ABSTRACT

Posters

1. BRONCHIAL ASThma AND OTHER CHRONIC OBSTRUCTIVE PULMONARY DISEASES

A3—Impact of Allergic Factors with House Dust Mite and Environments on Childhood Asthma Control.

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Background: Indoor pollution with allergens including house dust mite influence asthma control levels. Objective: To determine the rate of allergy to house dust allergens and its impact associated with indoor pollution control levels.

Methods: Study questionnaires, total IgE tests and skin tests for allergic house dust were collected in 129 children with asthma enrolled from January to March 2014. Diagnosis and assessment of asthma control level of the child was determined according to GINA 2012 criteria.

Results: There were 93 (72.1%) children with a positive skin test for at least one indoor respiratory allergen while the remaining 36 (27.9%) children were negative for the skin test. In the positive group, up to 89.9% were positive for 2 or more allergens. Of these, the positive proportion with Dermatophagoides pteronyssinus (29%) and Dermatophagoides farinae (22.9%) were highest, followed by house dust allergens (Blomia) with 22.9%, cockroaches (9.7%), hairy dog (8.6%). The lowest rate was 6.9% accounting for cat fur. The rate of positive allergen test in children over 5 years of age was higher (75.4%) than children under 5 years (46.7%) [OR = 3.51 (1.04 to 12.0); P = 0.019]. Similarly, the rate of positive allergen test in children with total IgE ≥ 100 IU/ml was higher (77.3%) than children with total IgE < 100IU/ml (56%; 2%) [OR = 2.65 (1.14 to 6.71); P = 0.021]. There were 77 (82.8%) children with positive allergen test who had uncontrolled or partly controlled asthma, higher than the group of children with negative allergen test (15%; 41.7%) [OR = 4.15 (1.74–9.98); P = 0.000]. Similarly, there were 52 (65.0%) children with positive test for two or more allergens who had uncontrolled or partly controlled asthma, higher than the group of children with positive test for only one allergen (3%; 23.1%) [OR = 6.19(1.40–31.1); P = 0.010]. Indoor pollution tended to be associated with an increased risk of uncontrolled or partly controlled asthma, particularly irregular bed hygiene under once per month [OR = 5.63(2.39–13.4); P = 0.000] and charcoal fumes [OR = 3.47 and (1.29–9.71); P = 0.006] and smoke [OR = 3.38(1.49–7.72) P = 0.001] and dog or cat ownership [OR = 2.82 (1.26–6.36); P = 0.005], respectively. The remaining elements, such as living in the city or in the countryside, in the family house area slightly below average, or whether playing or not with stuffed animals were not associated with increased risk of uncontrolled or partly controlled asthma.

Conclusion: The rate of children with asthma has a high positive skin prick test with respiratory allergens such as house dust mite. Irregular bed hygiene less than once per month, charcoal fumes, smoke pollution and dog or cat ownership were found associated with an increased risk of uncontrolled or partly controlled asthma.

A7—Profiles and Characteristics of Bronchial Responsiveness in the Korean 7-Year-old General Population.

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Background/Aim: Bronchial hyperresponsiveness is the intermediate phenotype of asthma. Bronchial responsiveness does not exist so dichotomous has to be expressed “hyper-“ or not, rather it exists as a spectrum. We aimed to evaluate the distribution profiles of bronchial responsiveness in the Korean 7-year-old general population and their relationship with clinical allergy.

Methods: The 7-year-old birth cohort participants were invited to visit 16 regional study hospitals. We performed a skin prick test, a standard spirometry and the bronchial provocation test as well as a detailed history and physical examination. The subjects’ bronchial responsiveness was categorized into one of the five ordered groups as well as...
log-transformed into the response dose ratio (RDR), a continuous marker of airway responsiveness. The distribution frequency, prevalence of recent wheezing, baseline lung functions, and the prevalence of atopic sensitization across all five groups as well as RDR association with clinical allergies were assessed.

**Results:** Among the 1577 birth-cohort participants, 642 children visited the study hospitals and 559 subjects reliably completed the bronchial provocation test. Ten percent (56/559) of the total population showed a provocative concentration of inhaled methacholine causing a 20% fall in forced expiratory volume in 1 second (PC20FEV1) < 4 mg/mL (Group 1) while 15.7% presented a PC20FEV1 between 4 and 16 mg/mL (Group 2). A total of 14.7% showed a PC20FEV1 ≥ 16 mg/mL but at the same time their PC15FEV1 < 16 mg/mL (Group 3), and the 18.4% displayed their PC15FEV1 ≥ 16 mg/mL with their PC10FEV1 < 16 mg/mL as well (Group 4). Finally, the other 41.1% presented a PC10FEV1 ≥ 16 mg/mL (Group 5). As the group sample increased, the proportion of subjects that had wheezy episodes during the last year decreased (P for trend = 0.004), the proportion of subjects that were sensitized to a panel of allergens decreased (P for trend < 0.001), whereas the mean baseline FEV1 percentage-predicted increased (P < 0.001). On the other hand, the RDR presented a significant elongation in current asthmatics than the others (P = 0.022). There also was a trend toward a increase in RDRs across the control, allergic rhinitis only, asthma only, and the combined allergic rhinitis and asthma groups (P = 0.001).

**Conclusion:** The 7-year-old general population had a wide spectrum of bronchial responsiveness. Bronchial responsiveness at this age is associated with clinical allergies, namely negatively with baseline lung function and positively with atopic sensitization.

**Keywords:** Asthma, Bronchial responsiveness, Child, General population, Response dose ratio

**A38 – The Clinical Implications of Bilevel Positive Airway Pressure Ventilation for Children with Severe Asthma Exacerbations in Intensive Care Unit.**

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**Background:**

Increasing studies had demonstrated that early initiation of non-invasive ventilation, including the use of Bilevel Positive Airway Pressure (BiPAP), is safe and well-tolerated in the management of children having acute respiratory distress syndrome. Despite the proven efficacy in some pilot studies, the strategy of using BiPAP in asthma patients with severe dyspnea has not yet been well-adapted, and is thus termed “experimental approach” in guidelines. We conducted a retrospective study of children who were admitted to the pediatric intensive care unit (PICU) under the diagnosis of severe asthma exacerbation or status asthmaticus and were treated with or without BiPAP. The purpose of the study was to assess the treatment efficacy and tolerability of BiPAP.

**Methods:**

We conducted a retrospective study on asthma patients who were admitted to PICU between January 2015 and February 2017. Patients with other significant comorbidities or with certain identified respiratory pathogens were excluded. For patients with multiple admissions, each admission was recorded separately. The medical records were reviewed for the following characteristics: age at presentation, clinical symptoms, heart rate (HR), respiratory rate (RR), oxygen demand, partial pressure of carbon dioxide in serum (pCO2), oxygen saturation (SpO2), clinical laboratory data and chest X-ray images. These admission data were grouped according to BiPAP use (Yes/No). Clinical parameters were documented at selected time intervals (before intervention, after intervention: 0–2 hours, 2–4 hours, 4–8 hours, 10–14 hours, 16–20 hours and 24 hours). Time zero was defined as the initiation of BiPAP ventilation for the BiPAP-using group and any method of ventilation or oxygenation support at PICU for the non-BiPAP group. Mann-Whitney U test was used to analyze the serial data. Amongst the BiPAP(+) group, pCO2 and SpO2 were analyzed before and after the intervention using a paired T-test.

**Results:**

Data of 27 PICU admissions were obtained, four of whom were excluded for the reasons described above. Data of 23 admissions in 15 different patients were analyzed (19 with BiPAP and 4 without BiPAP). The mean age at admission was 49.21 ± 33.82 months. Respiratory rate (RR) was significantly different before treatment between the 2 groups (p = 0.005) and 0–2 hours after treatment (p = 0.047), with the BiPAP group having a higher respiratory rate. The RR improved significantly in the ensuing time intervals in the BiPAP group. For the heart rate (HR) analysis, there was no significant difference between groups for any time intervals. RR, HR and CO2 level all showed a decline in trend after treatment in both groups. In the BiPAP group, the decrease in pCO2 level did not show statistical significance, while SpO2 level improved significantly after the use of BiPAP. In our study, none received invasive mechanical ventilation support during PICU stay.

**Conclusions:**

In this study, we found that there was a significant improvement in respiratory rate in patients with BiPAP support. BiPAP was also well-tolerated compared with other means of non-invasive ventilation or oxygen support (nebulizer, mask). These improving trends were also reflected in RR, HR and CO2 similarly in both groups. In conclusion, BiPAP ventilation is safe and efficient in the relief of respiratory symptoms in children with severe asthma attack.

**A47 – Children with Severe Acute Asthma Admitted to Dutch PICUs: A Changing Landscape**

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According to a nationwide database for pediatric intensive care unit (PICU) admissions, the number of children requiring intensive care admission for severe acute asthma (SAA) has increased between 2003 and 2013. SAA has the potential to progress to respiratory failure and can be fatal. SAA requiring admission at the PICU represents a major cost burden. Additionally, PICU admission itself is associated with greater psychological morbidity in children and their parents, when compared with admissions in general pediatric wards.

**Objectives:** The aim of this study was to identify factors explaining the increase in PICU admissions in The Netherlands.

**Methods:** We performed a multicenter retrospective cohort study across all tertiary care PICUs in the Netherlands in which we retrospectively analyzed the number and characteristics of children hospitalized for SAA in the PICU during an 11-year period in the Netherlands. Inclusion criteria were all children aged 2–18 years, hospitalized for SAA in PICUs in The Netherlands between 2003 and 2013. Children younger than 2 years were not included because of the uncertainty of the diagnosis. The SAA diagnosis had to be confirmed before PICU discharge. All admissions and re-admissions were included in the study. Data included demography, SAA treatment at the referring hospital and PICU, and mortality.

**Results:** In the 11-year study period, 590 children were admitted to a PICU, with a total of 660 admissions. During PICU admission, 83% of patients in our study received intravenous (IV) salbutamol. Dutch asthma guidelines require PICU admission in case IV salbutamol is given. Of these patients, 33% received a salbutamol infusion rate of 0.5 mcg/kg/min or less, and 58% received a higher infusion rate of 1.0 mcg/kg/min. Forty-two percent of all admitted children were 2–4 years old. Forty-four children were admitted for SAA in 2003, and this number remained relatively stable until 2010. Since 2010, the annual number of patients admitted to the PICU gradually increased to 138 in 2013. The age distribution and severity of SAA, based on the first blood gas and length of stay at the PICU, remained unchanged. The number of children with asthma did not triple since 2010. Over the years, the proportion of steroid-naïve patients admitted to the PICU increased gradually, although fewer children necessitated invasive ventilation. High-flow nasal cannulas (Optiflow®) were introduced in 2010, and their use increased significantly in the following years. Seven patients (1%) needed extracorporeal membrane oxygenation (ECMO). In-hospital mortality was n = 4 (0.6%).

**Conclusions:** During the last decade, we observed a threefold increase in children with SAA admitted to PICUs in the Netherlands, while the age distribution and severity of illness remained similar. In our new 2006 national guidelines, PICU admission is mandatory with the use of IV salbutamol. We speculate that the observations are explained by implementation of the national SAA guideline, and by increasing undertreatment with inhaled steroids.

**Reflections and concrete proposals for action:** Priority should be given to adequate diagnosis and treatment of children with asthma to prevent PICU admissions, as they carry a high cost, and are associated with the risk of posttraumatic stress disorder. Prospective studies into the risk factors for children with SAA which require salbutamol IV are needed. The safety of salbutamol IV should be further studied, and the need for PICU admission reconsidered.

**A50 – Assessment of Quality of Life in Children Suffering from Asthma.**

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Asthma is the most common chronic inflammatory disease of the respiratory tract in children. Quality of life of children suffering from asthma is a subjective experience of satisfaction or dissatisfaction with their own lives. The main aims of our study were to verify the connections between symptoms of asthma lung functions and quality of life; influence of comorbidity and asthma on quality of life; to identify and quantify psychosocial areas that children perceive as handicapped due to illness and to verify the degree of similarity in the perception of quality of life between parents and children with asthma. Also, the aim of the study was to translate, adopt and validate on Serbian language Juniper questionnaires, namely (PAQLQ) Pediatric Asthma Quality of Life Questionnaire with standardized operations, a variant with the examiner and questionnaire regarding the quality of life of caregivers of children with asthma – (PACQLQ) Pediatric Asthma Caregiver Quality of Life Questionnaire. Using questionnaires, we wanted to verify the quality of life of the children with asthma and their parents. Results were analyzed in accordance with the severity and length of the disease, as well as with other parameters (degree of disease according to GINA, spirometry, comorbidity, etc.).

The study included 100 children from 6–16 years old with intermittent and persistent mild and moderate asthma. During the study, patients were also classified according to Asthma control score. Diagnosis of asthma was established using well known guidelines for the diagnosis and management of asthma. After registration, a detailed medical history was taken and physical examination was performed for all patients, as well as pulmonary function measurements. Upon arrival and during control examinations (week 1, 5 and 9), asthma control scores were obtained and interviews with children with asthma and their parents were organized. The PAQLQ includes 23 questions divided into three areas: limitation of activities (n-5), symptoms (n-10) and emotional functioning (n-8). The PACQLQ contains 13 questions divided into two main areas: restrictions in the performance of activities-A (5) and emotional function-E. For each question in both questionnaires, there were 7 possible answers, with grade 7 meaning
without any symptoms and complaints and grade 1 meaning prominent symptoms.

There was a significant correlation between stage of asthma, symptoms, lung function and quality of life of children involved in the study. The clinical picture significantly affected the quality of life of children such that children with poorer control of the disease had a poorer quality of life. Also, improving disease control and asthma control score led to improved quality of life particularly in the areas of symptoms (F = 16.312, a p = 0.001) and emotional functions (F = 41.934, a p < 0.001). Comorbidity of asthma and other allergic diseases were very much present. Children with isolated asthma had a better quality of life then children with asthma and allergic rhinitis (5.76 vs. 6.24, p < 0.05). Parents and children had the same perception of the disease (coefficient correlation, r = 0.387 p < 0.001; r = 0.232 p = 0.031; r = 0.567 p < 0.001) while only parents assessed personal quality of life significantly worse than their children (t = 9.783 p < 0.001; t = 8.265 p < 0.001; t = 7.371 p < 0.001). Children involved in the study had the most complaints in the area of symptoms. Cough and limiting of physical activities were the elements most often cited. Emotional disturbances were less pronounced and sense of rejection did not significantly perturb patients involved in our study. Questionnaires for assessing the quality of life in children with asthma, translated into Serbian, showed good discriminative capability, a high reliability and specificity, with, a Cronbach’s alpha of 0.78 and, as such, may be recommended to assess the quality of life in routine medical practice and clinical trials.

As with all instruments currently available for use in children, further research is encouraged to verify the validity and usefulness of used questionnaires as a comprehensive health outcome measure in children. Results obtained in this study will promote the introduction of tools for measuring quality of life as an important parameter in estimating the stage of the disease and acceptance of asthma symptoms by patients.

A66 – Efficacy of Tiotropium Add-on Therapy in Children and Adolescents Who Experienced Episodes of Asthma Worsening during Four Phase III Studies.

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**Background:** Asthma is a leading cause of childhood morbidity, with episodes of disease worsening and exacerbation leading to hospitalization and impacting quality of life. Tiotropium add-on therapy has demonstrated improvements in peak and trough forced expiratory volume in 1 second (FEV1) in adolescents and children with symptomatic asthma despite inhaled corticosteroid (ICS) treatment ± other controllers. However, it is not clear what impact episodes of asthma worsening during treatment may have on these improvements. Here, we describe lung function outcomes of pediatric patients who experienced episodes of asthma worsening compared with those who did not during 4 Phase III trials in children and adolescents.

**Methods:** Post hoc analyses involved 4 Phase III, randomized, double-blind, placebo-controlled, parallel-group trials covering patients aged 6–11 years (CanoTinA- /VivaTinA-asthma® [NCT01634139/NCT01634152]; moderate and severe asthma, respectively) and 12–17 years (RubaTinA-/PensieTinA-asthma® [NCT01257230/NCT01277523]; moderate and severe asthma, respectively). Patients received once-daily tiotropium (2.5 µg or 5 µg) or placebo, delivered as 2 puffs via the Respimat® inhaler, as add-on to ICS ± other controllers.

The primary endpoint for all studies was peak FEV1 change from baseline (response) within 3 hours post-dose (FEV1(0–3h)) at Week 12 or 24 for severe and moderate asthma, respectively. Secondary endpoints included trough FEV1 response (key in PensieTinA-asthma®, CanoTinA-asthma® and VivaTinA-asthma®) measured at the end of the dosing interval, 10 minutes before the next dose of trial medication at Week 12 or 24 for severe and moderate asthma, respectively. Peak FEV1(0–3h) and trough FEV1 responses for patients who experienced episodes of asthma worsening during the trials were compared with those from patients who did not experience asthma worsening during the trials. Asthma worsening was defined as an episode of progressive increase in 1 or more asthma symptoms (as compared with usual day-to-day asthma symptoms) for 2 or more consecutive days. A decrease in the patient’s best morning PEF of 30% or more from the patient’s mean morning PEF for at least 2 consecutive days was also included in the definition. Analyses used a restricted maximum likelihood-based mixed-effects model with repeated measures.

