PIP, PEEP, FiO2, SaO2 and ABG analysis. Complications encountered during ventilation and duration of ventilation was noted. Relevant investigations were done. Finally, outcome was recorded. For data entry and analysis SPSS version 17 was used.

Results: Total 225 neonates were put on mechanical ventilator. Out of them 96(42.67%) survived. Mean weight and gestational age was significantly low among non-survivors (P < 0.05). Perinatal asphyxia (37.3%), preterm LBW with refractory apnoea or respiratory failure (29.4%) and neonatal sepsis (15.7%) contributed majorly. There was significant finding between mortal and pneumonia cases (P < 0.05). Weight <1500 gm and gestation <32weeks, mean initial arterial pH and HC03, initial PH <7.1, high PC02, BE and high initial FiO2 to maintain oxygen saturation, hyponatraemia, hypokalaeemia, complication during ventilation were associated with mortality (P < 0.05). Significant association was found between complication related to ventilation and outcome (P < 0.05). Ventilator associated Pneumonia (VAP) and Sepsis showed high mortality.

Conclusions: Early identification of need for respiratory support and initiation of ventilation before metabolic derangement should be necessary. Proper ET tube care and control of infection should be ensured. Fluid and electrolyte balance should be look after meticulously.

#115 - THE ROLE OF THE HIGH-RESOLUTION LUNG CT IN THE DIAGNOSIS AND CLASSIFICATION OF CHILDREN BRONCHIOLITIS OBLITERANS.

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Objective: To explore the role of the high-resolution lung CT in the diagnosis and classification of children bronchiolitis obliterans.

Methods: We retrospectively summarize the HRCT sign of 147 cases of children bronchiolitis obliterans, diagnosed in Beijing Children’s Hospital during April 2001 to April 2012. Compared with the HRCT sign of children asthma diagnosed in the same period and try to find the differences. We divide the 147 cases into 2 different groups according to their clinical severity and try to find the differences between CT findings. BO children were followed up.

Results: In BO patients, there are 147cases of Mosaic perfusion sign, 86 cases of bronchial wall thickening, 80 cases of bronchiectasis, 44 cases of mucus plug and 32 cases of atelectasis. The control group, only show 2 cases of Mosaic perfusion sign. The difference is statistically significant. The severe BO children show more bronchiectasis in HRCT than mild children. The signs of HRCT of 49 cases of BO who were followed up persist.

Conclusion: Mosaic perfusion sign, bronchial wall thickening and bronchiectasis are the most common sign in HRCT of children bronchiolitis obliterans. The severe patients show more bronchiectasis in HRCT. The signs of HRCT of BO persist.

Keywords: bronchiolitis obliterans diagnosis HRCT
METHODOLOGY: Observational Analytic Study of type Cross Sectional.

INTRODUCTION: Congenital and acquired lesions of the pediatric airway frequently pose perplexing problems in children, infants and newborns. Prompt investigation into the etiology and early intervention are essential to decrease the morbidity and to prevent some tragic events. Bronchoscopy grants access to the lesion sites for either diagnostic or therapeutic purposes.

MATERIAL AND METHODS: From January 2009 to December 2013, totally 224 endoscopic procedures, including 98 flexible and 126 rigid endoscopic procedures were performed in 236 pediatric patients at pediatric department of Hassan II hospital in morocco.

RESULTS: The median age of our patients was 52 months (range 5 month–15 years). They were 61% males. Interventional bronchoscopy was indicated for foreign body inhalation in (54.7%), stridor (21.6%), dyspnoea (14%). Bronchoscopy for diagnostic was performed for recurrent/persistent pneumonia(32%), wheezing that does not respond to appropriate therapy (16, 5%), and persistent atelectasis (14.2%). The X ray showed lung hyperinflation in 28% of patients, segmental or lobar pneumonia in 23% of cases, atelectasia in 15%, emphysema in 5%.

Interventional bronchoscopy was performed in 122 patients, foreign body was organic in 98 cases (peanut in 46.8% patients, almond in 16.1%, sunflower in 13.6% seeds, maize seed in 7.3%, olives in 5.8%) and inorganic in 12 cases (pins 45.4%, pieces of plastic 32.6%, metallic screw 17.3%). For 6 patients rigid bronchoscopy was necessary to resect obstructive granuloma due to tuberculosis or sequelae of a foreign body. Diagnostic bronchoscopy was indicated for 114 patients. The commonest finding were foreign body in 24%, tuberculosis in 12.4%, airways malacia in 11.1%, External compression of trachea / bronchi in 9.6%, structural deformity in 8.9%, hydatid cyst membrane in 2.6%.

There was not post operative major complication. Only reasonable bleeding in 10 patients, bronchospasm in 5 cases, transient hypoxemia in 4 childrens, and post bronchoscopy fever in 3 patients. These complications were managed accordingly and all patients recovered without any serious consequences.