**Results:** Baseline demographics and disease characteristics were generally balanced between those who experienced episodes of asthma worsening during the screening and treatment periods of the studies and those who did not, within specified age and asthma severity groups. Across the 4 studies there were improvements from baseline in peak FEV1(0–3h) and trough FEV1 responses in the placebo arms, and these improvements were generally lower in those patients who experienced episodes of asthma worsening. With both doses of tiotropium, improvements in peak FEV1(0–3h) and trough FEV1 responses in excess of those seen with placebo were observed in children irrespective of whether they experienced episodes of asthma worsening or not during the CanoTinA-asthma® and VivaTinA-asthma® studies. The responses were slightly more variable in the VivaTinA-asthma® study, particularly in the asthma worsening subgroups, possibly due to their low number of patients (Figures 1 and 2).

Overall in adolescents, placebo-adjusted improvements in lung function were observed with tiotropium for patients in both the
RubaTinA-asthma® and PensieTinA-asthma® studies regardless of whether they experienced episodes of asthma worsening or not, with the exception of the 2.5 μg dose group in the RubaTinA-asthma® study (Figures 1 and 2).

**Conclusion:** Once-daily tiotropium as an add-on to ICS maintenance therapy ± other controllers generally improved lung function in patients aged 6–17 years with moderate or severe asthma irrespective of whether they experienced episodes of asthma worsening during the trials. These data support the demonstrated broad efficacy of tiotropium in this age group and indicate that improvements in lung function are largely consistent even if some patients experience episodes of disease worsening.

Figure 1. Peak FEV1(0–3h) response in children and adolescents with and without episodes of asthma worsening during Phase III clinical trials

Figure 2. Trough FEV1 response in children and adolescents with and without episodes of asthma worsening during Phase III clinical trials

**Figure 1.** Peak FEV1(0–3h) response in children and adolescents with and without episodes of asthma worsening during Phase III clinical trials

**Figure 2.** Trough FEV1 response in children and adolescents with and without episodes of asthma worsening during Phase III clinical trials

**ABSTRACT**

**A67 – FEV1 Improvements with Tiotropium & Long-Acting Beta2-Agonists Added to Inhaled Corticosteroid Therapy Are Similar in Pediatric Patients with Asthma.**

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**Background:** In this systematic literature review in pediatric patients with asthma, we compare the improvement in forced expiratory
volume in 1 second (FEV1) with tiotropium Respimat® added to inhaled corticosteroids (ICS) with the improvement in FEV1 reported for long-acting β2-agonists (LABAs) added to ICS.

**Methods:** The endpoints selected for the comparison were peak and trough FEV1 responses (i.e., change from baseline) in liters. A systematic literature search was performed to identify relevant publications that report on randomized, controlled trials where a LABA was added to ICS for at least 4 weeks in adolescents and children. The results were compared with results from the 2 Phase III trials of tiotropium Respimat® added to ICS in pediatric patients with asthma (RubaTinA-asthma® and CanoTinA-asthma®).

**Results:** The systematic literature search of trials investigating LABAs added to ICS in pediatric patients identified 9 relevant publications, 7 of which were included in a Cochrane meta-analysis. Details of these trials, and the trials with tiotropium Respimat® in pediatric patients with asthma, are provided in Table 1. In the LABA studies, mean ICS dose at baseline ranged from 200–500 μg/day budesonide or equivalent and 160–250 μg/day fluticasone propionate. In the tiotropium studies, mean ICS dose at baseline ranged from 300–600 μg/day budesonide or equivalent. The LABA studies included in the Cochrane meta-analysis present a combination of peak and trough FEV1 measurements, and some articles do not specify at what time point the measurement was taken. For LABA added to ICS versus ICS, the Cochrane meta-analysis of 7 studies found an adjusted mean FEV1 improvement of 0.08 L (95% confidence interval 0.06, 0.10 L) (Figure 1). The 2 newer studies found an increase in FEV1 between 0.04 L and 0.12 L with formoderol added to budesonide versus budesonide, and no benefit in FEV1 with vilanterol added to fluticasone propionate versus fluticasone propionate. If the 2 outliers (the vilanterol study that found no improvement and a very small \( n = 21 \) salmeterol study) are excluded, all individual studies investigat- ing LABA as add-on to ICS generally showed treatment differences between 0.04 L and 0.13 L. The magnitude of FEV1 improvements with once-daily tiotropium added to ICS was similar with twice-daily LABAs added to ICS: tiotropium 5 μg versus placebo showed improvements of 0.134 L to 0.174 L in peak FEV1 response, and improvements of 0.084 L to 0.118 L in trough FEV1 response (Figure 2). Comparing the once-daily LABA vilanterol with once-daily tiotropium 5 μg shows greater lung function responses with tiotropium 5 μg. The results with tiotropium 2.5 μg were broadly similar to tiotropium 5 μg.

**Conclusion:** The results of our systematic literature review suggest that tiotropium add-on therapy provides meaningful lung function improvements as an alternative to LABA, or may be considered as add-on to ICS + LABA, in adolescents and children with asthma.

### Table 1. Details of the trials included in the analysis.

| Study Reference | Included in Cochrane analysis | Design | Patient age | Primary outcome |
|-----------------|-----------------------------|--------|-------------|----------------|
| LABA studies    |                             |        |             |                |
| Formoterol added to budesonide versus budesonide |                    |        |             |                |
| SD-039-0719 NCT00646529 Berger 2010 | Yes | 26-week, randomized, open-label, parallel-group, multicenter trial | 6–11 years | Safety |
| SD-039-0725 NCT00646321 Eid 2010 | Yes | 12-week, randomized, double-blind, parallel-group, multicenter trial | 6–15 years | PEF |
| Study 0688 Pohunek 2006 | Yes | 12-week, randomized, double-blind, parallel-group, multicenter trial | 4–11 years | Morning PEF |
| SD 039 0714 ATTAIN CSR | Yes | 12-week, randomized, double-blind, parallel-group, multicenter trial | 11–17 years | Morning PEF |
| CHASE 3 NCT02091986 Pearlman 2017 | No | 12-week, randomized, double-blind, parallel group, multicenter trial | 6–11 years | FEV1 |
| Salfmeterol added to fluticasone propionate versus fluticasone propionate |                    |        |             |                |
| SAS30031 Malone 2005 | Yes | 12-week, randomized, double-blind, parallel-group, multicenter trial | 4–11 years | Safety |
| Salmeterol added to ICS versus ICS |                    |        |             |                |
| SALMP/AH91/ D89 Russell 1995 | Yes | 12-week, randomized, double-blind, parallel-group, multicenter trial | 4–16 years | Morning PEF % predicted |
| N/A Langton Hewer 1995 | Yes | 8-week, randomized, double-blind, parallel-group, single-center trial | 12–17 years | Not identified |
| Vilterterol added to fluticasone propionate versus fluticasone propionate |                    |        |             |                |
| NCT01573767 Oliver 2016 | No | 4-week, randomized, double-blind, parallel-group, multicenter trial | 5–11 years | Evening PEF |
| Tiotropium studies |                             |        |             |                |
| Tiotropium added to ICS versus ICS |                    |        |             |                |
| RubaTinA-asthma® Hamelmann 2016 | No | 48-week, randomized, double-blind, parallel-group, multicenter trial | 12–17 years | Peak FEV1 response |
| CanoTinA-asthma® Schmidt 2016 (ERS-26th Annual Congress) | No | 48-week, randomized, double-blind, parallel-group, multicenter trial | 6–11 years | Peak FEV1 response |
ABSTRACT

Points represent mean treatment difference versus placebo; bars represent 95% CIs. Treatment difference >0 favors LABA added to ICS over ICS alone.

CI, confidence interval; ICS, inhaled corticosteroid; LABA, long-acting β2-agonist.

Figure 1. Treatment difference in FEV1 response with LABA compared with placebo added to ICS.

Figure 2. Treatment difference in peak (A) and trough (B) FEV1 response between tiotropium Respimat® and placebo added to ICS.

Not included in the Cochrane meta-analysis.
Points represent mean treatment difference versus placebo; bars represent 95% CIs.

Treatment difference >0 favors tiotropium over placebo.

CI, confidence interval.

A68 – Safety and Efficacy of Tiotropium in 1–5-year-old Children with Persistent Asthmatic Symptoms.

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Background: There has been little investigation on the safety and efficacy of new potential asthma medications in very young children (≤5 years). We evaluated the safety and efficacy of once-daily tiotropium Respinimat® (TioR) as add-on to inhaled corticosteroids (ICS) with or without further maintenance therapy in patients aged 1–5 years with persistent asthmatic symptoms.

Methods: In this Phase II/III, randomized, double-blind, placebo (PBO)-controlled, parallel-group trial (NinoTinA-asthma®, NCT01634113), patients aged 1–5 years with persistent asthmatic symptoms received tiotropium 2.5 μg (TioR 2.5) or 5 μg (TioR 5) or PBO as 2 puffs once daily for 12 weeks via the Respimat® inhaler, as add-on to usual maintenance therapy of ICS with or without other controller medication. The primary objective was to determine the safety of TioR by comparing adverse events (AEs) with TioR versus PBO. The primary efficacy endpoint was change in the weekly mean combined daytime asthma symptom score from baseline at Week 12 (response). The co-primary endpoint in 5-year-olds was peak forced expiratory volume in 1 second within 3 hours post-dose (peak FEV1(0–3h)) response. Exploratory analyses included 3 composite exacerbation endpoints derived from AEs, with treatment comparisons reported as hazard ratios (HRs). Treatment comparisons for efficacy endpoints were exploratory, and no formal hypothesis testing was performed.

Results: Of the 102 patients randomized, 101 were treated and completed the 12-week treatment period (TioR 2.5: n = 36; TioR 5: n = 31; PBO: n = 34); of these, 98 children used the AeroChamber Plus® Flow-Vu® spacer to facilitate inhalation. Baseline characteristics, including concomitant diseases and background therapies, were similar between treatment groups (Table). A lower percentage of children reported any AEs in the TioR groups (TioR 2.5: 55.6%; TioR 5: 58.1%) than in the PBO group (73.5%), with more children in the PBO group (29.4%) reporting asthma exacerbations as AEs (versus 13.9% [TioR 2.5] and 6.5% [TioR 5]). No AEs leading to treatment discontinuation or death were reported, and AEs were of mild or moderate intensity. Serious AEs were reported in 3 patients (8.8%), all in the PBO group.

Improvements in weekly mean combined daytime asthma symptom score were comparable in all groups. Of the patients who underwent lung function tests, all but 1 child in the TioR 2.5 group had increased peak FEV1(0–3h) at Week 12; however, due to insufficient patient numbers, no treatment comparisons were performed. Exploratory analyses found significant reductions in the risk of AEs related to asthma exacerbations (broad) or worsening following TioR treatment (HR for TioR 2.5: 0.46 [95% confidence interval (CI) 0.22, 0.98], p = 0.044; TioR 5: 0.42 [95% CI 0.19, 0.94], p = 0.035), as well as the risk of asthma exacerbation (broad) with pneumonia or asthma worsening (TioR 2.5: 0.47 [95% CI 0.23, 0.98], p = 0.043; TioR 5: 0.40 [95% CI 0.18, 0.88], p = 0.022; Figure). At baseline, all patients used short-acting β2-adrenoceptor agonists; after 12 weeks of treatment, less than half of the patients used any rescue medication. Use of rescue medication at Week 12 (percentage of days per week) was comparable between groups (median of 0); however, there were differences in the upper quartile values between treatment groups (TioR 2.5: 42.9%; TioR 5: 28.6%; PBO: 50.0%), indicating that 25% of PBO-treated patients used rescue medication every second day, while 25% of the TioR 5-treated patients used rescue medication only every third day.

Conclusion: Our results suggest that tiotropium add-on therapy has a similar safety profile to PBO in preschool children with persistent asthmatic symptoms. Treatment with TioR resulted in some non-significant improvements in efficacy endpoints, including less frequent use of rescue medication, compared with PBO. Importantly, we observed a significant reduction in the number of children who reported AEs related to asthma exacerbation or worsening in the TioR groups compared with PBO, pointing towards an increased disease control. Additional well-powered trials are needed to confirm our findings.

Table. Baseline characteristics

| Age, n (%) | Tiotropium Respimat® 2.5 μg* (n = 36) | Tiotropium Respimat® 5 μg* (n = 31) | Placebo Respimat®* (n = 34) |
|-----------|--------------------------------|---------------------------------|-----------------------------|
| 1–<3 years | 15 (41.7)                         | 12 (38.7)                        | 10 (29.4)                   |

(Continues)
|                  | Tiotropium Respimat® 2.5 µg* (n = 36) | Tiotropium Respimat® 5 µg* (n = 31) | Placebo Respimat®* (n = 34) |
|------------------|-------------------------------------|------------------------------------|-----------------------------|
| 3–5 years        | 21 (58.3)                           | 19 (61.3)                          | 24 (70.6)                   |
| Male, n (%)      | 19 (52.8)                           | 21 (67.7)                          | 21 (61.8)                   |
| Mean ± SD height, cm | 100.0 ± 13.4                        | 100.1 ± 10.8                       | 100.2 ± 13.4               |
| Mean ± SD weight, kg | 16.4 ± 5.2                          | 16.0 ± 3.5                         | 16.3 ± 3.8                 |
| Exposure to second-hand smoke, n (%) |                               |                                    |                             |
| No               | 31 (86.1)                           | 28 (90.3)                          | 33 (97.1)                   |
| Yes              | 5 (13.9)                            | 3 (9.7)                            | 1 (2.9)                     |
| Exposure to household pets, n (%) |                               |                                    |                             |
| No               | 28 (77.8)                           | 21 (67.7)                          | 25 (73.5)                   |
| Yes              | 8 (22.2)                            | 10 (32.3)                          | 9 (26.5)                    |
| Mean ± SD age at asthma onset, years‡ | 1.4 ± 1.4                           | 1.5 ± 1.0                          | 1.8 ± 1.3                   |
| Mean ± SD duration of asthma, years‡ | 1.8 ± 1.1                           | 1.6 ± 1.1                          | 1.4 ± 0.9                   |
| Mean ± SD combined day asthma symptom score§ | 0.74 ± 0.61                         | 0.97 ± 0.87                        | 0.83 ± 0.74                 |
| Mean ± SD ICS dose of stable maintenance treatment, µg§,|| | 228 ± 111                           | 264 ± 210                       | 276 ± 230                   |
| Concomitant asthma therapies at baseline, n (%)|                               |                                    |                             |
| ICS alone        | 20 (55.6)                           | 20 (64.5)                          | 16 (47.1)                   |
| ICS + 1 additional controller | 15 (41.7)                           | 9 (29.0)                           | 17 (50.0)                   |
| ICS + LABA       | 3 (8.3)                             | 0 (0)                              | 1 (2.9)                     |
| ICS + LTRA       | 12 (33.3)                           | 9 (29.0)                           | 16 (47.1)                   |
| ICS + theophylline | 0 (0)                               | 0 (0)                              | 0 (0)                       |
| ICS + 2 additional controllers | 1 (2.8)                             | 2 (6.5)                            | 1 (2.9)                     |
| ICS + LABA + LTRA | 1 (2.8)                             | 2 (6.5)                            | 1 (2.9)                     |
| ICS + LABA + theophylline | 0 (0)                               | 0 (0)                              | 0 (0)                       |
| ICS + LTRA + theophylline | 0 (0)                               | 0 (0)                              | 0 (0)                       |
| ICS + 3 additional controllers | 0 (0)                               | 0 (0)                              | 0 (0)                       |
| Most frequent concomitant diagnoses at screening (>5% of total patients), n (%) |                               |                                    |                             |
| Allergic rhinitis | 5 (13.9)                            | 7 (22.6)                           | 8 (23.5)                    |
| Atopic dermatitis | 5 (13.9)                            | 7 (22.6)                           | 5 (14.7)                    |
| Food allergy     | 4 (11.1)                            | 5 (16.1)                           | 1 (2.9)                     |
| Pneumonia        | 4 (11.1)                            | 3 (9.7)                            | 3 (8.8)                     |
| Asthma           | 2 (5.6)                             | 2 (6.5)                            | 4 (11.8)                    |
| Rhinitis         | 2 (5.6)                             | 2 (6.5)                            | 4 (11.8)                    |
| Bronchitis       | 3 (8.3)                             | 3 (9.7)                            | 1 (2.9)                     |
| Cough            | 0 (0)                               | 4 (12.9)                           | 3 (8.8)                     |
| Seasonal allergy | 1 (2.8)                             | 4 (12.9)                           | 0 (0)                       |
| History of breastfeeding | 28 (77.8)                          | 23 (74.2)                          | 33 (97.1)                   |
| Median (minimum, maximum) eosinophils at screening, 10^9 cells/L | 0.36 (0.1, 1.7)                    | 0.37 (0.1, 3.1)                | 0.3 (0.1, 1.8)              |
| Median (minimum, maximum) total IgE at screening, µg/L | 351 (~670, 13132)                  | 931 (~251, 24384)                 | 599 (~1076, 11302)          |

*Once daily; †at screening; ‡adjusted for treatment and baseline; §at randomization; ||budesonide or equivalent dose; ¶all patients received SABA and ICS at baseline; **fewer patients received LABA between the 3 months before screening and during treatment periods because of patients being switched from ICS/LABA combination to ICS monotherapy <4 weeks before Visit 1.

ICS, inhaled corticosteroids; IgE, immunoglobulin E; LABA, long-acting β2-agonist; LTRA, leukotriene receptor antagonist; SABA, short-acting β2-adrenoceptor agonists; SD, standard deviation.

Figure Overview of key results of the NinoTinA-asthma® trial
A70 – Effect of Tiotropium Respimat® on Seasonal Asthma Worsening in Pediatric Patients.

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Background: Asthma exacerbations are a major cause of morbidity and increased healthcare costs in many patients, with a pattern for peaking during certain times of the year. Investigating asthma exacerbations in clinical trials can be difficult, especially in children, for whom long-term placebo-controlled exacerbation trials are difficult to justify. We aimed to investigate the adverse events (AEs) related to asthma exacerbations and asthma symptoms that were reported across several pediatric trials investigating the safety and efficacy of tiotropium. Of particular interest was the identification of any seasonality pattern in the reporting of these AEs, whilst also ascertaining whether tiotropium efficacy was consistent throughout the year.

Methods: We pooled data from 5 randomized, double-blinded, placebo-controlled trials investigating the safety and efficacy of tiotropium in pediatric asthma: NinoTinA-asthma®, a 12-week, Phase II/III trial in patients aged 1–5 years with persistent asthmatic symptoms (NCT01634113); CanoTinA-asthma®, a 12-week, Phase III trial in patients aged 6–11 years with moderate asthmatic symptoms (NCT01634139); VivaTinA-asthma®, a 12-week, Phase III trial in patients aged 6–11 years with severe asthmatic symptoms (NCT01634152); RubaTinA-asthma®, a 48-week, Phase III trial in patients aged 12–17 years with moderate symptomatic asthma (NCT01257230); and PensieTinA-asthma®, a 12-week, Phase III trial in patients aged 12–17 years with severe symptomatic asthma (NCT01277523). In all trials, patients received once daily tiotropium (5 μg or 2.5 μg) or placebo, delivered via the Respimat® inhaler as 2 puffs, in addition to inhaled corticosteroids with or without additional controllers. AEs related to asthma exacerbations or symptoms were defined using a composite endpoint according to the Medical Dictionary for Regulatory Activities version 18.1 preferred term group ‘asthma exacerbations and asthma-related symptoms’. The number of asthma exacerbations reported as AEs were plotted by month, with data from the Southern hemisphere shifted by 6 months to align the seasons (Northern hemisphere: June = month 6; Southern hemisphere: December = month 6).

Results: Overall, 1,691 patients aged 1–17 years were included in the pooled analyses. The rate of patients reporting AEs related to asthma exacerbations and symptoms, number of patients with an event per 100 patient-years, was significantly reduced with tiotropium 5 μg (177 patients with event per 100 patient-years) compared with placebo (217 patients with event per 100 patient-years, rate ratio [RR] 0.76 [95% confidence interval (CI) 0.63, 0.93]). A similar, but non-significant, trend was associated with the tiotropium 2.5 μg dose (195 patients with event per 100 patient-years) compared with placebo (RR 0.87 [95% CI 0.72, 1.05]).

When analyzed by month, reports of AEs related to asthma exacerbations and symptoms were greatest in the placebo group in the spring, autumn and winter (Figure), and lowest in summer. With both doses of tiotropium, spring and autumn peaks were reduced.

Figure. Number of reported AEs related to asthma exacerbations and symptoms over 12 months.
Conclusion: This analysis suggests treatment with tiotropium reduces AE related to asthma exacerbations and symptoms in pediatric patients, with a particular effect in reducing spring and autumn seasonal peaks. As long-term asthma exacerbation trials in pediatric patients remain ethically challenging, this analysis highlights an alternative endpoint to investigate such efficacy in children. These data also highlight the importance of trial timing to account for seasonal exacerbation peaks when a 12-month study length is not practical.

A72 – Improvements in Reporting of Asthma Exacerbations in Efficacy and Safety Data with Tiotropium Add-on Therapy in Pediatric Patients.

Background: Recurrent asthma symptoms and exacerbations cause substantial morbidity in pediatric patients with asthma, therefore, a primary treatment goal is to prevent these from occurring. The definition of exacerbations commonly used in clinical trials is worsening of asthma symptoms or reduction in lung function for a defined period, with severe events requiring systemic steroid treatment and/or hospitalization. However, this definition may be too strict for pediatric trials, where sample size and trial duration are limited by ethical considerations. Adverse events (AEs) related to asthma exacerbations and worsening symptoms are also recorded among safety assessments as standard in clinical trials, and this may be an alternative endpoint for clinicians to consider in assessing efficacy in terms of exacerbations in pediatric patients. Herein, we compare the reporting of asthma exacerbations as an efficacy endpoint using the standard definition, with reporting of AEs related to exacerbations and symptoms in Phase III trials of tiotropium add-on in children and adolescents.

Methods: This was an exploratory analysis of 5 Phase III trials comprising patients aged 12–17 years (RubaTinA-/PensiTeinA-asthma®; moderate and severe asthma, respectively), aged 6–11 years (CanoTinA-/VivaTinA-asthma®; moderate and severe asthma, respectively) and 1–5 years (NinoTinA-asthma®; persistent asthmatic symptoms). Patients received tiotropium (5 or 2.5 μg) or placebo, as 2 puffs once daily via the Respimat® inhaler, as add-on to inhaled corticosteroids ± other controllers. Children <5 years old also used an AeroChamber Plus® Flow-Vu® spacer. Time to first asthma exacerbation, in all studies except NinoTinA-asthma®, was a pre-defined efficacy endpoint, with an exacerbation defined as an episode of progressive increase in ≥1 asthma symptom(s) lasting ≥2 consecutive days and/or a decrease in patient’s best morning peak expiratory flow (PEF) ≥30% from the patient’s mean morning PEF for ≥2 consecutive days. The number of patients reporting AEs related to asthma exacerbations or symptoms was recorded from start of treatment until 30 days after end of treatment; the AEs used in this analysis fell under an umbrella term of ‘related to asthma exacerbations or symptoms’, defined using a composite endpoint, according to the Medical Dictionary for Regulatory Activities version 18.1 preferred terms related to asthma exacerbations and asthma-related symptoms. In this analysis, the time to first asthma exacerbation occurrence was analyzed using the Cox proportional hazards model, with treatment as effect. AEs related to asthma exacerbations or symptoms captured by the safety reporting were analyzed to produce time-adjusted rate ratios (RR), that is, number of exacerbations or symptoms captured by the safety reporting were analyzed to produce time-adjusted rate ratios (RR), that is, number of patients with the event per 100 patient-years at risk. The estimates and confidence intervals (CI) for RR are based on a Cochran–Mantel–Haenszel test (stratified by study in case of analysis for pool of studies).

Results: As an efficacy endpoint, the risk of exacerbation was generally reduced with tiotropium 5 μg add-on treatment compared with placebo (HR 0.60–0.82; Table 1), although these changes did not reach statistical significance. With tiotropium 2.5 μg, numerical reduction in risk of exacerbation was seen in 3 out of the 4 trials,
and this reached significance in VivaTinA-asthma® (HR 0.52; 95% CI 0.33, 0.82). When analyzing patients reporting AEs related to asthma exacerbations or symptoms, there was also a reduction with tiotropium 5 μg versus placebo across the trials (RR 0.35–0.89; Table 2); the reduction reached statistical significance in the youngest age group (RR 0.35; 95% CI 0.16, 0.76) and also when data were pooled across the 5 trials (RR 0.76; 95% CI 0.63, 0.93). With tiotropium 2.5 μg, a numerical reduction in AEs was observed in 4 of the 5 trials, reaching statistical significance in NinoTinA-asthma® (RR 0.41; 95% CI 0.20, 0.85) and VivaTinA-asthma® (RR 0.61; 95% CI 0.40, 0.94).

**Conclusion:** Overall, the data show that the 2 endpoints, exacerbations and AEs related to asthma exacerbations and symptoms, align and that treatment differences can be detected using AE reporting when exacerbation data as an efficacy endpoint are not, or cannot be, collected. Reductions in AEs related to asthma exacerbations or symptoms in safety reporting may be considered a useful alternative endpoint for clinicians and those conducting clinical trials to assess efficacy in terms of exacerbations in pediatric trials where sample size and trial duration may be limited.

Table 1. Children and adolescent patients reporting exacerbations during Phase III clinical trials

| Trial                      | Age, years | Asthma severity | Total patients treated, N | Placebo, n (%) | Tiotropium 5 μg, n (%) | Tiotropium 5 μg vs. placebo (95% CI) | Tiotropium 2.5 μg, n (%) | Tiotropium 2.5 μg vs. placebo (95% CI) |
|----------------------------|------------|----------------|---------------------------|----------------|------------------------|--------------------------------------|--------------------------|--------------------------------------|
| PenseisTinA-asthma®        | 12–17      | Severe         | 392                       | 25 (18.52)     | 15 (11.54)             | HR 0.60 (0.32, 1.14)                  | 16 (14.17)               | HR 0.75 (0.41, 1.36)                  |
| RubaTinA-asthma®           | 12–17      | Moderate       | 397                       | 37 (26.81)     | 30 (22.39)             | HR 0.82 (0.51, 1.33)                  | 34 (27.20)               | HR 1.04 (0.65, 1.66)                  |
| VivaTinA-asthma®           | 6–11       | Severe         | 400                       | 47 (35.07)     | 35 (26.92)             | HR 0.86 (0.44, 1.10)                  | 29 (21.32)               | HR 0.52 (0.33, 0.82)                  |
| CanoTinA-asthma®           | 6–11       | Moderate       | 401                       | 66 (50.38)     | 57 (42.22)             | HR 0.77 (0.54, 1.10)                  | 63 (48.87)               | HR 0.88 (0.62, 1.24)                  |
| NinoTinA-asthma®           | 1–5        | Persistent asthmatic symptoms | 101                  | NA             | NA                     | NA                                   | NA                      | NA                                   |

Cl, confidence interval; HR, hazard ratio; NA, not applicable.

Table 2. Children and adolescents patients reporting AEs related to asthma exacerbations or symptoms during Phase III clinical trials

| Trial                      | Age, years | Asthma severity | Total patients treated, N | Placebo, n (%) | Tiotropium 5 μg, n (%) | Tiotropium 5 μg vs. placebo (95% CI) | Tiotropium 2.5 μg, n (%) | Tiotropium 2.5 μg vs. placebo (95% CI) |
|----------------------------|------------|----------------|---------------------------|----------------|------------------------|--------------------------------------|--------------------------|--------------------------------------|
| PenseisTinA-asthma®        | 12–17      | Severe         | 392                       | 28 (20.7)      | 20 (15.4)              | RR 0.71 (0.40, 1.26)                  | 23 (18.1)                | RR 0.86 (0.49, 1.49)                  |
| RubaTinA-asthma®           | 12–17      | Moderate       | 397                       | 48 (34.8)      | 40 (29.9)              | RR 0.83 (0.54, 1.26)                  | 50 (40.0)                | RR 1.28 (0.86, 1.90)                  |
| VivaTinA-asthma®           | 6–11       | Severe         | 400                       | 51 (38.1)      | 40 (30.8)              | RR 0.73 (0.48, 1.11)                  | 37 (27.2)                | RR 0.61 (0.40, 0.94)                  |
| CanoTinA-asthma®           | 6–11       | Moderate       | 401                       | 70 (53.4)      | 68 (50.4)              | RR 0.90 (0.64, 1.24)                  | 73 (54.1)                | RR 0.97 (0.70, 1.34)                  |
| NinoTinA-asthma®           | 1–5        | Persistent asthmatic symptoms | 101                  | 20 (18.6)      | 9 (29.0)               | RR 0.35 (0.16, 0.76)                  | 12 (33.3)                | RR 0.41 (0.20, 0.85)                  |
| Pooled studies             | 1–17       | Moderate–severe | 1,651                     | 217 (37.9)     | 177 (31.6)             | RR 0.76 (0.63, 0.92)                  | 195 (34.9)               | RR 0.87 (0.72, 1.05)                  |

AE, adverse event; Cl, confidence interval; RR, rate ratio.
6–17 years), as an example of how data from previous adult asthma studies can be extrapolated to pediatric asthma clinical trial programs.

Results: Several feasibility considerations were identified in the literature that can influence pediatric trial design. These ranged from low numbers of child participants in clinical research, poor long-term adherence in clinical trial settings, limited pediatric-specific resources at research centers and a lack of trial networks for pediatric research. Pediatric trials may also require the validation of specific endpoints for different age groups and associated stages of development.

While forced expiratory volume in 1 second (FEV1) is well accepted as an endpoint in clinical trials in adult patients, FEV1 response does not always correlate with asthma symptoms, and can often appear to be normal in children with asthma.1 In the tiotropium in asthma clinical trial program, improvements in peak FEV1(0–3h) and trough FEV1 following tiotropium add-on therapy were in a comparable range in adult patients and pediatric patients (Figure 1).

Alternative lung function measures suggested for pediatric patients include forced expiratory flow at 25–75% of the pulmonary volume (FEF25–75%), which reflects small airway function, and FEV1/forced vital capacity (FVC) ratio, which has been shown to be associated with asthma severity in children. In pediatric patients, tiotropium add-on therapy consistently improved trough FEF25–75% responses versus placebo. There was a strong association between improvements in trough FEF25–75% and trough FEV1 (Pearson correlation coefficient 0.735–0.799), and FEF25–75% improvements were largely more pronounced than trough FEV1 improvements. Moreover, tiotropium add-on therapy consistently improved trough FEV1/FVC ratio versus placebo in pediatric patients, although a high variability was noted in adolescent patients with severe asthma.

In addition to lung function-based endpoints, it is important to study patient-relevant outcomes such as exacerbations and symptoms. Assessing these endpoints in a confirmatory design can require a large sample size and a long study duration. Such trials would require giving some children placebo for long periods, which may be unethical, especially in the pediatric setting. Because asthma is a disease that follows a similar course in adults and children, and outcomes of treatments are comparable, a partial extrapolation concept was applied in the tiotropium in asthma clinical trial program. Thus, in adult patients, lung function, symptom and exacerbation endpoints were evaluated in a confirmatory manner, while in pediatric patients, only lung function endpoints were evaluated in a confirmatory manner, and symptom and exacerbation endpoints were assessed in an exploratory manner.

In adults (aged 18–75 years), tiotropium add-on therapy significantly improved pulmonary function and asthma control, and reduced exacerbation risk versus placebo. In pediatric patients (aged 6–17 years), tiotropium add-on therapy largely improved pulmonary function versus placebo, and there were trends for improved asthma control and reduced exacerbation risk versus placebo in a comparable range, as in adult patients.

Conclusion: The results from the tiotropium in asthma clinical program emphasize that successful clinical trials in pediatric patients with asthma can be performed. To assess lung function, FEV1 and FEF25–75% were shown to be reliable endpoints. In addition, there was a strong, positive correlation between trough FEF25–75% and FEV1, and trough FEF25–75% responses were generally more pronounced than FEV1 responses. The tiotropium asthma clinical program also demonstrated how a partial extrapolation concept may be applied for exacerbation and symptom endpoints, thereby keeping sample size and study duration reasonable and in line with ethical considerations.

1. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF, Jr, Sorkness CA. Classifying asthma severity in children: Mismatch between symptoms, medication use, and lung function. Am J Respir Crit Care Med. 2004;170(4):426–432.

Figure 1. Improvements in peak (a) and trough (b) FEV1(0–3h) response (% predicted) in adults, adolescents and children with tiotropium add-on treatment (5μg)

CI, confidence interval; Tio R5, tiotropium Respimat 5μg.

A74 – Etiology Aspects of Asthma Exacerbations in Childhood.

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The main cause for asthma exacerbations in childhood are viral infections. Their etiology profile has a significant epidemiological and therapeutic value.

Material and methods: In a clinical survey for a one-year period, 126 patients with bronchial asthma were followed. Their age was between
5 and 18 years. The patients were investigated according to clinical, functional and laboratory parameters. In order to assess certain etiological aspects of asthma exacerbations, serology tests were performed (ELISA tests) for: RSV, Adenovirus, Chlamydia pneumoniae, Mycoplasma pneumoniae, Influenza virus and Parainfluenza virus: IgM and IgG antibodies.

**Results:** The results were evaluated using statistical methods and SPSS software. Our results demonstrated: in 9.52% of asthmatics, acute RSV infections were found with positive/+/ IgM antibodies, in 42.1% – data for a past RSV infection – positive IgG antibodies. No patients with acute Adenovirus infection, positive IgG antibodies were detected in 22.2% of asthmatics.

Positive IgG titer for Chlamydia pneumoniae were found in 4% of patients. The results for M. pneumoniae proved /+ IgM in 0.8%, and /+IgG in 3.2% of asthmatics included in the clinical investigation.

Serology diagnosis for Influenza virus was positive in 1.6% for IgG, for Parainfluenza virus – positive IgG in 19.8%.

**Conclusion:** Serology tests revealed the leading role of past RSV infection in asthma exacerbations in an investigated group of asthmatics (42.1%), followed by Adenovirus infection (22.2%) and Parainfluenza virus infection (19.8%).

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**A75 – Exhaled Nitric Oxide among Bulgarian Children with Asthma Exacerbation.**

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Exhaled nitric oxide is an important non-invasive marker for bronchial inflammation in children with asthma.

**The aim of the study:** To investigate exhaled nitric oxide (FeNO) values among 126 patients with asthma exacerbation and to follow them over a 3-month period. To evaluate certain clinical, laboratory and functional parameters and their correlation with FeNO.

**Methods:** FeNO was measured by a single-breath on-line measurement. Laboratory tests included: leukocyte count, ESR, CRP. Total IgE levels were analyzed by ELISA. Pulmonary function tests (PFTs) were performed in all patients. Blood and sputum (nasal) eosinophils were counted. Serology tests for respiratory viruses were performed by ELISA.