CONCLUSION: The development that bronchoscopy has experienced in the recent years has been spectacular, especially in the field of pediatrics. Both the diagnostic and the therapeutic applications of bronchoscopy have increased considerably.

OBJECTIVE To determine whether there are factors associated to the inappropriate management of acute bronchiolitis in Colombia

METHODOLOGY: Observational Analytic Study of type Cross Sectional. 267 physicians were surveyed during the second half of 2013. Logistic regression models were fitted to identify whether there were factors associated to the possibility to assign an inadequate treatment during the infant’s stay in the emergency room and hospitalization.

RESULTS A total of 267 surveys were conducted to physicians in 8 different cities of Colombia. In relation to the type of hospital, 164 (61.4%) of respondents were practicing their care activities in university hospitals, and 57 (21.3%) in non-university hospitals. With respect to the academic level of the physicians surveyed, it was noted that 75 (28.1%) were pediatric fellows, 69 (25.8%) pediatricians, 48 (18%) general physicians, 32 (12%) medical interns and 18 (6.7%) pulmonologists or neonatologists. Based on survey responses, 80 (30%) physicians would assign an inappropriate handling to infants with bronchiolitis in the emergency department and 66 (24.7%) during hospitalization. Of caregivers surveyed, 232 (86.9%) confirmed their institutions had acute bronchiolitis management guidelines and 31 (11.6%) did not have them. In the case they had them, 41 (15.4%) said no to apply them. Bivariate analysis confirmed that for both scenarios to work in an university hospital (P = 0.00), became a significative factor associated with a better chance of receiving appropriate management. Additionally, academic level was significant factor associated with a better chance of receiving appropriate treatment in the hospitalization scenario. Multivariate analysis concluded that for the case of hospitalization, to work in an university hospital was associated, with the ability to receive appropriate management (OR 0.40 95% CI: 0.17–0.92, P = 0.031). Besides, decision making in the Pacific Coast Region (OR 4.68 95% CI: 1.11–19.77, P = 0.03) and Coffee Region (OR 4.95 95% CI: 1.10–16.48, P = 0.03) in Colombia was also associated with the possibility of prescribing an inappropriate treatment at the same stage.

CONCLUSION: The study showed that in Colombia 30% of physicians surveyed may assign improper treatment for acute bronchiolitis in emergency room and 25% of them in hospitalization. The existence of guidelines does not guarantee the application of them as 29% of the physicians decided not to apply them. To work in an university hospital reduced by 60% the chance of being assigned to improper treatment during hospitalization. It is necessary to develop continuing medical education activities with emphasis on Hospitals that have no physicians on training and in the Regions of Colombia that were mentioned. It must be ensured greater adherence to management guidelines of the institutions.

ETIOLOGY AND OUTCOME OF LOWER RESPIRATORY TRACT INFECTION IN CHILDREN

Background: Lower respiratory tract infection (LRTI) remains the leading cause of mortality in children worldwide. Mixed viral-bacterial infections are common. The respiratory viruses pave the way for airway colonization bacteria. There was severe acute respiratory infection (SARI) surveillance in Indonesia including Hasan Sadikin General Hospital. Aim of the study to investigate the respiratory pathogens and outcome of the disease.

Methods: Since 2007–2009 NIHRD, Ministry of Health Indonesia developed SARI surveillance. The study enrolled 352 children hospitalized with LRTI (pneumonia and bronchiolitis). Blood culture for bacteria and PCR Luminex of nasopharyngeal swab for viral detection were assayed in 160 subjects. Outcome of LRTI was observed until discharge.

Results: Of the 160 subjects, bacterial cultures positive in 61 blood specimens. The most common bacteria was coagulase negative staphylococci (CONS) 35 (57%), Serratia marcescens in 10 (16%), Pseudomonas aeruginosa 7 (11%), Staphylococcus aureus 2 (3%), others 8 (13%). Viral infections were identified in 44 subjects. The most common viruses are Influenza A 18 (41%) and Coxsackie virus 18 (41%), Rhinovirus 3 (7%), Parainfluenza virus 3 (7%), Respiratory syncytial virus (RSV) in 1 (2.3%). Bacillus and Influenza B 1 (2%). Mixed viral-bacterial infections were detected in 21 subjects. The outcome of LRTI was 6 (4%) death, four subjects positive
CONS, and 2 subjects with mixed-infection by CONS and viruses (Coxackie and Rhinovirus).

Conclusion: The proportion of mixed viral-bacterial infection in LRTI in children is high. The most common cause of mortality are CONS and mixed viral-CONS.

Keywords: Etiology-LRTI-Outcome

#42 - BLOODY PLEURAL EFFUSION AT A GIRL OF 10 YEARS OLD

Author:

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Bloody pleural effusions are very rare in children, excluding trauma. This could lead to false diagnosis and to delay the treatment. A girl of 10 years old is admitted to our clinic, as an emergency, for fever, cough, abdominal and chest pain, anorexia, malaise. Onset of the disease is 9 months before, when she got abdominal pain, poor appetite, was treated for parasitosis and got analgesics seemingly with good evolution. After 1 month she was readmitted for cough and abdominal pain. Clinical examination, lab tests, abdominal ultrasound, chest radiograph showed bilateral pleural effusions. Thoracocentesis evacuate small amount of bloody pleural exsudate in which no microorganism was isolated. After 3 weeks of antibiotics she was better and she was discharged. Two weeks after, she came back with the same symptomatology. She had bilateral pleural effusions and at repeated thoracocentesis bloody pleural liquid was identified. Diagnosis of tuberculosis was done, even QuantiFERON-TB, ADA in positive autoimmunity tests, serum amylase and BAL amylase were high. She had anti-TB drugs for 4 months. During this time she continued to suffer of cough, abdominal and chest pain and repeated hemoptysis. In our clinic after clinical exam, she had chest radiography and bronchoscopy with bronchoalveolar lavage (BAL). No microorganism was found but measuring Gold Score for hemosiderin laden macrophage was found 94. Blood tests showed the presence of inflammatory markers, no positive autoimmunity tests, serum amylase and BAL amylase were high. Abdominal ultrasound, chest and abdominal MRI – established the diagnosis: mediastinal pancreatic fistula, bilateral bloody pleural effusion, chronic pancreatitis. She had caudal pancreactectomy, fistulotomy, spleen was preserved. Post surgery evolution was good. The histopathology result confirms chronic pancreatitis and pseudo pancreatic cyst. We emphasize the difficulty of the diagnosis explained by the rarity of pleural and pulmonary complications of pancreatitis at pediatric age and by the developing of a fistula and not a typical pancreatic pseudo cyst image. Causes of bloody pleural effusion and of pancreatic diseases in children are discussed.

#45 - A CASE OF SEVERE COMBINED IMMUNODEFICIENCY (SCID)

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Severe combined immunodeficiency (SCID) includes a group of rare life-threatening disorders. At least 15 different single gene defects result in profound deficiency in T- and B-lymphocyte function. The estimated annual incidence of SCID is approximately one case per 50,000 live births. SCID usually is diagnosed when an infant has repeated or chronic unusual infections or complications following live vaccines (BCG or viral vaccines). We report a seven month old girl who presented with left axillary lymphadenitis, difficult wound healing after BCG vaccination and pneumonia. SCID was diagnosed – T-, B-. All attempts to clarify the etiology of the pneumonia (blood cultures, sputum, gastric aspirate, PCR for viruses) failed. She was treated with antibiotics, trimethoprim and sulfamethoxazole and anti-tuberculous chemotherapy (comprising Isoniazid, Rifampicin, Ethambutol), intravenous immune globulin. After partial improvement of the symptoms of pneumonia and BCG lymphadenitis the patient was sent for hematopoietic stem cell transplantation.

The case adds up to the well-known discussion about BCG vaccination - when and whether to do it.

#61 - CONGENITAL SYSTEMIC ARTERY-PULMONARY ARTERY SHUNT IN A MASSIVE HEMOPTYSIS CHILD: CASE REPORT

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Background: Congenital Pulmonary Arteriovenous Malformation (PAMV) is a communication between artery and vein in lung. According to the source of supply vessel PAMV can be divided into three types. Shunt between pulmonary artery and pulmonary vein (95%). Shunt between pulmonary artery and systemic artery with pulmonary artery to pulmonary vein shunt. Shunt between pulmonary artery and systemic artery without pulmonary artery to pulmonary vein shunt.

Case presentation: A 9-year-old girl presented with recurrent hemoptysis for 4 months. Her past history was normal. She tested negative for pneumonia, tuberculosis, idiopathic pulmonary hemosiderosis, auto-immune disease and hematological disease. The results of CXR showed atelectasis or infiltration. CT scans showed extensively diffuse infiltration in pulmonary parenchyma but was normal 9 days later. Based on Digital Subtraction Angiography (DSA), which showed the right and left bronchial arteries were aberrant with bronchial artery to pulmonary artery shunt in right middle and low lobe, she was diagnosis as pulmonary artery-systemic artery shunt without pulmonary artery to pulmonary vein shunt. She was treated by Transcatheter Embolotheraphy (TCE). During 6-year of follow-up the patient remained well without recurrence.

Conclusions: Congenital pulmonary artery-systemic artery shunt can be the rare cause for massive hemoptysis in children. It had no specific sign of CXR and CT scans. It was confirmed by DSA. TCE can be used as treatment. Follow-up should be recommended with its unclear natural history and the long-term effects of TCE.
#165 - HEMOPTYSIS IN PEDIATRIC PRACTICE - THREE DIFFERENT CASES

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Hemoptysis can range from blood-streaking of sputum to the presence of gross blood in the absence of any accompanying sputum. It’s a symptom in variety of diseases of upper or lower respiratory tract as well as some with vascular origin. The most common source of hemoptysis is the airways disease (inflammatory diseases, neoplasms, foreign body and airway trauma, fistula between a vessel and the tracheobronchial tree).