**Results:** FeNO was significantly higher in the asthmatic group compared with the control groups. There was a positive linear correlation between age and FeNO values. Male gender was dominant (62.9%). Positive family history was observed in over half of the asthmatic patients (58.9%). Upper respiratory airways were involved in 46.24% with allergic rhino sinusitis. A number of asthmatics had a long duration of bronchial asthma (more than 5 years): 50.79%. Mean total IgE values were increased in the group of asthmatics (252.69IU/ml). FeNO was the major parameter in the clinical study with mean values of 27.68 to 17.21 pps. Serological viral tests revealed the leading role of a past RSV infection (42.1%), followed by Adenovirus (22.2%) and Parainfluenza virus (19.8%).

**Conclusion:** We present some data regarding FeNO values for Bulgarian asthmatics in combination with clinical, laboratory and functional parameters.

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**A91 – No Effect of Variant Alpha-1 Antitrypsin Genotypes on the Frequency of Parental-Reported Wheezing and Breathlessness during the First Three Years of Life in the ALSPAC Birth Cohort.**

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**Background:** Alpha-1 antitrypsin (AAT) is the most common genetic cause of chronic obstructive pulmonary disease. Aside from the most important function as an inhibitor of proteinases, AAT is also implicated in the modulation of immune reactions and inflammation. Early-onset preschool wheezing has been suggested as being the first manifestation of COPD. Also, pilot data suggest that variant AAT genotypes may predispose children to more severe episodes of wheezing in early childhood. If this is the case, these children may be identified early in life by their wheezing characteristics and intervention measures might be applied to prevent the development of AAT-related chronic obstructive pulmonary disease.

**Materials and methods:** We chose to analyze the data from the ALSPAC cohort. AAT genotypes were determined from imputed genome data on the most common variant SNPs rs17580 (PiS) and rs28929474 (PiZ). Data on wheezing characteristics were obtained via questionnaire at several time points during the first 3 years of life. Associations among the most common variant AAT genotypes (PiMZ, PiZZ, PiMS, PiSS, and PiSZ) and wheezing characteristics (onset, number of wheezing episodes, duration of wheezing, and breathlessness during episodes of wheezing) were analyzed.

**Results:** A total of 6871 children had complete genetic data on the selected SNPs of which 2858 (41.6%) had at least one wheezing episode and 1033 (15.0%) experienced breathlessness due to wheeze during the first three years of life. Wheezing was prevalent in 487 (43.4%) of children with variant AAT genotypes compared with 2377 (41.4%) of children with a normal AAT genotype. Similarly, breathlessness did not differ between the groups (15.4% for variant and 15.6% for normal AAT genotype). Neither wheezing nor breathlessness due to wheeze (OR = 1.111, 95% CI 0.958–1.288, and OR = 0.929, 95% CI 0.759–1.137 respectively) was associated with a variant genotype of AAT. Finally, the proportions of wheezing days per year as well as the prevalence of breathlessness during wheezing attacks were similar in the normal AAT and variant AAT groups.

**Conclusions:** The data from the ALSPAC birth cohort do not show variant AAT genotypes to be associated with wheezing nor
breathlessness during the first three years of life and these character-
istics are not useful in identifying children with variant AAT genotypes.

A99 – Three Oxygen Saturation Targets for Discharge in
Children with Wheeze – An Observational Study.

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Objective: To assess the potential effect of three guideline discharge
oxygen saturation (SpO2) targets (≥90%, ≥94% and ≥94%) on length of
hospital admission in children with acute wheeze.

Methods and patients: Children aged 1 year up to 16 years admitted
with wheeze (requiring supplementary oxygen for SpO2 (≥94%)) were
assessed in air every 4 h over nine months (11/14 – 08/15). Time from
admission for SpO2 to become stable for at least 4 h at ≥90%, ≥92% and
≥94% was recorded. In addition, time to clinical stability was also
collected, defined as requiring a frequency of four hourly salbutamol
inhaled or less.

Results: 140 children, median age 2.8 years, were included. Median
length of stay was 71 hours (h). Five children were admitted to high
dependency. Sixty-three percent (88/140) had a viral or bacterial agent
identified. Details on inhaler frequency were missing in five children and
eleven children did not receive inhaled salbutamol during admission.

SpO2 became stable for at least 4 h at 8h (IQR 5–20), 17h (IQR 7–30),
and 22h (IQR 11–33) for targets of ≥90%, ≥92% and ≥94% respectively.
Time to achieve a stable SpO2 ≥90% was a median of
0h (IQRRO-12h) and 4h (IQR 0-16h) sooner than SpO2 at ≥92% and ≥94,
respectively. There was a time lag in 47% (66/140) children between
SpO2 targets of 90% and 92%, and 57% (80/140) between SpO2 targets of
90% and 94%. The median time lag in these children was 12h
(IQR 8-19h) and 15.5h (IQR 8-24h) for SpO2 of ≥92% and ≥94%
respectively.

The median time to stability of inhaler frequency in all children in
whom this was recorded (n = 124) was 14h (IQR 10–21.5h). 68% (84/
124) of children reached stability of inhaler frequency after achieving a
stable SpO2 ≥90%, 51% (63/124) for ≥92% and 44% (54/124) for
≥94%. For those children with a time lag between different oxygen
saturation targets, 58% (SpO2 90–94%) and 20% (SpO2 92–94%)
reached stability of inhaler frequency after achieving a stable SpO2.

Discussion and Reflections: Our results show that reducing SpO2
targets could potentially reduce the length of stay in approximately
50% of children above 1 year of age with acute wheeze. However, in
58% of these children, clinical stability, as defined by only requiring
regular four hourly salbutamol inhalers, was reached after achieving
stable SpO2 reducing the potential number of children fit for earlier
discharge at lower SpO2 targets to 25% (31/124) and 9% (11/124) for
targets of SpO2 ≥ 90% and SpO2 ≥ 92% respectively. Results indicate
the need to ensure wheeze control is achieved before a potential
discharge at lower accepted SpO2 targets.

Conclusions: Allowing lower SpO2 of ≥90% as discharge targets
could reduce length of stay in around a quarter of children with
wheeze. Although this SpO2 target level has been shown to be safe
in infants with bronchiolitis, safety and the effect on clinical status
post discharge needs to be studied in older children with acute
wheeze and a randomized control trial is merited to answer these
questions.

A102 – Heterogeneity of Childhood Asthma in Korea:
Cluster Analysis of Children with Asthma from the Korean
Childhood Asthma Study (KAS)

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Background: Asthma is a heterogeneous airway disease with various
clinical phenotypes in children. It is important to clearly identify clinical
phenotypes to achieve better asthma management and to predict the
prognosis. Investigating the asthma phenotype remains rarely under-
stood in Korea. This study aimed to identify the phenotype of asthma
in Korean school-aged children.

Methods: We enrolled 706 children with physician-diagnosed asthma
from the Korean childhood Asthma Study (KAS) cohort which is a
3-year prospective follow-up study at 6-months intervals. At every
visit, questionnaire survey and pulmonary function tests were
conducted, and methacholine challenge test, blood tests, and skin
prick tests were conducted at the first time visit. We classified 183
children with asthma from the Korean childhood Asthma Study (KAS)
cohort into 4 clusters using hierarchical cluster analysis.
ABSTRACT

Results: Cluster analysis of the KAS cohort indicated four asthma phenotypes. Cluster 1 (40.3%) of children was characterized by late-onset, male-dominant, atopic asthma; cluster 2 (39.8%) was early-onset, male-dominant, atopic asthma with a history of bronchiolitis; subjects in cluster 3 (8.2%) consisted of puberty-onset, female-dominant atopic asthma having the lowest lung function; and cluster 4 (11.7%) was associated with early-onset non-atopic asthma.

Conclusions: Our results indicate that Korean children with asthma can be classified into four distinct clusters. Identification of asthma phenotypes may facilitate prediction of prognosis and response to treatment in heterogeneous phenotypes of asthma.

Funding: This study was supported by a grant (2016ER670300) from the Research of Korea Centers for Disease Control and Prevention, Republic of Korea.

Key words: Asthma, children, cluster analysis, classification, phenotype

A133 – Asthma Knowledge, Attitudes and Practices of Parents of Asthmatic Children in the Outpatient Department of a Tertiary Care Institution

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Introduction: Bronchial asthma is a common childhood respiratory condition. Objectives of management of patients with asthma include decreasing exposure to environmental triggers and decreasing the use of anti-inflammatory controller medications. The knowledge, attitudes and practices (KAP) of parents of asthmatic children have a big influence on the quality of life of asthmatic children as these determine the care that they give.

Objectives: This study investigated the asthma KAP of parents with asthmatic children who consulted at the outpatient department of a tertiary hospital. It determined if there was a difference in the asthma KAP of parents of children with controlled versus uncontrolled asthma and if there was a correlation between the asthma KAP of parents of asthmatic children and the number of emergency room (ER) consults and hospital admissions for asthma in the immediate past year.

Methods: In this descriptive, cross-sectional study, parents of patients one-year-old and older diagnosed with bronchial asthma during the past six months were included. Excluded were parents who were younger than 18 years old and those whose children had other active chronic conditions aside from asthma.

Results: A total of 66 subjects participated in the study. Partly and uncontrolled asthma was observed in 21.2% of the subjects’ children. Most parents had a good knowledge of asthma, its signs and symptoms (87.9%), and its management (86.4%). Half of the parents (50%) were anxious about their children practicing physical activities for fear that these will provoke an asthmatic attack. The majority of parents were able to initiate home measures (80.3%), administer the correct drug in the proper timing (98.5%), seek the physician early on (92.4%), institute proper timing (98.5%), seek the physician early on (92.4%), institute early treatment in mild symptoms (92.4%), and adhere to the physician’s medication orders (97%) to decrease the occurrence of attacks. There was no difference in the asthma KAP of parents of children with controlled versus uncontrolled asthma. Among the subjects with children with frequent ER consults and hospital admissions, their asthma KAP scores were higher than those with no ER consults and hospital admissions, although these variables were not statistically significant.

Conclusion: Parents of asthmatic children in a tertiary hospital had a good level of KAP on bronchial asthma comparable to those in other countries. The asthma KAP of parents with children whose asthma was controlled did not differ from those whose children had uncontrolled asthma. Frequent ER consults and hospital admissions may provide parents with opportunities to achieve higher asthma KAP scores.

A150 – The Prevalence of Passive Smoke and Impact on Childhood Asthma Symptoms

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Introduction: Asthma is a chronic, frequent disease with high morbidity in childhood. Indoor exposure to allergens and irritants, including cigarette smoke, affects the control of asthma symptoms.

Objective: We aimed to verify the prevalence of passive smoke and repercussions on childhood asthma symptoms.

Methods: The sample consisted of 384 asthmatic patients, aged 2 to 14 years. A complete interview with the child and his/her parents regarding asthma symptoms, treatment in use, exacerbations and hospitalizations as well as a clinical evaluation were performed. Social and economic aspects were also evaluated.

Results: Exposure to passive smoking was present in 55% of the children. Household agglomeration, lower family income, lower level of maternal and paternal schooling were significantly observed in the exposed group. The exposed population showed a higher frequency of asthma classified as moderate, greater use of inhaled corticosteroids and greater frequency of diurnal symptoms (present at least once a week in 60% of patients). The prevalence of asthmatic children exposed to passive smoking was high. Low socioeconomic condition was confirmed in the exposed group. Moderate severity, greater use of inhaled corticosteroids and greater frequency of diurnal symptoms were observed in the exposed group. Effective measures to combat passive smoking should be taken immediately as an essential strategy for the control of childhood asthma.

A151 – Clinical, Functional and Sputum Cytology Evaluation in Patients with Post-infectious Bronchiolitis Obliterans.

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Introduction: Bronchiolitis is a common respiratory infection in early childhood. Post-infectious bronchiolitis obliterator is a complication of bronchiolitis that can cause persistent or recurrent wheezing, requiring hospitalization and difficult to treat. The prevalence of this condition is unknown. The clinical, functional, and cytology evaluation of sputum in patients with post-infectious bronchiolitis obliterator is important to assess the severity of the disease and guide the treatment.

Objectives: The objectives of this study were to evaluate the clinical, functional, and sputum cytology in patients with post-infectious bronchiolitis obliterator.

Methods: This was a prospective, observational study of patients with post-infectious bronchiolitis obliterator. The clinical evaluation included symptoms, physical examination, and laboratory tests. The functional evaluation included pulmonary function tests and sputum cytology. The sputum cytology was analyzed for the presence of eosinophils, lymphocytes, and neutrophils.

Results: A total of 30 patients were included in the study. The majority of patients (76.7%) had a history of bronchiolitis. The clinical evaluation showed persistent or recurrent wheezing in 86.7% of patients. The functional evaluation showed a decrease in forced expiratory volume in one second (FEV1) in 90.0% of patients. The sputum cytology showed an increase in eosinophils in 53.3% of patients.

Conclusion: The clinical, functional, and sputum cytology evaluation in patients with post-infectious bronchiolitis obliterator are important to assess the severity of the disease and guide the treatment. Eosinophils in the sputum are an important marker of the disease.

Conclusion: The clinical, functional, and sputum cytology evaluation in patients with post-infectious bronchiolitis obliterator are important to assess the severity of the disease and guide the treatment. Eosinophils in the sputum are an important marker of the disease.
**ABSTRACT**

**Introduction:** Post-infectious bronchiolitis obliterans is a rare lung disease that occurs after severe insult to the small airways caused by viral bronchiolitis or viral pneumonia before 3 years of age. It is characterized by respiratory symptoms compatible with lower airways obstruction, lung function tests (LFT) demonstrating obstructive pattern and tomographic changes such as mosaic attenuation, bronchial thickening, bronchiectasis and atelectasis.

**Objective:** The aim of this study was to evaluate the clinical findings, lung function and sputum cytology in patients with bronchiolitis obliterans who attend an outpatient clinic.

**Methods:** Twenty-three patients aged less than 21-years-old diagnosed with bronchiolitis obliterans were invited to participate. They underwent LFT, CT scan, skin prick test (SPT) for aeroallergens, induced sputum using Pizzichini et al. methodology, and were classified according to Spanevello et al.

**Results:** Thirteen patients were included and signed the consent, 12 underwent LFT and all had an induced sputum sample collected. Three sputum samples were discarded due to low cellular viability. Five (38%) patients reported daily symptoms while 8 (61.5%) reported symptoms during physical activity. All patients showed tomographic alterations, mosaic pattern (84%) and bronchial thickening (76%). Nine (90%) demonstrated obstructive ventilatory disorder and 4 (25%) had positive bronchodilator LFT. Four sputum samples showed a neutrophilic cytological pattern, while 2 were eosinophilic, and 4 were mixed (eosinophilic-neutrophilic). Eight patients reported associated allergic diseases and were positive for SPT.

**Conclusion:** A correlation was not demonstrated between daily symptoms or exercises, severity of the obstructive ventilatory disorder, tomographic findings and cytological sputum patterns. There is a possibility of asthma and bronchiolitis obliterans coexistence.

**A171 – Vitamin D Levels in Asthmatic and Healthy Children in Singapore.**

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**Background:** Asthma is one of the most common chronic diseases affecting children, and there has been much interest in the relationship between vitamin D and asthma symptoms. Vitamin D is involved in the support of immune regulation, by regulating the actions of lymphocytes, mast cells, antigen-presenting cells and structural cells to dampen excessive inflammatory responses. Establishing a causal relationship between vitamin D and asthma could result in a simple yet important preventive and therapeutic strategy in the management of asthma. Several case-control studies showed that vitamin D insufficiency is more prevalent among asthmatic children. However, there is a lack of uniformity among studies in the current literature body in demonstrating correlation between vitamin D levels and control of asthma. Obtaining local data on the prevalence of vitamin D insufficiency in both asthmatic and control populations is important in justifying further research on this relationship, as this is currently unknown in Singapore. Our hypothesis was that asthmatic children had significantly lower vitamin D levels than controls.

**Methods:** We conducted a cross-sectional study with a case-control design on children aged 7–16 years of age attending pediatric outpatient clinics at a tertiary hospital in Singapore. Children were recruited as cases if they fulfilled the following criteria: they had a diagnosis of asthma made on clinical grounds, and either (1) uncontrolled asthma, as defined as an Asthma Control Test score of 19 or less, or (2) asthma requiring control with at least 200mcg of inhaled beclometasone-equivalent dose per day at time of entry into the study. Serum 25-hydroxy vitamin D (25-OH vitamin D) levels were measured by the hospital laboratory from blood samples taken by venepuncture from these children. Vitamin D levels were categorized as sufficient (30 μg/l or greater), insufficient (20–30 μg/l), or deficient (20 μg/l). Controls were selected to match the age, gender and ethnicity of cases. Children were excluded if they had a history of consumption of calcium and vitamin D supplementation or drugs that modulate vitamin D levels, a history of significant chronic medical diseases (other than asthma in cases), or had a first-degree family history of vitamin D deficiency.

**Results:** 20 cases of children with asthma who fulfilled the inclusion criteria were recruited for the study. This group was comprised of 12 males and 8 females. Nine children were of Chinese ethnicity, 9 were of Malay ethnicity, and 2 were of Indian ethnicity. Age range was 8 years 0 months to 16 years 11 months (men age 12 years 5 months). The control group consisted of 20 healthy children who were age, gender and ethnically matched (age range 8 years 11 months to 16 years 11 months, mean age 11 years 11 months). There was no significant difference in household income between the two groups (p = 0.53). The mean vitamin D level for the asthma group was 23.5 μg/l (range 8.4–44.5 μg/l, standard deviation 9.47 μg/l), and the mean level for the healthy controls was 20.1 μg/l (range 5.3–31.9 μg/l, standard deviation 7.63 μg/l). There was no significant difference in vitamin D levels between the two groups (p = 0.27). Thirty-three of the 40 children (82.5%) had vitamin D levels that fell below our threshold for sufficiency (30 μg/l), with 6 children from the asthma group showing vitamin D deficiency (<20 μg/l) and 8 healthy controls showing vitamin D deficiency.

**Discussion:** A recent systematic review on vitamin D levels and asthma in children found that mean vitamin D levels pooled from 10 case-control studies had shown significantly lower vitamin D levels in asthmatic children compared to non-asthmatic children. However, taken separately, five of these studies showed no significant difference in vitamin D levels between asthmatic and non-asthmatic children. Our data did not show a significant difference in vitamin D levels between asthmatic and non-asthmatic children, consistent with the findings of these studies. We have therefore not shown an association between vitamin D levels and asthma in our study population. The sample size was small, and this may account for the statistically non-significant association. What our study did show, however, was a high prevalence
of vitamin D insufficiency and deficiency in our study population, regardless of whether the children were asthmatic or not. Our data is at the higher end of the spectrum of prevalence of vitamin D deficiency and insufficiency compared to other studies in the literature body looking at vitamin D deficiency among asthmatic and non-asthmatic children. The prevalence is slightly higher than a previous study in Singapore which showed a prevalence of 76.1% for vitamin D insufficiency and deficiency in adults. In studies looking at vitamin D deficiency in tropical countries, several factors have been postulated to contribute to poor vitamin D status—unfortified food in the local diet and a lack of sun exposure due to lifestyle habits being two of the more likely factors. While these may account for the high prevalence of vitamin D insufficiency found in our study participants (children in Singapore tend to spend more time indoors than outside the home due to the hot weather and high humidity), we did not investigate for these factors in our study, and can therefore not draw conclusions from our data.

Conclusion: There was no significant difference in vitamin D levels in asthmatic children compared to non-asthmatic healthy controls in our population. However, the prevalence of vitamin D insufficiency is high. Further studies are needed to investigate why vitamin D insufficiency is so highly prevalent in children living in a tropical country such as Singapore.

A176 – Inflammatory Phenotypes and Instability of Induced Sputum Inflammation in Children with Severe Therapy-Resistant Asthma: A Case-Control Study.

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Background: Induced sputum (IS) has been an important tool to assess airway inflammation in children with asthma. However, the pattern of airway inflammation in children with severe therapy-resistant asthma (STRA) has not been widely studied. We report in this study the characteristics of the inflammatory pattern and granulocytic cell counts in children with severe asthma compared to mild to moderate asthma, including sequential sputum procedures.

Methods: Children and adolescents (6–18 years) with STRA and mild to moderate asthma (MMA) were selected according to GINA and ERS/ATS criteria. Induced sputum was collected from all patients, and was repeated between 6 and 12 months in a sub-group of subjects. The type of inflammation, granulocytic cell counts and instability of inflammation of the induced sputum was analyzed. The association of inflammatory cell counts and lung function results was also assessed.

Results: 99 subjects were selected, with a mean age of 11.3 ± 2.1 years, and 53% female subjects (STRA: n = 23 and MMA: n = 76); 182 induced sputum procedures were performed (success rate: 64%). The group of STRA children exhibited the following inflammatory phenotypes: 6/23 (26%) were eosinophilic, 26% neutrophilic, 4/23 (17.5%) mixed and 7/23 (30.5%) paucigranulocytic. There was no significant difference in the inflammatory phenotypes, eosinophil and neutrophil counts in induced sputum between the STRA and MMA groups. When abnormal lung functions were selected, neutrophil counts were significantly and negatively correlated with FEV1 (r = −0.69, p = 0.01). In those STRA children with sequential sputum performed, 10/12 (83%) subjects changed inflammatory phenotype. All children with neutrophilic sputum did not respond clinically to a trial of macrolide therapy.

Conclusions: The inflammatory phenotype of induced sputum in children with asthma is very heterogeneous, regardless of the severity of disease, and most children with STRA changed inflammatory phenotype in sequential induced sputum procedures. The role of induced sputum in the management of children with STRA is still unclear, and the understanding of neutrophilic inflammation should be better explored in this group of patients.

A187 – Defining and Diagnosing Asthma in the Infant and the Preschooler: A Systematic Review.

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Introduction: There is disagreement among Spanish pediatrician experts relative to asthma diagnosis in infants and preschoolers. We present the results of a systematic review of asthma guidelines to answer some key questions regarding the diagnosis of asthma in infants and preschoolers, as a preliminary step to reaching a consensus among Spanish pediatricians on this subject.

Methods: Key questions:

Is there a specific definition for asthma in children under 6 years old?

Is it possible to diagnose asthma at any age, including the first year of life?

Is it necessary to perform pulmonary function tests in order to make the diagnosis of asthma in children under 6 years of age?

Are there defined and objective criteria for the diagnosis of asthma in children under 6 years old?

Is it possible to diagnose asthma in preschoolers even though the disease may remit at 6 years of age or later?

Search strategy: We performed a systematic search of scientific literature published between 2007 and 2016 to identify and select clinical practice guidelines (CPGs) related to asthma management. We initially searched in the database of clinical guidelines Trip Database
Inclusion and exclusion criteria: We included CPGs that aimed to provide diagnostic and therapeutic recommendations on the care for children and/or adolescents and adults. The documents were considered as a guideline if they met the following criteria: provided practical clinical recommendations for children, adolescents or adults, and collected all related documents and supporting materials. We excluded documents without information regarding the concept or diagnosis of asthma in childhood, including the first 6 years of life.

Analysis: The guidelines included in the review were subjected to several exploratory analyses conducted by LM, with the participation of all the researchers. Given the descriptive nature of the sections related to the concept and diagnosis of asthma, questionnaires were designed to find out how the guidelines considered the diagnosis of asthma in young children, especially in terms of the age at which it could be established, the diagnosis and the premises (clinical criteria or complementary tests) to make this diagnosis. The authors responded to these questionnaires and they contributed with comments via e-mail to clarify the discrepancies. Discrepancies were resolved by agreement among reviewers.

Results: We obtained 2338 references with the initial search in Trip Database and PubMed (Figure 1). Through manual search, we added 7 more guides. Finally, 22 documents were analyzed and grouped into 20 guides, given that 2 of the guides were considered to be integrated by 2 different documents whose contents were judged as complementary. Nine guidelines referred to patients of all ages, 8 were pediatric and 3 were dedicated exclusively for preschoolers. Regarding questions, the results were:

In most guidelines, the concept and definition of asthma are closely linked to their diagnosis. In the general guidelines, distinction is not made between the definitions of adult or pediatric asthma.

Most asthma guidelines recognize, generally implicitly, that there is not an age limit to establish the diagnosis of asthma, but highlight the difficulty to establish the diagnosis under 5–6 years.

Spirometry is not considered essential to establish the diagnosis in preschoolers, although the difficulty in carrying it out is an inconvenience that makes it difficult to confirm the diagnosis.

In most of the guidelines, asthma diagnosis in preschool children is based on the subjective interpretation that the pediatrician makes of the clinical findings, treatment response and exclusion of other alternative diagnoses. They also rely on the performance of some complementary tests that rule out or increase the probability of diagnosis.

The ERS guideline on preschool wheezing is the only one to indicate that the disappearance of symptoms in later years is what distinguishes those who really suffer from asthma from those who do not. Some guidelines accept that asthma may remit over time (for example, ICON and Japan's child) and, therefore, it would not be an impediment to establish the diagnosis.

Conclusion: There is an apparent agreement among most national and international guidelines to consider that the diagnosis of asthma in preschool child is syndromic and that it can be established at any age, even though respiratory function tests cannot be performed.

Reflection: We believe that there is, therefore, a good basis for the performance of a consensus that formalizes the findings of this review.
ABSTRACT

Methods: The immune status of pediatric patients diagnosed with healthcare-associated pneumonia as a potential agent to specifically alter the inflammatory response and immune function of an individual during the disease process that is measured indirectly by soluble human leukocyte antigen type DR (sHLA-DR) level.

Objective: To determine the effect of adjunctive arginine therapy on the immune status of pediatric patients diagnosed with healthcare-associated pneumonia.

Study Design: Randomized, Double-Blinded, Placebo-Controlled Trial

Methods: All patients aged 1 month old to 18 years old admitted at the Pediatric ER, Wards 6, 9, 11, Trauma and Burn Unit, diagnosed with a first bout of healthcare-associated pneumonia regardless of the current hospital stay, empirically treated with IV antibiotic and on enteral nutrition either per orem or through feeding tubes, were included in the study. Patients who were enrolled in the study were randomized into two (2) groups by means of a computer-generated randomization table. One group received the dietary supplement and the other the placebo. The dietary supplement group received L-arginine 200 mg/kg/day three times a day per orem for 7 days as an adjunct to the appropriate intravenous antibiotics not exceeding 3 grams/day. Blood samples were collected from all recruited subjects for baseline levels of plasma arginine and serum sHLA-DR and repeat blood extraction after 7 days of supplementation and treatment for healthcare-associated pneumonia.

Data were encoded in Microsoft Excel and analyzed using SPSS. All variables were numerical variables and expressed as mean and standard deviation. All variables underwent T-test for numerical variables. Pearson correlation was also used to test the relationship of the plasma level of L-arginine with sHLA-DR level between the dietary supplement and placebo groups.

Results: There were a total of 40 patients recruited in the study. Seven (7) subjects were withdrawn from the study; five (5) of whom were due to protocol non-compliance and two (2) had deceased due to acute respiratory failure as complication of the underlying disease, thus only 33 subjects were included. There were 16 and 17 subjects recruited to the respective supplement and placebo groups. There was no significant difference between the two groups in terms of age, weight, gender and use of oxygen support.

The Arginine levels on Day 1 of both supplement and placebo groups were the same and showed no significant difference (p value = 0.71). The Arginine levels on Day 8 of the supplement group however had a higher level compared to the placebo group but was not statistically significant (p value = 0.27). Regarding the sHLA-DR levels of both groups, the supplement group had a lower level on Day 1 as well as after supplementation (Day 8) compared to levels of the placebo group. Both sHLA-DR levels of the two groups were not statistically significant. However, both sHLA-DR levels of both groups were below the set threshold level, hence both groups had low sHLA-DR levels.

Further analysis of the data comparing arginine and sHLA-DR levels on day 1 to levels after 7-day supplementation (Day 8) showed that, in the supplement group, arginine levels at baseline and after 7 days of supplementation increased which was statistically significant (P value = 0.04). In the placebo group, the Arginine levels at baseline and after 7 days of supplementation also increased, however they were not significantly different (P value = 0.31).

Data on arginine and sHLA-DR levels both at baseline (Day 1) and after 7 days of supplementation (Day 8) were compared although showed no correlation between the level of arginine and sHLA-DR in both groups with Pearson’s r values of less than 0.8.

Conclusion/Recommendations: In this study, the data of 33 patients were analyzed. There was no general trend and no correlation between arginine level and soluble HLA-DR level from baseline and after 7 days of supplementation. In conclusion, arginine supplementation as an adjunct to IV antibiotics did not improve the immune status of patients with healthcare-associated pneumonia. Further studies are needed focusing on the dietary intake of each subject prior to supplementation as well as during the duration of therapy. It is recommended that future studies have a longer duration of supplement intake. Furthermore, arginine and sHLA-DR levels should be monitored even after 7 days of supplementation as well as a greater number of patient subjects recruited for the study.

C9 – Lobectomy as a Life-Saving Procedure Following Life-Threatening Necrotizing Pneumonia in a Toddler – A Case Study.

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Necrotizing pneumonia is a severe form of pneumonia caused by highly virulent bacteria, mainly Streptococcus pneumoniae and Staphylococcus aureus. Treatment is primarily conservative, while surgical intervention is still controversial.

We report a unique case of necrotizing pneumonia due to group A streptococcus infection in an 18-month-old boy. Severe respiratory failure required extracorporeal membrane oxygenation (ECMO) support as a bridge to recovery. Following surgical lobectomy, the child was weaned off ECMO and recovered uneventfully.

Cases of necrotizing pneumonia requiring ECMO support present a unique clinical challenge. A conservative approach includes watchful waiting for respiratory improvement while on ECMO support. However, an alternative approach stipulates surgical intervention to facilitate ECMO withdrawal.
Our patient’s necrotizing pneumonia was successfully treated by surgical lobectomy while he was on ECMO support. Thus, we suggest surgical lobectomy as a suitable option in select cases of necrotizing pneumonia not responding to conservative medical treatment.

C16 – Prevalence of Extrapulmonary Tuberculosis among Patients Aged 1–18 Years Admitted in a Government Hospital from 2014–2016 – A Retrospective Study.

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Background: Tuberculosis or TB is an infectious disease caused by the bacteria called Mycobacterium tuberculosis which is a curable and preventable. Extra-pulmonary TB (EPTB) refers to tuberculosis involving organs other than the lungs. According to the Department of Health (DOH Philippines, 2014), tuberculosis remains a major public health problem in our country. In 2010, TB was ranked as the 6th leading cause of mortality across all ages, with 26.3 deaths for every 100,000 population and accounted for 5.1% of all total deaths. There may also be an increased risk of having more cases of EPTB in our country. This study aims to provide an overview on the prevalence of EPTB among pediatric patients and help increase awareness of the magnitude of the problem in order to improve management of Tuberculosis programs among the pediatric population in the country.

Objective: To describe the prevalence of extrapulmonary tuberculosis among pediatric patients aged 1–18 years old in a tertiary government hospital.

Study Design: Retrospective, descriptive study (chart review).

Setting: A Tertiary Government Hospital in Manila (Ospital ng Maynila Medical Center)

Population: Patients diagnosed with extrapulmonary tuberculosis aged 1–18 years old admitted in a tertiary hospital between 2014 and 2016.

Study Methods: Permission was obtained from Ospital ng Maynila Medical Center. The consent of all patients who were admitted at Ospital ng Maynila Medical Center with the diagnosis of extrapulmonary TB from year 2014–2016 was obtained. The charts or patient’s file were retrieved from medical records. Demographic and socio-economic features, clinical findings, laboratory, treatment and outcome information were obtained. Data were arranged in tables expressed as proportions and percentages.

Results: This study showed that there was a prevalence rate of 0.35% for extrapulmonary TB among all pediatric admission for the years 2014–2016. The majority of the cases were children aged 1–5 years old, 64% with a mean age 10 years old. There appeared to be no sex predilection with regards to extrapulmonary TB. A majority of the cases had no known TB disease or TB exposure. Common cases of EPTB included TB meningitis (84%) presenting with changes in behavior or decrease in sensorium. Gastrointestinal TB (8%) presented with abdominal distention and one case of TB Uveitis who presented with whitish lesion in the cornea of the eye. Among these patients, 33% were discharged as improved including and 42% died all of whom were TB meningitis patients.

Conclusion: With these data, we can say that there is a need to strengthen the National TB program in terms of active case finding so that we can further decrease the transmission of TB in the country and initiate early treatment. There is also a need to educate health care workers to identify possible cases of EPTB to prevent possible fatal outcomes. Since TB meningitis has a poor outcome, health care professionals should be vigilant and be more aggressive in treating these cases.

C33 – Effect of Passive Smoking Exposure on Development of Childhood Pneumonia and Illness Severity.

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Objective: Previous research has shown that passive smoking exposure is associated with wheezing, chronic cough, asthma and bronchiolitis in children. Research studies on pneumonia are limited and based on questionnaire studies. Since 2008, smoking cessation has begun to be applied in closed areas in Turkey. In previous studies, urine cotinine / creatinine threshold value, which shows passive smoking exposure is associated with wheezing, chronic cough, asthma and bronchiolitis in children. Research studies on pneumonia are limited and based on questionnaire studies. Since 2008, smoking cessation has begun to be applied in closed areas in Turkey. In previous studies, urine cotinine / creatinine threshold value, which shows passive smoking exposure in children, was evaluated as 60 ng / mg in our country. Our aim is to objectively evaluate the effect of passive smoking on pneumonia development and illness severity in childhood.

Methods: Between December 2015 and April 2016, children under the age of 5 with pneumonia and age-matched healthy controls were included in the study in three pediatric pulmonology centers. A questionnaire was applied to the parents regarding demographic data and smoking status at home. Urine cotinine / creatinine levels were measured as objective indicators of passive smoking exposure. The pneumonia group was grouped as mild and severe according to disease severity. The data of patient and control groups as well as children with mild and severe pneumonia in the pneumonia group were compared with each other.

Results: There were 74 children in the study group and 153 children in the control group. Overall, 52% of children in the study group and 54% of children in the control group had passive smoking exposure. Urine cotinine / creatinine levels of children exposed to passive smoking were higher than unexposed children. There was a significant difference between the study and control groups in terms of age, monthly income, number of people living at home, age of mother and father, and time spent outside the home (p < 0.05). The cotinine /
creatinine level of the study group was higher than the control group. There was a significant difference between age and urine cotinine / creatinine levels in mild and severe cases in the study group (p < 0.05); 64.1% of the children with smoking exposure had severe pneumonia while 35.9% had mild pneumonia. ROC analysis revealed a urine cotinine / creatinine threshold of 2.47 ng / mg for passive smoking exposure.

Discussion: Objectively, it was shown that passive smoking exposure is associated with the development of severe pneumonia in children. The present findings are considered as promising given that the threshold value of passive smoking exposure after smoking cessation in our country was considerably lower than in previous studies.

C39 – Necrotizing Pneumonia Caused by Refractory Mycoplasma pneumoniae Pneumonia in Children.

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Objectives: The aim was to evaluate the clinical features of necrotizing pneumonia (NP) caused by refractory Mycoplasma pneumoniae pneumonia (RMPP).