We present three different cases of children admitted in the clinic in which the only initial symptom is hemoptysis.

The first case is well developed 17 year old girl, without any significant premorbidity but with a very hazardous behavior and many risk factors (including drug, alcohol and tobacco abuse). At the admission the X-ray was suggestive for massive bilateral pneumonia in both lower lobes of the lung. At the careful examination, specific diagnostic tests and follow up Goodpasture Syndrome was diagnosed, and she received an appropriate treatment.

The second case is well developed 11 year old boy, without any significant premorbidity. On the X-ray oval shape behind the heart shadow was found. After CT scan, the patient was transferred for surgical removal of hydatid cyst. The third case is of a 9 year old boy with signs of mild mental and physical retardation, with repeated pneumonias in early childhood. On the X-ray and the CT scan – localized bronchiectasis were found and appropriate treatment was conducted.

These cases illustrate different entities with an onset with only one symptom – hemoptysis. Careful diagnosis and imaging examination helps for the correct treatment. While surgery remains the only truly definitive therapy for massive hemoptysis, it should not be used in the acute emergent setting unless it cannot be avoided.

#176 - A TODDLER CASE OF HYPER-IgE SYNDROME WITH A MUTATION OF THE STAT3 GENE

Author(s):

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Introduction: Hyper-IgE syndrome (HIES), so called Job’s syndrome, is a rare primary immunodeficiency (PID), which is characterized by recurrent respiratory tract infection and markedly elevated serum IgE levels. Signal transducer and activation of transcription 3 (STAT3) gene mutation is known as a major cause of HIES, and we report a toddler HIES case with STAT 3 mutation who suffered recurrent respiratory infection.

Case: 2 year-old boy had a history of frequent upper respiratory infection (> 6/year) and at least 3 times pneumonia history confirmed by chest x-rays. Chest X-ray in remote phase revealed persistence of the opacification. He also suffered oral and finger nail candidosis, skin infection caused by MRSA. Laboratory data showed an elevated eosinophil count (1320/μL) and extremely high total IgE level (371001U/mL). In addition, his right clavicle fractured with a minor injury. High arched palate was observed on his physical examination. Total National Institutes of Health (NIH) score for HIES was 44. Direct sequencing of the STAT3 gene showed heterozygous for a missense mutation in the DNA binding domain of the STAT3 protein (c.1144C>T, p. Arg382Trp). STAT3 deficiency is associated with excessive lung inflammation and is consistent with the development of pneumococles. His chest computed tomography revealed bronchial wall thickening without pneumococles. Thereafter he has been treated with sulfamethoxazole/trimethoprim (SMX/TMP) and fluconazole to prevent further respiratory tract infection and following respiratory complications.

Conclusion: PID/HIES should be suspected in a patient with the recurrent respiratory tract infection and other specific clinical features. Detection of the STAT3 gene mutation leads to the early diagnosis of PID/HIES, which is beneficial to prevent progression of the structural changes in the lungs.

15. Miscellaneous

#38 - DOES 3 WEEKS OF AZITHROMYCIN IMPROVE CLINICAL OUTCOMES OF INDIGENOUS CHILDREN HOSPITALISED WITH BRONCHIOLITIS: A PLACEBO-CONTROLLED RANDOMISED TRIAL

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Background: Hospitalised bronchiolitis imposes a significant health burden upon young children globally, particularly in Indigenous children. In settings where children have high rates of nasopharyngeal bacterial carriage and frequent prolonged illness, macrolides may be beneficial. We aimed to determine if 3 once-weekly doses of azithromycin (30 mg/kg) vs. placebo improve clinical outcomes (length of hospitalisation and duration of supplemental oxygen). Secondary aims include (i) effect of treatment on respiratory readmissions to hospital within 6 months; (ii) whether macrolide-resistant respiratory pathogens in nasopharyngeal swabs (NPS) influence clinical severity; (iii) the short term impact of azithromycin on macrolide resistance patterns of respiratory pathogens in the nasopharynx; and (iv) point prevalence and diversity of respiratory viruses.

Methods: Indigenous children aged ≤24 months were enrolled in a placebo-controlled randomised trial from two Northern Australian and one New Zealand hospital from 2010 to 2013. Primary endpoints were monitored 12 hourly until discharge. NPS were collected at baseline and 48 hours. Children were reviewed clinically on day-21 to determine presence of persistent respiratory symptoms and signs. Respiratory readmissions within 6 months post discharge were recollected. All investigators, care providers, and participants remain blinded to treatment groups until the final chart review.

Results: The mean age of 219 children randomised was 7 months (SD = 5). One family withdrew consent after enrolment and another refused NPS. summarises the results. The most common viruses found at baseline were respiratory syncytial virus (RSV) 91/215 (42%) and human rhinovirus (HRV) 79/215 (37%). Respiratory bacteria detected at baseline include Haemophilus influenzae 78/217 (36%), Moraxella catarrhalis 80/217 (37%) and Streptococcus pneumoniae 42/217 (19%). At day-21, a wet cough was present in 29/218 (13%), crackles in 22/218 (10%) and wet cough plus crackles in 40/218 (18%) children. 50/186 (27%) children have had a respiratory readmission within 6 months. Table-1: RCT summary

Conclusion: RSV and HRV were the most common viruses detected. Nasopharyngeal bacterial carriage was common in these children. Persistent symptoms 3 weeks post hospitalisation is high. We will report the primary and secondary outcomes by treatment group after breaking treatment codes in April 2014.

Support: NHMRC (grant 605809), NHMRC Centre for Research Excellence in Lung Health of Aboriginal and Torres Strait Islander Children (grant 1040830). GBM is supported by a NHMRC scholarship (grant 1055262).

Conflict of Interest: None

#65 - DYSREGULATION OF THE RESPIRATORY CONTROL AND AUTONOMIC NERVOUS SYSTEM IN CHILDREN. PARADIGMATIC CLINICAL REPORTS.

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In all children with evidence of hypoventilation, without a primary cardiopulmonary, metabolic, neuromuscular or brainstem dysfunction, a diagnosis of congenital central hypoventilation syndrome (CCHS) should be considered. We report 2 paradigmatic cases of central hypoventilation with different forms and timings of presentation.

Pediatric Pulmonology

CCHS is a rare disorder, presenting mostly in the neonatal period, characterized by the failure of automatic control of breathing. It is caused by mutations in the PHOX2B gene, which also plays a role in neural crest cell migration, hence the autonomic nervous system dysregulation (ANSD), particularly Hirshprung’s disease, identified in some patients in addition to the hypoventilation.

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) is a different and even less common syndrome, for which there is no genetic mutation identified.

We report the cases of 2 children with central hypoventilation treated in this center. One is a 5-year-old girl, who presented in the newborn period with episodes of cyanosis, apnea and, later, the diagnosis of Hirshprung’s disease, requiring mechanical ventilation and parenteral nutrition in the first days of life. A 29 polyalanine repeat expansion mutation (PARM) was later identified in the PHOX2B gene. This patient was never tracheostomized, and, in order to ensure adequate ventilation during sleep, is ventilated using bi-level positive airway pressure ventilation (BIPAP) via face mask. The other patient is a 10-year-old boy, with a history of normal development until the age of 3. He then stopped achieving psychomotor developmental milestones and consecutively developed hyperphagic obesity, hypersomnolence, disordered temperature, altered sweating, gastrointestinal dysmotility, strabismus, behavioral disorder, sodium and water dysregulation, central hypothryoidism, recurrent respiratory tract infections and alveolar hypoventilation, leading to the diagnosis of ROHHAD syndrome. The cerebral spinal fluid (CSF) neurotransmitter analysis showed reduced levels of serotonin metabolites, which was also reported in a ROHHAD case in Southeast Asia. Both the alveolar hypoventilation and the psychomotor disorder improved significantly with positive pressure ventilation (PPV) via tracheostomy.

#67 - TUBERCULOSIS EMPYEMA: A CASE REPORT

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Empyema due to tuberculosis usually occurs in older children and is rarely associated with miliary disease. It is a complication of pleural tuberculosis, which is responsible for 5% of the tuberculosis in children in endemic regions.

Objective: Describe a case of empyema due to tuberculosis in a 6 year old girl.

Methodology: The information needed for the study was obtained from hospital records.

Case report: IMMC, a 6 year old girl from Belem, Pará, Brazil was admitted after experiencing progressive dyspnea, fever and productive cough for 16 days and had a previous admission to another hospital. A chest X-ray exposed opacification of the right hemithorax and pneumothorax. She underwent a chest tube drainage procedure in which green, purulent fluid was drained.

Cytology of pleural effusion: Neutrophils 99%; Lymphocytes 1%; Glucose 10 mg/dl

Ph:6.98; TST: 00 mm; Gastric lavage: 3 negative samples; HIV serology test: dot-ELISA negative. Intravenous(IV) Piperacillin-Tazobactam was started and she exhibited no fever for 18 days. Later, complications evolved despite antibiotic therapy and she still had drainage of purulent fluid. Chest Computedized Tomography (CT) showed a large right pneumothorax with fluid and bronchopleural fistula. Thoracoscopy with decortication was performed and a double chest tube inserted. The antibiotic was changed to imipenem and vancomycin.

Another Chest CT was implemented and showed air fluid level and pulmonary collapsing. She underwent a flexible bronchoscopy on the 57th
day and the bronchoalveolar lavage (BAL) showed AFB. A standardized treatment regimen of 2 RHZ/4RH (R-Rifampicin; H-Isoniazid; Z-Pyrazinamide) for Tuberculosis was started and after 67 days she was discharged from the hospital.

Conclusion: Tuberculosis in children remains difficult to diagnose. In this case, the acute non-typical form of the disease delayed a proper diagnosis and treatment.