Methods: A retrospective, observational study of NP cases caused by RMPP, who were hospitalized in our hospital from January 2008 to December 2015 was conducted, and clinical manifestations, laboratory data, imaging performance, hospital course and outcomes were analyzed.

Results: A total of 25 NP cases caused by RMPP were identified, with a median age of 5.1 (4.0 – 7.9) years. The mean length of total fever days and hospital stay days of these patients were 21.0 ± 8.9 days and 19.9 ± 9.9 days, respectively. The abnormal laboratory findings of elevated C-reactive protein (CRP), lactate dehydrogenase (LDH), interleukin (IL)-6, IL-10 and interferon gamma (IFN-γ) were observed in many of our patients. Meanwhile, pleural fluid characteristics associated with NP in the present study, particularly the high value of pleural fluid cell count, LDH and protein, was also observed. Most of the patients (80.0%) in our study were associated with pleural effusion, and had a high incidence of lobar atelectasis and pulmonary consolidation. Interestingly, the mean delay time for detecting necrotic lesions from onset of symptoms was 21.0 ± 6.9 days. Eighty percent (80.0%) of patients were administered corticosteroid and 100% of patients underwent bronchoalveolar lavage (BAL). Of the 20 patients who presented with pleural effusion, 11 had thoracocentesis alone and 2 had chest drainage. All patients received prolonged course of antibiotics (32.2 ± 8.7 days), and discharged without death. Follow-up studies showed that all patients recovered without surgical intervention, and chest radiographs revealed resolution or only minimal residual fibrotic change within 3.0 (2.0 ~ 6.0) months.

Conclusions: NP caused by RMPP should be recognized as a severe, yet self-limiting and reversible disease through appropriate managements.

C52 – Determinants of Pulmonary Complications in Childhood Mycoplasma pneumoniae Pneumonia

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Background: Mycoplasma pneumoniae (MP) is the major pathogen causing community-acquired pneumonia in children. Although Mycoplasma pneumoniae pneumonia (MPP) is usually benign and self-limited, it may develop into pulmonary complications. The aim of this study was to elucidate the clinical and laboratory characteristics of patients with early-onset (pleural effusion, necrotizing pneumonia, and acute respiratory failure) and late-onset (bronchiectasis and bronchiolitis obliterans) pulmonary complications after MPP.

Methods: A retrospective analysis was performed in children with MPP who were admitted to our hospital from January 2011 through December 2016. Of a total of 464 patients, 85 and 11, respectively, had early and late-onset pulmonary complications.

Results: The median age was higher in patients with early-onset complications (ECx) than in those without ECx, while it was not different between patients with and without late-onset complications (LCx). The median levels of lactate dehydrogenase (LDH), C-reactive protein, ferritin, C-X-C motif ligand 9, C-X-C motif ligand 10, interleukin (IL)-2Ra, IL-10, IL-18, interferon-γ and the median percentage of neutrophils in patients with ECx were higher than in those without ECx. In logistic regression analysis, ferritin >37.01 pg/mL (OR 11.75, 95% CI 1.07–229.29) and IL-10 >809.13 pg/mL (OR 6.57, 95% CI 1.05–50.58) increased the risk for ECx while LDH >1002IU/L (OR 20.31, 95% CI 3.45–386.38) increased the risk for LCx. Cox regression analysis showed that macrolide treatment for over 15 days (HR 13.83, 95% CI 1.68–113.61) and LDH >1002IU/L (HR 27.41, 95% CI 3.23–232.86) were significant determinants for LCx.

Conclusions: During the course of MPP, ferritin >37.01 pg/mL and IL-10 >809.13 pg/mL may promote timely recognition of early-onset complications and LDH >1002IU/L might be the significant predictor of late-onset complications.

C63 – Multidrug-Resistance in Congenital Disseminated Tuberculosis: A Rare Case Report from Indonesia

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Introduction: Recently, although childhood Multidrug-Resistance (MDR) Tuberculosis (TB) is increasing in Indonesia, congenital MDR TB however is still rare. We report a late diagnosed congenital
disseminated MDR TB case to increase awareness, particularly in countries with high-burden TB cases.

**Case Presentation:** A five-month-old girl infant was admitted to Hasan Sadikin General Hospital with respiratory distress, abdominal distention, hepatosplenomegaly, and poor feeding with failure of weight gain. She was referred by a private hospital in Bandung with disseminated TB and no improvement after 4 months of standard TB treatment. Her mother had died 1.5 months postpartum because of meningitis TB and low CD4 count, but negative HIV status. Tuberculosis and HIV screening of all family member results were negative.

The baby was normal until she exhibited fever and abdominal distention at 1 month after birth. She was diagnosed with pneumonia and hospitalized for 13 days without any improvement, leading her father to bring her to another hospital. In this hospital, she was diagnosed with pulmonary TB, and treated with antituberculosis drug. Furthermore, she was hospitalized several times because of pneumonia, recurrent pleural effusion, and also miliary TB with Antituberculosis Drug-Induced Hepatotoxicity (ADIH). She also had low CD4 but negative HIV status, anemia, thrombocytopenia, hypoalbuminemia, and high C-reactive protein (CRP) level. MRI and chest-abdominal CT scanning showed bilateral pulmonary TB, pleural effusion, multiple lymphadenopathy, hepatosplenomegaly with multiple nodules with central necrotic areas, adrenal TB, and spondylitis TB.

The Xpert MTB/RIF results in both induced sputum and feces specimen were *Mycobacterium tuberculosis* detected with Rifampicin resistance, although the AFB smear result was negative. In day 4 after admission, respiratory distress worsened accompanied with decreased hemoglobin level and sepsis, thus blood culture-based antibiotic and PRC transfusion were given. Sensory neural hearing loss (SNHL) found by audiometry screening resulted in capreomycin being chosen as injection drug combined with levofloxacin, ethionamide, cycloserine, ethambutol, and pyrazinamide for the MDR TB regimen. After 30 days of treatment, respiratory distress decreased, hepatomegaly was smaller, and bodyweight increased. She was finally discharged after being hospitalized for 2 months, and the MDR regimen was continued.

**Conclusion:** TB screening in pregnancy and infants born from mothers with suspected TB is very important. MDR TB should be suspected in an infant with unresponsive pneumonia and standard TB treatment who are born from a mother deceased due TB. Late diagnosis, disseminated TB and MDR resulted in poor prognosis in this congenital TB case.

**Keywords:** Multiple Drug Resistance; Congenital Tuberculosis; Disseminated Tuberculosis; Infant

C86 – Miliary Tuberculosis and Its Associating Factors

**Objective:** To investigate the epidemiology and characteristics of miliary tuberculosis in children in an Indonesian top referral hospital, Cipto Mangunkusumo Hospital (CMH).

**Methods:** A retrospective study from 2014 to 2017 was performed to investigate the profile of miliary tuberculosis in children.

**Results:** From 2014 to 2017, 483 children were treated as tuberculosis. Miliary tuberculosis was diagnosed in 21 children (4.35%). Among these, 57% were female, 23.8% were under 2 years of age, while a majority (61.9%) were older than 10 years old. BCG vaccination was administered in 61.9% of children. Forty-two percent were mildly malnourished, and 38% were severely malnourished. No HIV infection was found in these patients. GeneXpert was positive in 47% and all were rifampicin-sensitive. Only 9 children underwent a tuberculin test, which yielded a positive result in 1 child. Mortality rate among miliary tuberculosis children was 28.6%.

**Conclusions:** Miliary tuberculosis is prevalent among children older than 10 years old (adolescents). Most of these children are female, and have been vaccinated. Bacteriological confirmation should be performed in miliary tuberculosis patients since positive results are high. Almost 30% of the cases result in mortality. This may raise the notion for prophylaxis among adolescents in high endemic countries.

**Keywords:** tuberculosis, miliary, adolescent.

C87 – Pulmonary Tuberculosis and Scrofuloderma in Marasmic Kwashiorkor Children: A Case Report.

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**Background:** Pulmonary tuberculosis (TB) and extrapulmonary TB can sometimes simultaneously occur, especially in child malnutrition. Scrofuloderma is one form of cutaneous TB whose infection route is always endogenous, usually secondary to joint and lymph node TB and dependent on individual immunity and environmental factors. Clinical lesions appear as nodules, gumma and ulcers due to fistulae, occurring in children and young people. Very few pediatric patients with pulmonary TB and scrofuloderma have been reported.

**Case:** A 10-year-10 month-old boy was referred to the department of child health with shortness of breath, abdominal enlargement and swelling of the leg, with normal urination and defecation, for 2 weeks. History of low grade fever, chronic cough, loss of appetite, decreased body weight, nodules in the neck, armpit, upper chest, no pain, since 1 year. Then, in 1 month, the nodules became reddish and ruptured, discharging pus, after which other nodules started to appear. We found signs of dyspnea with rales, multiple hypertrophic crustied ulcers with skin tract at the colli, axilla and infraclavicular regions, abdominal enlargement due to ascites and edema of the leg, and clinical marasmic kwashiorkor. Tuberculin skin and HIV rapid tests were negative, a rapid molecular test detected very low *Mycobacterium tuberculosis* (Mtb), and hypoalbuminemia. Skin biopsy showed specific chronic
inflammatory granulomatous. Anti-tuberculosis therapy (ATT), albumin, antibiotic, and nutritional therapy was administered. Significant improvement was observed after 1 week of treatment.

Discussion: One-third of the world’s population is infected with Mtb and the global burden of the disease continues to grow, depending on the individual immunity and environmental factors of the children. The typical patient is adolescent with malnutrition and low socioeconomic conditions from crowded environments. In the present case, specific scrofuloderma lesions, skin biopsy results, positive rapid molecular Mtb test and a good response to ATT favored the diagnosis of pulmonary TB and scrofuloderma in a marasmic kwashiorkor child. Scrofuloderma must be differentiated from some other similar lesions such as sporotrichosis and hidradenitis suppurativa by skin biopsy.

Keywords: pulmonary tuberculosis, scrofuloderma, marasmic kwashiorkor, children

C121 – Pneumological Endosonography in a Child with Tuberculosis – A Case Report.

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Background: Endobronchial ultrasound (EBUS & EUS-B) is an essential part of the bronchoscopic diagnosis of lung cancer and mediastinal lymphoma, especially in sarcoidosis and tuberculosis. To date, the possible uses in children have only been explored through a limited number of individual case reports, one prospective multicenter study (1) and one retrospective analysis (2).

Methodology: We report on a three-year-old boy with mitochondrialopathy and suspected tuberculosis due to contact with a tuberculosis patient and prolonged cough. Further diagnosis revealed a positive tuberculin skin test, a right lobe atelectasis and a bilateral hilum prominence. Gastric aspirates remained without germ detection. Despite triple therapy with INH, RMP and PZA, an increasing stenosis of the left main bronchus developed after 2 months. Bronchoscopically, lymph node penetration was the cause of the stenosis. Endosonographically (EBUS PENTAX), it was possible to visualize pathological lymph nodes via EBUS and EUS mediastinally on the left (position 2L, 7 and 9) and to perform a transesophageal EUS-B-FNA from position 7 and 9.

Results: Bronchoalveolar lavage showed acid-fast bacilli. The PCR for M. tuberculosis complex was positive. The EUS-B-FNA revealed a granulomatous inflammation of the TB type as well as the molecular pathological evidence for tuberculosis. Resistances were not found. After escalation of the therapy with EMB and passable prednisolone, the local findings and clinical picture improved.

Conclusion: The course shows that EBUS can be helpful in pediatric pulmonology. However, transesophageal puncture has to be preferred in very small patients, to reduce possible complications, especially bleeding, and to account for device limitations because of limited airway diameter. Further diagnosis of mediastinal lymphoma is also possible in children and recommended due to the broad range of possible causes.

C126 – Clinical Features of Tuberculosis in Pediatrics.

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Background: Tuberculosis (TB) infection and disease are still a global health problem in Indonesia, especially in children. Clinical presentation for childhood TB may vary depending on the epidemiological situation of TB.

Objective: To study the clinical features and investigation profiles of pediatric TB patients at various ages.

Methods: Retrospective analysis of 50 children with TB who were admitted to the Dr. Moewardi Hospital from November 2016 to November 2017 and included in the study. Clinical features and investigation profiles of patients were obtained.

Results: From the overall 50 pediatric TB patients, 20 were males and 30 were females. Pulmonary TB was more common (76%) than extrapulmonary TB (24%). BCG scar was present in 50% of cases. History of TB contact was present in 2%. The most common symptoms were fever (72%), cough (70%) and malnutrition (40%). Tuberculin skin testing was positive in 68%. GeneXpert was positive in 46%.

Conclusion: Fever is the most common presentation of pediatric TB, but it is not a specific symptom. GeneXpert and tuberculin skin tests are important diagnostic tools.

C127 – Characteristics of Tuberculosis in Children in Kariadi Hospital Semarang Indonesia.

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Background: Tuberculosis (TB) still remains a major problem in Indonesia, especially in children. Characteristics of the disease may differ between regions as well as site of infection.

Objective: To report the characteristics of pulmonary and extrapulmonary TB in children.

Methods: A retrospective descriptive study was undertaken in children aged 0 to 18 years admitted to Kariadi Hospital between 2015 and 2017. Data regarding TB, nutritional status, history of contact, demographics, sputum smear and GeneXpert result, HIV status and Tuberculin Skin Test (TST) were recorded. Chi-square was performed to analyze the variables.
**Results:** Of 215 children admitted with TB, 64.2% showed pulmonary TB and 35.8% extrapulmonary TB. There were 119 (55.3%) males and 96 (44.7%) females, with a median age of 6 years (range 0–18 years).

Nutritional status was 47% mild/moderate and 25.6% severe malnourished. HIV status was 6% positive, and 92.3% were pulmonary TB. History of TB contact was only 60% of whom 61.4% had positive TST. Positive sputum smear was found in 15.8% cases and GeneXpert was positive in 10.2% with 1 Rifampicin resistance. There was a statistical difference between pulmonary and extrapulmonary TB with regard to history of contact (p = 0.01). Fifty-five percent of over 14-year-old children had extrapulmonary TB compared to 26% and 37.1% in under 5 years old and 5–14 years old, respectively (p = 0.03).

**Conclusion:** Incidence of extrapulmonary TB was found higher in adolescence, and history of contact was higher in pulmonary TB.

**Keywords:** Pulmonary TB, extrapulmonary TB, children

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**C128 – Disseminated Tuberculosis in a Boy with HIV.**

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**Background:** HIV alters the pathogenesis of TB, increasing the risks of developing severe disseminated TB.

**Objective:** To describe a case of disseminated tuberculosis in a boy with HIV.

**Case:** A 3-year, 10-month-old boy was referred to the Kariadi Hospital with swelling in the left knee, chronic diarrhea, and severe malnutrition. Physical examination: oral thrush, multiple cervical lymphadenopathy, diffuse rales and crackles, inflamed left knee; ulcer with necrotic tissue and pus. TST was negative. Anthropometric score showed severe chronic malnutrition (WAZ –6.39 SD, HAZ –6.12 SD, WHZ –5.71 SD). He had normocytic normochromic anemia (5.4 gr/dL), a CD4 count 167 cells/µL and HIV screening was indeterminate although HIV viral load level was 9.060.457 copies/mL. Sputum smears revealed no AFB, and culture showed *Staphylococcus aureus* (ESBL). Left knee X-ray results suspected periosteal osteomyelitis; sonography suggested septic arthritis and periosteal reaction. Wound swab smears revealed positive AFB. Knee effusion staining was positive for AFB with Xpert MTB-RIF high detection of MTB but no rifampicin resistance. Biopsy of the left knee resulted in non-specific chronic inflammation. Wound culture and blood culture revealed *Staphylococcus aureus* (MRSA). Stool smears were positive for AFB and *Cryptosporidium* sp cyst. The patient was treated with cefoperazone sulbactam and vancomycin intravenously; RHZE, ART (zidovudine, lamivudine, efavirenz); azithromycin and paromomycin for *Cryptosporidiosis*; and cotrimoxazole. He was programmed for debridement and drainage, with application of back slab splinting. After 4 weeks, the child was discharged with improved condition. After 9 months of TB treatment, his left knee was no longer inflamed and the wound was improving, with X-ray showing no periostal inflammation although there remains joint effusion; no AFB was detected in wound swab smears. Physiotherapy was subsequently programmed. He still continues the maintenance phase of TB treatment and ART.

**Keywords:** Disseminated TB, HIV, children

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**C140 – Outcomes of Children Hospitalized with Pneumonia in West Nusa Tenggara Province General Hospital Indonesia.**

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**Background:** Pneumonia is a major cause of death in children younger than 5 years old, particularly in developing countries. Aside from a high mortality rate, pneumonia also causes a significant number of hospitalizations. We conducted this study to present the outcomes of children hospitalized with pneumonia in West Nusa Tenggara Province General Hospital.

**Methods:** A respirology registry of children aged 2 months to 15 years of age admitted with pneumonia from January 2015 to December 2016 was retrospectively reviewed. Demographic data, physical examination, laboratory and radiology findings, and outcomes were carried out in all children admitted with pneumonia.

**Results:** Out of the 392 children admitted with pneumonia, 187 (47.7%) were admitted in 2015 and 205 (52.3%) in 2016. The majority were male – 224 (57.1%), aged between 2 and 12 months – 259 (66.1%), and had Fe deficiency anemia – 215 (54.8%) as co-morbidities. Nine of 392 (2.3%) had very severe pneumonia, while 383/392 (97.7%) were hospitalized for more than 5 days, with an average length of hospital stay of 7.4 days (2015) and 6.8 days (2016). Overall, the mortality rate was 24/392 (6.1%), with 8/187 (4.3%) in 2015 and 16/205 (7.8%) in 2016, respectively. Eighteen of 24 (75%) were aged between 2 and 12 months, of whom 6/24 (25%) were admitted with very severe pneumonia, and 18/24 (75%) with severe pneumonia with two or more co-morbidities.

**Conclusions:** Although the mortality rate of children hospitalized with pneumonia in our hospital had increased from 2015 through 2016, the average length of stay in hospital nevertheless declined. These findings highlight the need for further prospective studies to identify the risk factors of prolonged hospital stay and mortality as poor outcomes in children hospitalized with pneumonia.

**Keywords:** outcome, pneumonia, hospitalized, children

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**C163 – Characteristics of Children Who Are in Close Contact with MDR TB Patients in Persahabatan Hospital.**

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**Background:** There are increasing MDR TB cases in Indonesian adults, which render the need for children who are in close contact with these MDR TB cases to be closely observed, because of the risk of contracting MDR TB from adult patients.

**Objective:** To examine the pediatric population in the household of adult MDR TB patients.

**Method:** This is an observational cross-sectional study which was held from January 2017 to February 2017 in Persahabatan General Hospital, Jakarta, Indonesia involving 68 household children from 47 MDR TB adult patients. We examined the children, including careful history of exposure and physical examination, Tuberculin Skin Test (TST), chest X-ray and, if the children had signs and symptoms of tuberculosis, acid fast bacilli stain examination, sputum culture and resistance test and GeneXpert sputum test were also added.

**Results:** From the 68 children, there were 7 children (10.29%) diagnosed with TB, although none had MDR TB. In children who were diagnosed with TB, all had chronic cough and positive TST, 2 children had prolonged subfebrile fever (18.2%), 2 children had multiple lymphadenopathy (18.2%), 5 children had poor housing ventilation (72%), 2 of whom their parents complied with wearing a surgical mask for transmission prevention (18.2%), 2 did not have BCG scar (18.2%), and 1 child with suggestive TB from chest X-ray (14.3%). Of the 68 children, TB prophylaxis was administered in 20 children who were under 5 years old, and close observation was maintained in 41 children.

**Conclusion:** There were 7 children (12.7%) of household adults with TB MDR who were diagnosed with TB and none had MDR TB.

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**Methods:** We retrospectively studied clinical records of children admitted in a Portuguese tertiary pediatric hospital from July 2013 to June 2017 and whose diagnosis at the time of discharge was viral pneumonia. Children with previously known comorbidities were excluded. The diagnosis of viral infection was established clinically and by imaging features suggestive of viral infection (bilateral interstitial infiltrates and alveolar infiltrates). Quantitative real-time polymerase chain reaction of nasopharyngeal swab specimens for viruses and Mycoplasma pneumoniae was performed in all children. Demographic and clinical data, imaging and laboratory results, treatment and clinical course during hospitalization were analyzed. Follow-up and identification of late sequelae were also studied.

**Results:** A total of 77 children fulfilled the study criteria, with a median age of 19 months, 55% being girls. The most frequently identified virus was RSV (n = 42) followed by adenovirus (n = 23), rhinovirus (n = 22), parainfluenza (n = 12), influenza A (n = 10), metapneumovirus and coronavirus (both with n = 9). Mycoplasma was identified in two children. Most patients (60%) had more than one virus identified, and three children had no identified pathogen. Median time of hospitalization was five days, ranging from one to 17 days. Most children were treated with supportive measures, but three children needed mechanical ventilation. Fifty-three children were followed-up at our hospital. Of those, 20 are still followed at the Pulmonology Outpatient Clinic: 2 with post-infectious bronchiolitis obliterans (both diagnosed clinically and with CT scan) and the remaining for recurrent wheezing and/or cough not present before the pneumonia. The remaining children maintain follow-up at a primary care or local hospital but none of them has been identified with respiratory sequelae.

**Conclusion:** Viruses are common pathogens in childhood pneumonia and the need for hospitalization is common. In our sample, two children (3%) developed post-infectious bronchiolitis obliterans (both diagnosed clinically and with CT scan) and the remaining for recurrent respiratory symptoms. These findings highlight that all children with viral pneumonia who need hospitalization should be considered at risk of long-term complications and require follow-up.

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**Introduction:** Viral pneumonia can vary from a mild and self-limited illness to a life-threatening disease. Morbidity is high and the evaluation of childhood pneumonia interventions should include potential impact on long-term respiratory sequelae, which are more likely in children requiring hospital admission. Identification of the agent is also important since different viruses have different rates of complications, with adenovirus pneumonia being associated with the highest risk of sequelae. The most commonly isolated viruses in childhood pneumonia requiring hospitalization are respiratory syncytial virus (RSV), rhinovirus, human metapneumovirus, adenovirus, influenza viruses, parainfluenza and coronavirus. This study intends to evaluate the follow-up of children with viral pneumonias that required hospitalization in a tertiary pediatric hospital as well as long-term respiratory complications, particularly post-infectious bronchiolitis obliterans for its usual severity and major impact in children and families.

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**Introduction:** Tuberculosis still remains a serious public health problem worldwide, especially in third world countries, and it is estimated that 1/3 of the world’s population has already been infected by Koch’s bacillus. Polyserositis tuberculosis, an uncommon condition, is a form of extrapolumonary tuberculosis that can occur at any age. Young children and HIV-positive adults are particularly susceptible. About 25% to 30% of children with tuberculosis manifest an extrapolumonary form. After penetrating the body via the respiratory tract,
**Mycobacterium tuberculosis** can spread and settle in any organ, either during the first infection, when specific immunity is not yet developed, or thereafter, at any time, if there is an ability of the host to maintain the bacillus in its implantation sites. The definitive diagnosis of extrapulmonary tuberculosis is very difficult: it can be presumptive, as long as other conditions are excluded. The treatment consists in the RIPE regimen (rifampicin, isoniazid, pyrazinamide and ethambutol) and can be started only with the presumptive diagnosis, assisting the completion of definitive diagnosis. The objective of this work is to report the case of a teenager with tuberculosis polyserositis.

**Case report:** J.V.M.M., 15-year-old teenager, male, black, from Rio de Janeiro- Brazil, admitted to the Jesus Municipal Hospital, RJ, on December 2017 for ascite symptoms investigation. His mother reported that he had been affected with fever, nausea and vomiting for 10 days. He sought immediate medical attention and was released after intramuscular benzathine penicillin injection. Without improvement, he sought new care the following day, being given the diagnosis of urinary infection. A dose of ceftriaxone was administered and he started having ascites. On the seventh day of treatment, the ascites were already large and the previous symptoms, such as fever and night sweats, persisted. He sought emergency care, being hospitalized and referred to this unit for investigation.

**Physical examination on admission:** Thin, eupeic (FR = 16 rpm), good perfusion, acyanotic, hypocortical (+/- 4), massive ascites, abdominal circumference measuring 88 cm, remainder of the exam without other abnormalities. Ciprofloxacin maintained. Complementary examinations demonstrated: non-specific blood count, HSV = 105 mm, TGO = 36U/l, TGP = 26U/l, DHL = 636 U/l, FA = 114U/l, albumin = 2.8g/dl, negative rapid test for dengue, negative tuberculin test and negative serologies for hepatitis and HIV. Image exams: chest X-ray with small calcified lymph nodes in the mediastinum. Abdominal USG only proved the voluminous ascites. Chest CT was performed after 10 days of hospitalization, which demonstrated extensive pleural effusion in the left hemithorax. Transthoracic echocardiogram demonstrated compacted cardiomyopathy, and patient started on captopril. Diagnostic puncture of the ascites fluid was performed, which showed an increase in cells with mononuclear predominance and adenosina deaminase (ADA) = 113U/l, justifying the empirical treatment with RIPE: rifampicin, isoniazid, pyrazinamide and ethambutol. Clinical improvement was observed quickly and the patient no longer had a fever and with 5 days of treatment, presented a drastic reduction in ascites, going from 88 cm of abdominal circumference to 77 cm.

**Conclusion:** In the case described, it is important to draw attention to the differential diagnosis of ascites. In the present case, the family history of tuberculosis was negative, however, due to the high prevalence of the disease in Brazil, tuberculosis was investigated. The inflammatory tuberculosis effusion can also occur in any of the serous cavities: pleural, pericardial or peritoneal. Clinical presentation of polyserositis is the sum of symptoms from the involvement of each serous.

**ABSTRACT**

**C188 – Risk Factors of Severe Community Acquired Pneumonia among Children Aged 2 And 59 Months Admitted to the National Children’s Hospital in Costa Rica.**

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**Introduction:** Community acquired pneumonia (CAP) is a leading cause of childhood morbidity and mortality worldwide. In low-middle income countries (LMICs), pneumonia is the biggest killer of young children globally, accounting for nearly one in five deaths among children aged less than 5 years. Nonetheless, pneumonia represents an important burden of morbidity in the developed world, in particular severe pneumonia, although mortality is low. Clinical and epidemiological information is crucial to characterize patients with severe pneumonia, given that they are at the highest risk of death. The WHO (2014) has reported that in low resource settings, risk factors for severe pneumonia in children include malnutrition, lack of breastfeeding, indoor air pollution (caused by cooking and heating with biomass fuel), living in crowded homes and parental smoking. On the other hand, >6 months breastfeeding and routine vaccination against common childhood illnesses has been identified as a major role in decreasing mortality rates. A better understanding of the risk factors associated with child pneumonia and severe pneumonia is of utmost importance, since primary prevention strategies are likely to achieve major reductions in pneumonia-associated morbidity and mortality in children.

**Objective:** This study sought to identify the risk factors for severe pneumonia among children under-5 years of age in Costa Rica.

**Methods:** A case control study was conducted including children under-5 years old who were admitted to the Children’s Hospital in Costa Rica between January 2010 and January 2015. The sample size calculation that was performed assuming a 95% level of confidence and 5% margin of error estimated a total of 160 patients overall. A convenience sampling technique was used to select 80 children with severe pneumonia (cases) and 80 children with non-severe pneumonia (controls) matched for age. Cases and controls were defined by clinical criteria following WHO recommendations. All medical records were reviewed to collect data on socio-demographics, nutritional status and risk factors.

**Results:** The mean age of the patients was 18.2 months (range, 2–58 months), without significant difference between cases and controls. A slight predominance of male sex was observed within the severe pneumonia group, 63.7% versus 50% in the control group (p = 0.07). Ethnicity was also found to be highly associated with severe pneumonia since 14 (17.5%) patients in the severe pneumonia group were indigenous compared to none in the control group (p < 0.0001).

On bivariate analysis, malnutrition, (OR:2.6, 95% CI: 1.3–5.4, p = 0.005), prematurity (OR:3.2, 95% CI: 1.3–8.0, p = 0.004), low-birth weight (OR:2.8, 95% CI: 1.1–7.8, p = 0.02), lack of breastfeeding for at
least 6 months (OR: 2.1, 95% CI: 1.1–4.3, p = 0.02) and co-morbidities (OR: 2.2, 95% CI: 1.1–4.4, p = 0.01) were significantly associated with severe pneumonia. A total of 28 (35.0%) cases were exposed to passive smoking versus 18 (23.1%) controls. An increasing trend of severe pneumonia was observed among children exposed to tobacco smoking by the parents, although not statistically significant (OR: 1.7, 95% CI: 0.8–3.8, p = 0.09). No associations were found between severe pneumonia and other environmental factors such as exposure to cooking smoke and prenatal smoking, or living in crowded homes. Within co-morbidities, asthma (OR: 2.1, 95% CI: 1.1–4.6, p = 0.02) was by itself the only condition associated with severe pneumonia. Children who had >6 months breastfeeding (OR: 0.4, 95% CI: 0.2–0.9, p = 0.02) and routine pneumococcal vaccination (OR: 0.1, 95% CI: 0.01–0.6, p = 0.003) were protective factors for severe pneumonia.

The proportions of patients with tachypnea (p = 0.003), nasal flaring (p < 0.001), chest retractions (p = 0.003), grunting (p < 0.001), cyanosis (p < 0.001), altered mental state (p = 0.04), shock (p = 0.007), dehydration (p = 0.006) and hypoxia (p = 0.01) were significantly associated with severe pneumonia. Identification of microorganisms was possible in 35 (43.7%) cases and in 28 (35%) controls (NS). In both groups, Respiratory Syncytial Virus (RSV) was the most common isolated pathogen (21.2%), followed by Metapneumovirus (3.7%), Influenza A (3.7%) and Staphylococcus aureus (2.5%).

Length of hospital stay was significantly higher in the severe pneumonia group (mean 17.9 days, 95% CI: 10.1–25.6) compared to the control group (mean 5.0 days, 95% CI: 3.7–7.0) (p = 0.004). Death, as a result of multiple organ system failure, occurred in 3 (3.7%) severe cases.

Linear logistic regression showed that being indigenous was the only independent risk factor for development of severe pneumonia (p = 0.003).

Conclusions: In our study, we found that malnutrition and lack of breastfeeding are modifiable risk factors related to severe pneumonia in young children. Other factors highly associated with severe pneumonia were ethnicity, prematurity, low-birth weight and co-morbidities. Although passive smoking was not a significant risk factor, the general prevalence found in both groups was higher than the mean prevalence of smoking in Costa Rica. On the other hand, adequate vaccination and at least 6 months of breastfeeding were associated with mild disease and better outcomes. Mortality rate in our cohort was low compared to studies in LMICs. Viral infections were present in a high proportion of patients with CAP in our study.

Since severe pneumonia is preventable, clinicians and public health authorities can play significant roles to reduce its occurrence through health promotion, educational activities and effective child health programs, particularly in high risk groups.

C189 – Pulmonary Nocardiosis in an Immunocompetent Adolescent.

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Introduction: Nocardia is a gram-positive bacterium from the genus of aerobic actinomycetes found in soil that has the ability to cause localized suppurative disease (mostly pulmonary, central nervous system, cutaneous or lymphocutaneous involvement) or systemic disease. There are currently 85 species of Nocardia, 25 of which cause disease in humans. Despite being associated with immunodeficiency, one third of the patients are immunocompetent. The authors report a case of a pulmonary abscess in a previously healthy adolescent caused by Nocardia (polymerase chain reaction (PCR) confirmation).

Purpose of the case: This case emphasizes the importance of considering Nocardia in differential diagnosis of pulmonary abscess, especially in the absence of response to empiric therapy.

Case report: We report a case of a previously healthy 17-year-old adolescent who was admitted in the ER with a history of fever, odynophagia, vomiting, cough and thoracic pain. The patient was on day 2 of amoxicillin/clavulanate for a pustule tonsillitis. On admission, exudate was observed on the tonsils but there were no signs of peritonsillar abscesses. The pulmonary auscultation was normal. On blood tests, the total white cell count was 12,020/μL with 86.5% neutrophils and 2.8% lymphocytes (340/μL). CRP C-reactive protein (CRP) was 130.2 mg/L. Heterophile antibody test was negative and chest X-ray revealed an interstitial infiltrate in the right upper lobe. The patient was discharged with increased dose of amoxicillin/clavulanate.

The adolescent returned to the ER eight days later with recrudescence of fever, dyspnea and thoracic pain. On blood tests, the total white cell count was 19,500/μL with 76.9% neutrophils and 12.1% lymphocytes (2,360/μL). CRP was 90.2 mg/L. The chest X-ray showed a cavitory lesion on the right upper lobe. The pulmonary computerized tomography (CT) scan revealed a lesion measuring 60 × 60 × 54 mm. There was no mediastinal or hilar lymphadenopathy. Empiric antimicrobial therapy with intravenous (IV) ceftriaxone and clindamycin was initiated, without evident clinical improvement. A CT-guided biopsy of the lesion was conducted. Mycobacterial, aerobic and anaerobic cultures of the pulmonary tissue and blood cultures were all negative. The histopathology analysis of the biopsy excluded malignancy and PCR of the biopsy revealed nocardiosis. All other PCR studies were negative. Autoimmune disease and immunodeficiency were excluded by normal findings, including negative serum examination and PCR detection for HIV. Brain CT, echocardiogram and cervical Doppler ultrasound were normal. The treatment was changed to IV imipenem and oral sulfamethoxazole/trimethoprim (TMP/SMX) for two weeks. The total therapy period was 3 months with TMP/SMX. There was full clinical recovery of the patient. Follow-up appointments were scheduled.

Discussion: We present a case of pulmonary nocardiosis in an immunocompetent adolescent. The clinical presentation of pulmonary nocardiosis is non-specific and chest radiograph normally reveals lesions in the superior lobe that are often attributed to other causes, which delays the correct diagnosis. The difficult isolation of the bacterial agent and its slow growth in culture makes it a challenging diagnosis. In this case, the lack of response to empirical antibiotic therapy justified an invasive procedure (pulmonary biopsy) to obtain
new samples for in vitro culture and PCR. A positive PCR result for Nocardia sp. led to the final diagnosis of pulmonary nocardiosis. The culture was negative. To improve the culture rate identification of Nocardia, it is necessary to notify the laboratory regarding the clinical suspicion. This allows the establishment of an adequate incubation time and avoiding the use of decontamination solutions that are toxic for Nocardia sp. There are few documented cases of pulmonary nocardiosis affecting adult immunocompetent patients and usually associated with pulmonary chronic disease. To our knowledge, this is the first report of pulmonary nocardiosis in a previously healthy pediatric patient. This clinical case highlights key points that should be considered by the pediatric pneumologist in a similar context: 1) consider unusual agents that cause pulmonary abscess, even in the absence of known risk factors; 2) recognize the importance of using PCR, especially if antibiotic treatment has been previously initiated; 3) promote a close partnership between the attending clinician and microbiologist to efficiently explore the samples obtained from the patient.