#70 - ADVERSE EFFECTS OF ANTI-TUBERCULOUS TREATMENT IN CHILDHOOD

Author:

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Tuberculosis is a disease requiring multi-drug treatment for a prolonged time. Simultaneous use of multiple drugs increases the risk for side effects. Seventy-five patients with a predigression of tuberculosis were followed between 2007 and 2012. Among these 61 were diagnosed with tuberculosis infection and 14 with tuberculosis disease. Six of the patients in the tuberculosis disease group were diagnosed with pulmonary tuberculosis, two with urinary and two with tuberculosis lymphadenitis. The remainders were diagnosed with tuberculosis arthritis, pericarditis, endobronchial and military tuberculosis.

Patients diagnosed with tuberculosis infection received isoniazid for 6 months (5–10 mg/kg/day). Except for a patient with elevated liver function tests, no adverse events were documented.

Patients diagnosed with tuberculosis disease were initially started on a 3 or 4-drug regimen for two months (isoniazid 10–15 mg/kg/day, rifampin 10–15 mg/kg/day, pyrazinamide 30–40 mg/kg/day, ethambutol 15–25 mg/kg/day) followed by a 2-drug regimen for 4–16 months (isoniazid 10–15 mg/kg/day, rifampin 10–15 mg/kg/day). Treatment was delayed in 2 patients with elevated liver function test results. Seven patients had elevated serum uric acid levels and they were encouraged to drink water and were prescribed allopurinol. Hyperuricemia is the most common side effect of the patients who were treated with pyrazinamide and these patients may require oral hydration therapy and allopurinol during the course of antiglucocorticoid regimen treatment.

#71 - ANALYSIS OF THE USE OF TOBACCO AND MARIJUANA IN JUNIOR HIGH SCHOOL IN 10 SCHOOLS IN THE WESTERN REGION IN SÃO PAULO – BRAZIL

Author:

Lotufo J. (Pediatrics, USP – São Paulo, Brazil)

Introduction: the use of tobacco and marijuana is appearing increasingly early in Brazil and worldwide. Although being the fourth country in the number of ex-smokers, the precocity of tobacco use in Brazil concerns us. Smoking and the use of marijuana are pediatric diseases, for they start at the age of 12 (+/-2) and must be understood as a reason for prevention by pediatric pulmonologists.

Methodology: We screened 2814 questionnaires from students from 10 schools in the western region of São Paulo, on the initiation of tobacco use. These were teenagers from Junior High School and High School, with ages ranging from 10 to 17 years.

Results: 48% were boys and 52% girls.

18% of them deny having received any guidance on drugs and tobacco.

About tobacco, 90% deny having smoked in the past year, 3% of them use tobacco less than once a week, 1% of them once or more times a week, 2% of them use it daily, 1% of them twice or more times a day and 3% did not answer this question.

About marijuana, 90% have never used, 2% used less than one time a week, 1% use once or more times a week, 1% of them use it daily, 1% twice or more times a week and 5% did not answer this question. The reasons to try smoking for the first time were:

1. Because I wanted to and friends offered (4%)
2. Because friends offered and I couldn't refuse it (1%)
3. Out of curiosity (9%)
4. Because it is charming (1%)
5. 5% did not answer and 80% have never used it.

When asked about the use of cigarettes, 80% denied the use, 3% do it to help reduce bad feelings, 1% to do things they wouldn't be able to, 5% because it is tasty, 1% because they are already used to doing it, 1% because their friends do it, and 9% did not answer it.

Of those who did not use tobacco products, 57% because they know it is harmful, 10% because “it’s against their principles”, 4% are afraid, 3% have never had the opportunity and 15% have never used them. 4% did not use for other causes, and 7% did not answer.

When asked about the best way to prevent the use of drugs, 57% said it would be family guidance, 8% radio and TV, 3% teachers, 4% school material, 12% school campaign and 16% did not answer it.

Conclusion: Pediatric Pulmonologists and Pediatricians must get involved in the tobacco control issues, and anti marijuana, mainly in the prevention, for Junior High and High School students (11–17 year olds) are already trying it and are becoming early users. And Pediatric Pulmonologists are not mentioned as a way of prevention of drug use among teenagers. There has to be a change. The brief intervention (using 3 minutes of the medical appointment to talk about tobacco and marijuana) should be part of our medical appointments.

#72 - IMPORTANT DETAILS OF A SMOKING CESSATION CLINIC, RELATED TO PEDIATRICS AND PEDIATRIC PULMONOLOGY

Author:

Lotufo J. (Pediatrics, USP – São Paulo, Brazil)

Introduction: Active smoking is the first cause and passive smoking is the third leading cause of preventable death in the world. I started a smoking cessation clinic by treating smoking parents of children with asthma. 3000 people are currently being treated with therapy related to drug addiction and psychological and behavioral dependence.

Methodology: we evaluated the situation of teenagers in the smoking cessation group, and all the important facts related to Pediatrics.

Results:

1. 24% of children aged zero to five years old who come to the Emergency Department of Pediatrics, have urine positive for cotinine levels (nicotine derived), which means, they had close contact with cigarette in the past 36 hours (index ranged from 6.9 to 273 ngramas /ml of blood).
2. 3% of those who come to us in order to quit smoking, started smoking before age ten, 53% before age 15, and 86% before 20 years of age.
3. There was no seeking for treatment for smoking cessation before age 20.
4. From 20 to 25 years of age, only 21% quit smoking, and from 25 to 30 years of age, 30% quit smoking.

Evaluation:

1. Passive smoking is real in children, it is important to quit smoking at home.
2. Smoking begins increasingly early and it starts in the pediatric phase.
3. The teenager is not worried about quitting smoking, for the age group that seeks treatment ranges mainly from 40 to 60 years of age.
Abstract

4. The rate of smoking cessation is lower by the age of 30, if compared to the rate after the age of 30 (45 to 50%)

Discussion: Smoking starts in the pediatric phase of life, and pediatricians and pediatric pulmonologists do not spend time in making the prevention of the disease called “Nicotine Dependence”. Young people are not interested in quitting smoking (pre-contemplation stage) and the pediatricians need to guide them on this regard (action stage).

Young university students are still teenagers, and even with potential for 6000 smoking students at USP campus (20% of the population) a clinic created for this age group did not succeed for lack of demand. Young people are not interested in quitting smoking.

Conclusion: pediatricians and pediatric pulmonologists need to embrace this issue about smoking, as well as of other drugs, for its beginning is increasingly early. We need to make tobacco prevention in the pediatric care, guide smoking parents properly and discuss this issue in every medical appointment.

#87 - THE EFFECT OF BODY MASS INDEX (BMI) ON PULMONARY FUNCTION IN SCHOOL AGED CHILDREN

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Introduction: Data on pulmonary function abnormalities as complications of obesity in children are limited and conflicting. Therefore, it is of great importance to study the effect of high BMI on pulmonary function parameters in children.

Methods: Healthy children between 9 and 15 years of age were recruited. The parents were given a detailed questionnaire. All the responders underwent a detailed clinical assessment.

High BMI group (obese & overweight) had BMI for age and sex more than 85th percentile according to Centre for Diseases Control reference charts. (Overweight- 85th - 95th and Obese >95th percentile). The control group had BMI between 3rd and 85th percentile. All the children in high BMI and a subgroup of normal children (control) underwent spirometry. Exclusion criteria were respiratory infections within 2 weeks, chronic respiratory disorders and neuromuscular system disease.

Weight (kg) and standing height (cm) were measured with a calibrated weighing scale and a stadiometer. Alpha Touch Vitalograph Spirometer in accordance with the American Thoracic Society and European Respiratory Society Guidelines was used for testing. All children performed forced expiratory maneuvers. The best of at least three technically acceptable values for forced expiratory volume in one second (FEV1), forced vital capacity (FVC), maximum mid-expiratory flow rate (FEF25-75%), and flow volume curves were selected.

Study was approved by the Ethics Committee, University of Sri Jayewardenepura.

Statistical analysis: Pearson’s chi square test to evaluate potential association and student’s t test to assess differences were used with categorical and ratio-scale variables among the two groups with SPSS for Windows. The level of significance was set at 5%.

Results: A total of 405 school children participated. Of them 93 were excluded (did not fulfill the inclusion criteria or refused consent for medical appointment).

No significant difference noted in age, gender, height, exposure to cigarette smoke (P = 0.552) and family history of atopy (P = 0.458) between the two groups. BMI has no significant relationship to any of the pulmonary function parameters (FVC (t = 1.060, df = 117, P = 0.291), FEV1/FVC (t = -1.796, df = 117, P = 0.075) and FEF 25-75% (t = -1.060, df = 117, P = 0.291).

Conclusion: In conclusion, we have shown that pulmonary function does not correlate with body mass index and there is no reduction in pulmonary function values in children with high BMI.

#134 - INFLUENZA VIRUS INDUCED DAMAGE TO THE PULMONARY EPITHELIAL-ENDOTHELIAL BARRIER

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Acute respiratory distress syndrome (ARDS) is a fatal complication of influenza virus infection that is observed in both pediatric and adult patients. Clinically, ARDS is characterised by severe respiratory insufficiency and a high case fatality rate. The severity of this disease is reflected in the lung lesions of infected patients. During the acute phase of ARDS, patients display diffuse alveolar damage characterised by the accumulation of fluid and leukocytes in the alveoli. Central to the development of these pulmonary lesions is damage to the epithelial-endothelial barrier. Destruction of this barrier results in fluid leakage from interstitium, fibrin deposition and pulmonary haemorrhaging. At present, the specific mechanisms by which influenza virus damages the epithelial-endothelial barrier remain unclear. Previous studies have suggested that the ability of influenza virus to infect the pulmonary endothelium and cause endothelial cell apoptosis results in vascular permeability and oedema. Others have suggested that the pro-inflammatory cytokines produced in response to influenza virus play a more significant role in lung damage. Pro-inflammatory cytokines may damage the lung via the recruitment and activation of leukocytes. Alternatively, pro-inflammatory cytokines can damage tight junctions between epithelial cells and facilitate intercellular fluid permeability – although this has yet to be demonstrated in the case of influenza virus infection. Here, we use an in vitro model to assess how influenza virus damages the pulmonary epithelial-endothelial barrier. Briefly, epithelial cells are seeded on the upper half of a transwell membrane whilst endothelial cells are seeded on the lower half. These cells are then grown in co-culture for approximately seven days and then influenza virus is added to the upper chamber. The presence of influenza virus damages this barrier, as determined by a significant decrease in the trans-epithelial resistance (TER) over time. Interestingly, we show that whilst the addition of influenza virus results in the infection of epithelial cells, endothelial cells are not infected. Instead, endothelial cells facilitated increased cytokine production by epithelial cells. This increased cytokine production was associated with a significant decrease in the expression of tight junction proteins and a significant decrease in the tightness of the endothelial barrier. Our data therefore suggest that endothelial cells may play an important role in influenza virus-induced ARDS by triggering cytokine production by epithelial cells. This then in turn disrupts epithelial cell tight junctions and facilitates paracellular permeability and pulmonary oedema.

#147 - SLEEP-RELATED RESPIRATORY EVENTS AND SLEEP STRUCTURE IN HYPOXIC-ISCHEMIC ENCEPHALOPATHY NEONATES

Author(s):

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Objective: To determine whether sleep-related respiratory events are more common in hypoxic-ischemic encephalopathy (HIE) neonates compared to normal controls and to investigate if sleep structure is impaired in HIE patients.

Method: HIE neonates were recruited in the neonatal wards from June to August in 2011. Newborns recovered from neonatal pneumonia were served as controls. All the subjects and controls had the polysomnography performed in the Sleep Unit for at least 4 hours. Sleep stage was scored and respiratory events were analyzed by technicians who were unaware of the subjects’ conditions.

Results: Twenty-two full term infant with mild to moderate HIE and eleven control neonates were included into the study. There were no differences regarding age, gender, height and weight between the two groups. The percentage of indeterminate, quiet, and active sleep of total sleep time was 39.9, 29.4 and 30.6 respectively in the HIE group, and 29.1, 33.7 and 37.2 respectively in the control group. The percentage of indeterminate sleep was increased and REM sleep was decreased in the HIE patients compared to the controls ($P = 0.002$ and $P = 0.031$ respectively). There was no difference regarding the percentage of quiet sleep between the two groups ($P = 0.12$).

The HIE patients had a higher apnea/hypopnea index and hypopnea index compared to the controls ($P = 0.03$, and $P = 0.01$ respectively), while no difference were found with respect to obstructive apnea index, central apnea index and Mixed apnea index($P = 0.08$, $P = 0.57$ and $P = 0.49$ respectively).

Conclusions: HIE neonates had increased proportion of indeterminate sleep and decreased proportion of active sleep. Further more, HIE patients were more likely to have apneas and hypopneas compared to the controls.

#162 - PERFORMANCES OF A VALVED HOLDING CHAMBER WITH DIFFERENT INHALED CORTICOSTEROIDS

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In young children with asthma, the use of a pressurised metered dose inhaler (PMDI) with a valved holding chamber is recommended. The objective of this study was to evaluate the performances of a valved holding chamber with different inhaled corticosteroids.

In this study, the performance of a valved holding chamber called Tipshaler (Protec’som, France) was evaluated with beclomethasone (QVAR®, 100 μg/dose, MEDICIS, Canada) and ciclesonide (Alvesco®, 200 μg/dose, Takeda, Canada). The method according to the European Pharmacopoeia used a constant flow rate (30 L/min) was used. Particle size distribution was measured using a NGI cascade impactor (Copley Scientific, Nottingham, United Kingdom). The beclomethasone and ciclesonide concentrations were assayed by spectrophotometry at 239 nm and 243 nm respectively.

In the trachea, the mass of beclomethasone was higher with pMDI alone in comparison with Tipshaler (11.6 ± 0.4 μg vs 1.2 ± 0.2 μg, $P < 0.05$). In addition, deposition of fine particles of beclomethasone was similar with pMDI alone compared to Tipshaler (77 ± 1 μg vs 75 ± 1 μg, $P < 0.05$). Concerning ciclesonide, in the trachea, the mass of drugs was lower with Tipshaler compared to pMDI alone (2,4 ± 0.7 μg vs 16,0 ± 0.6 μg, $P < 0.05$). However, the fine particle dose was higher with the pMDI alone compared to Tipshaler (158 ± 1 μg vs 153 ± 1 μg, $P < 0.05$).

In conclusion, the use of valved holding chamber reduces the deposition of ultra-fine particles of inhaled corticosteroids in the trachea and allows efficient lung deposition of drugs.