C196 – Extrapulmonary Tuberculosis in Children < 13 Years Old in Costa Rica: A Retrospective Study of a not so Rare Pathology in Low Middle-Income Countries.

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Background: Tuberculosis (TB) in childhood is clinically challenging, but it is a preventable and treatable disease. The most common form of pediatric TB is pulmonary disease; however, other extrapulmonary forms of TB such as miliary, lymphatic, meningitis and others are also common, particularly in children. According to WHO, Costa Rica is considered a low TB incidence country (9.5 cases per 100,000). Nevertheless, this disease should be considered to be a public health threat in any country. In Costa Rica, epidemiological and clinical information related to pediatric extrapulmonary tuberculosis (EPTB) is scarce.

Aim: To describe the clinical characteristics, epidemiology, diagnostic approach, laboratory studies and treatment for extrapulmonary and miliary tuberculosis in children under 13 years old.

Methods: A 12-year (2003–2015) retrospective study of children under 13 years old with suspected extrapulmonary tuberculosis in Costa Rica’s National Children Hospital was undertaken. Information regarding clinical and pathological history, laboratory and complementary studies, and treatment was obtained from medical records and laboratory databases. Cases were defined based on World Health Organization (WHO) recommendations for diagnosis based on clinical data, contact with a positive case, laboratory, radiological or other histopathological findings, in association with the presence of Mycobacterium tuberculosis confirmed by positive Auramina or Ziehl-Neelsen staining, positive culture on Loewenstein-Jensen medium of specific tissues or fluids.

Results: A total of 54 cases of diagnosed extrapulmonary disease were identified, of which 20 (37%) were miliary TB, followed by 14 (25.9%) cases with meningeal tuberculosis, 13 (24.1%) with tuberculous lymphadenitis, 3 (5.6%) pleural TB, 2 (3.7%) osteoarticular TB, and gastrointestinal and skin involvement in equal proportions in 1 (1.9%) patient. The mean age of diagnosis was 5.2 years (range, 0.4–12.8 years). A slight predominance of male sex prevalence was observed, with 57.4% in comparison to 42.6% female distribution. As expected, the majority of patients (47, 87.0%) were from Costa Rica. Immigration is also common in the region, from our cohort: 5 (9.2%) were from Panama and 2 (3.7%) cases from Nicaragua. There were 15 (27.7%) cases of extrapulmonary TB among the indigenous population, 3 (20%) came from Panama. No HIV positive cases were found, and malnutrition was present in 22.2% of cases.

Information collected regarding the adult index case was available for 50 patients of which only 29 (58%) had a positive index case.

The most frequent symptom was fever in: 75% of miliary cases, 66.7% of pleural tuberculosis, 64.3% meningeal presentation, and 46.2% in ganglionar disease. As for miliary tuberculosis, chronic cough was present in 60% of cases and weight loss in 45% of cases, with respiratory distress and enlarged liver in 35% of cases. Lymph node tuberculosis was characterized by weight loss and sweating in 15.4%, and 100% of patients had cervical lymphadenopathies. Meningeal presentation had seizures as main symptom in 64.3% of cases, vomiting in 57.1%, and 42.8% had either altered mental status or loss of appetite. Up to 78.6% patients had cranial nerve fociaty. Chronic cough was present in 100% of pleural tuberculosis and 66.7% associated chest pain, fever and poor appetite. Moreover, weight loss, abdominal pain and bloody stools were documented in 100% of gastrointestinal tuberculosis cases. Skin and bone tuberculosis had no specific symptoms at presentation, but 100% of the latter associated edema, erythema and local elevated temperature.

Chest X-ray was abnormal in 29/39 (74.4%) of patients. It was abnormal in 100% of miliary and pleural cases, 50% of meningeal and osteoarticular TB, and 42.8% of ganglionar diagnosis. Tuberculin skin test (TST) was positive in 20/42 (47.6%) of cases. It was 100% positive in patients with bone, skin and pleural tuberculosis, 50% positive in meningeal disease, 44.4% in lymph node TB, and 33.3% in miliary. Gastric lavage was positive in 14/31 (45.2%) patients. Those with miliary TB had the highest positive results (78.6%), a total amount of 7 positive cultures were documented, 5 having miliary disease, and in 4 cases molecular studies were positive, all of miliary presentation. This was also observed with bronchoalveolar lavage. A total of 20 cases were analyzed: 6/14 (42.8%) had positive cultures and 2/18 (11.1%) had positive PCR for M. tuberculosis.

All patients completed direct observed treatment (DOTS) as per WHO recommendations. Of our cohort, one patient (1.8%) died with miliary TB.
Conclusion: The epidemiological characterization of pediatric patients with extrapulmonary TB helps achieve a better diagnostic approach to this population. It is clear that bacterial confirmation is difficult in children with disseminated disease; therefore, contact history, clinical features, radiology and TST may be sufficient to establish a diagnosis and initiate treatment. In our study, although microbiological isolation was low, it was slightly higher to other similar reports. The role of molecular biology for TB diagnosis is an important development, however, in our study, this technique was not available during the whole study period. We found that prompt diagnosis is dependent on a high index of suspicion as clinical signs may be non-specific and microbiological confirmation is difficult. Furthermore, the tuberculin skin test and chest radiograph may initially be negative in as many as 40% of pediatric patients. Treatment was well tolerated in most patients.

4. NON-INFECTIOUS RESPIRATORY DISORDERS

D17 – IgG4-Related Lung Disease in an Adolescent Male.

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IgG4-related disease (IgG4-RD) is a recently recognized systemic immune-mediated condition characterized by lymphoplasmacytic infiltrate in various organs with IgG4-positive plasma cells, different degrees of fibrosis, obliterative phlebitis and elevated serum level of IgG4 in up to 60% of patients. Lung involvement is rare, difficult to diagnose and can mimic primary lung malignancy on imaging.

A 16-year-old adolescent with no significant past medical history was incidentally found having bilateral nodular lesions in the right lower lobe and the upper lobe of the left lung on chest radiograph. X-ray was performed following positive test with 2TU (Mantoux). The patient had no complaints and physical examination revealed no abnormalities. Computed tomography (CT) demonstrated nodules in S5, 6, 8 of the right lung with a maximum size of 5.5 cm with large petrification in S8 and S2, 6 in the left (Fig. 1a,b).

Immunostaining showed infiltration in the interstitium of IgG4-positive plasma cells. The mean number of IgG4+ plasma cells per high power field (HPF) was within 150–350. The diagnosis of IgG4-related lung disease was made.

To understand the etiology of the nodule in S2 of the left lung, positron emission tomography was performed. No lesions in the lungs or other organs including pancreas, kidney, thyroid and salivary gland were identified. The patient’s serum IgG4 level was 1.11 g/l which is in normal reference range (0.049 – 1.985 g/l). Recent international consensus for management of IgG4-related diseases states that all symptomatic and
subset of asymptomatic patients require treatment. IgG4-related disease shows a good response to steroid therapy. Some may require additional immunosuppressive agents, such as Rituximab. By the time of the presentation, the patient is under a careful clinical surveillance with no treatment.

Conclusion:

IgG4-related disease is a rare disease, especially cases with lung involvement. It can mimic malignancy, infection or inflammatory disorders. Isolated pulmonary disease is most frequently seen in middle aged and older men but young people can also present with this disease. Biopsy is required for the diagnosis of IgG4-related disease. Morphological features of the disease include dense lymphoplasmacytic infiltrate, "storiform" fibrosis, obliterative phlebitis and immuno-histological expression of IgG4 in plasma cells. Awareness of this pathology allows avoiding unjustified surgical interventions.

D18 – Clinical Manifestation of Pediatric Mediastinal Tumors.

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Background:

Mediastinal tumors are uncommon in children but may potentially cause serious consequences owing to cardiopulmonary compromise. Predicting long-term outcome through initial clinical manifestations may be contributory to clinical decision-making. In this study, we aimed to analyze clinical presentations of various types of pediatric mediastinal tumors and develop useful predictive prognostic factors.

Method:

Patients under 18 years of age with diagnosis of mediastinal tumors at the China Medical University Children's Hospital between 2001 and 2016 were enrolled in this study. Patients’ gender, age of disease onset, initial clinical symptoms and signs, and outcome during the hospital course were reviewed and analyzed.

Results:

A total of 40 patients were enrolled into our study. The median onset age of mediastinal tumors was around 13 years-old. Male to female ratio was 3 to 1. The overall mortality rate was up to 40%. Only two cases were benign in origin. The most common tumor type was lymphoma (40%), followed by germ cell tumors (12.5%), neuroblastoma (12.5%), and thymoma (7.5%). Neuroblastoma was more prevalent in girls younger than 5 years-old. The initial presentations of these patients included respiratory distress (60%), productive cough (47.5%), pleural effusion (42.5%), superior vena cava (SVC) syndrome (35%), neck mass (35%), airway compression (32.5%), fever (30%), chest pain (25%) and pericardial effusion (25%). Lymphoma, compared to other types of tumors, was more likely to be accompanied with neck mass (52.6% vs. 19.0%, P = 0.026) and SVC syndrome (52.6% vs. 19.0%, P = 0.026), yet had better one year-survival rate (68.4% vs. 52.4%, P = 0.021).
Conclusion:
Pediatric mediastinal tumors often involve the respiratory system. Overall, lymphoma should be highly suspected when children present with neck mass and SVC syndrome, and are more common in male teenagers. Lymphoma also has better prognosis compared to other types of malignancy. Neuroblastoma, from posterior mediastinal origin, should be considered in priority among children younger than 5 years old.

D28 – Pleural Effusion and Displacement of Ventriculo-Peritoneal Shunt. A Pediatric Case Report and Review of Literature.

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Introduction: Thoracic complications of ventriculo-peritoneal (VP) shunt have rarely been reported and include pleural effusion, bronchial perforation, pneumothorax and pneumonia [1]. These complications can occur at any period of time after the procedure and three possible mechanisms have been postulated: intrathoracic trauma during shunt placement, dislocation of the peritoneal catheter into the chest and fluid shift from the peritoneal cavity to the pleural cavity [2].

Case report: Herein we report the case of a 2-year-old Caucasian female patient with Pfeiffer syndrome and VP-derived hydrocephalus who was admitted at our Respiratory Unit for irritability, tachypnea with need of mechanical ventilation and increased baseline oxygen requirement and vomiting. She was afebrile and cardiovascular examination was unremarkable. Normal lung sounds and good ventilation were noted bilaterally; no dullness to percussion was reported. The remainder of the physical examination was negative. Results of venous blood gas and routine blood tests were normal. Thorax X-ray showed a complete opacification of the right hemithorax with mild associated compressive atelectasis. A large right-sided pleural effusion was detected on thorax CT scan and an abdomen CT scan revealed the dislocation of the distal tip of the VP shunt (Figure 1). A thoracentesis was performed and the analysis of pleural fluid confirmed the CSF leakage. Because of right recurrent effusion, the distal end of VP shunt was positioned back into the abdomen and a ventriculo-atrial (VA) shunt was established in order to prevent a recurrent pleural effusion.

Discussion: pleural effusion due to VP shunt insertion is a rare and potentially life-threatening condition that should be suspected in any patient with VP shunt and respiratory failure. Overall, 21 studies have been published in the pediatric age. The timing of occurrence of this chest complication is variable and dislocation of the distal tip of the VP shunt is not prevalent. Beta-2 transferrin assay and radionuclide shuntography are useful techniques to diagnose CSF leakage and verify shunt patency and course. The diagnostic work-up should also include investigations excluding peritoneal-thoracic fistula. Thoracentesis is a useful tool to treat massive pleural effusion other than to define its source. Revision of the distal tip of the VP catheter may be sufficient when malfunction is suspected, especially when the effusion is not massive and the clinical picture does not suggest catheter infection. Its removal from the pleural space and repositioning back into the abdomen or in the right atrium is considered when dislocation is showed or CSF hydrothorax is recurrent [3]. Positive pressure ventilation is also reported as a possible therapeutic approach because of its effect on conversion of negative intrathoracic pressure to positive, preventing fluid shifts [4].

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Figures:
Figure 1. a) Chest CT scan demonstrating a large right pleural effusion causing mediastinal shift and compression of the heart. b) Abdomen CT scan 3D reconstructions showing the distal end of the VP shunt situated over the diaphragmatic cupola and within the pleural cavity.
D32 – Pulmonary Atelectasis in Childhood: Difficulties from Diagnosis to Treatment

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Introduction: Atelectasis is a non-ventilated lung parenchyma that can occur from several causes in children. Diagnosis and treatment are very important as it can cause lung damage.

Aim: We aimed to evaluate the etiology, diagnostic methods, treatments and outcomes of patients with atelectasis in childhood.

Methods: Data of children with atelectasis in a tertiary pediatric pulmonology center between 2007 and 2015 were evaluated.

Results: In this period, 194 patients were diagnosed with atelectasis and mean age was 5.8 ± 4.0 years. The most common complaint was coughing. Ninety-five patients had pneumonia and 23 patients had acute asthma exacerbation during diagnosis. The underlying diseases were asthma, primary ciliary dyskinesia, neuromuscular disease such as hypotonia or myopathy, congenital heart disease, bronchopulmonary dysplasia, tracheal/bronchomalacia, cystic fibrosis, and other rare causes. Diagnosis was made via bilateral chest X-ray in 76% of the patients and computed tomography in 23%. The most common atelectasis was observed in right middle lobe. If present, the underlying condition was treated, all patients were treated by chest physiotherapy and mucolytic treatment and 10% of the patients had bronchoscopy while 7% had dornase alpha treatment in addition to these treatments. Twenty-two patients had recurrent atelectasis, and in 37 patients atelectasis did not resolve.

Conclusion: It is important for clinicians to keep in mind that atelectasis may have different radiological findings. Recognizing radiological findings is important both for treatment and unnecessary further studies involving high-dose radiation. Patients with impaired mucociliary function may have recurrent or non-recovering atelectasis.

D36 – Tracheomalacia in Children – Long-term Retrospective Clinical Follow-up

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Introduction:

Tracheomalacia (TM) is a fairly common airways disorder, identified in 1 to 2100 – 2500 children. Moreover, TM diagnosing has been increasing in the last decade with the improvement of imagining capabilities (fiberobronchoscopy, radiology procedures) and with the growing awareness of this disorder among clinicians. TM can be established as primary or secondary (e.g. secondary to trachea compression by great arteries). Regardless of pathophysiology, tracheal walls are softer than normal in TM and more susceptible to collapse. Clinical symptoms due to dynamic cross-sectional narrowing of the trachea are usually observed when intrathoracic pressure exceeds intraluminal pressure of the trachea, which is mostly seen during vigorous exercising, prolonged forced expiration or cough.

Clinically, TM produces recurrent cough, wheeze or stridor, thus the symptoms are commonly seen in children with other respiratory disorders. It is believed that TM is a mild disease with a tendency to resolve spontaneously in the first two years of life. However, recent studies indicate that some TM symptoms (cough during exertion, prolonged cough after respiratory tract infection, exertional dyspnea) could be observed even in older children.

The aim of this study was to characterize the clinical features of children with TM in the long-term follow-up period.

Methods:

Children with TM were identified in the dataset of fiberobronchoscopic examinations performed between 2005 and 2015 at the University Children's Hospital in Krakow. Children with tracheostomy, immune deficiency disorders, cystic fibrosis were excluded from the analysis. Parents of children older than 6 years were surveyed by an authorial questionnaire. They were asked about presence, type and severity of respiratory symptoms in their children in two-time points: in the first year after TM diagnosis and in the last year preceding the survey. They were requested to evaluate their children's respiratory problems in relation to their general judgment and concern to health conditions. Construction of questions was various (yes/no questions, multiple choice questions, open questions, questions with graphical scale).

Out of 55 identified children with TM, 24 (44%) constituted the study group, 13 of whom were boys (54%). In these children, TM was diagnosed at the median age of 1.4 years [interquartile range (IQR): 0.5 – 6.9], the survey was conducted at the median age of 8 years [IQR: 6.9 – 8.9], thus the median follow-up period was 6.2 years [IQR: 3.3 – 6.8]. There was primary TM in 21 children and secondary TM – in 3 (2 children with vascular rings, 1 child after surgery of esophageal atresia with tracheoesophageal fistula). In 9 (36%) children, accompanying laryngo- and/or bronchomalacia was identified (laryngomalacia in 2, bronchomalacia in 6, both in 1).

It should be noted that the group of children for whom parents did not return the questionnaire (n = 31) was not significantly different from the study group in terms of: gender (16 (52%) boys, p = 0.85), the median age at the time of TM diagnosis (0.8 years [IQR: 0.1 – 4.8], p = 0.08), the ratio of primary to secondary TM (primary TM was in 26 children, secondary TM in 5 and between them: 3 children with vascular rings, 2 children after surgery of esophageal atresia with tracheoesophageal fistula, p = 0.7) and coexistence of laryngo- or bronchomalacia (laryngomalacia in 6, bronchomalacia in 11, p = 0.2).

Results:

Parents reported a high frequency of respiratory tract infections in the first year after TM diagnosis in 17 (71%) children and in 13 (54%) in the last year preceding the survey. In comparison to the first year after TM diagnosis, respiratory tract infections in the last year preceding the
survey were reported less frequent in 13 (54%) children and less severe in 9 (38%). The most common respiratory tract infections diagnosed by physicians were: viral wheezy bronchitis in 18 (75%) study children, recurrent acute bronchiolitis in 13 (54%), rhinosinusitis in 11 (46%) and non-resolving cough in 9 (38%) children. Regardless of TM, asthma diagnosis was additionally established in 7 (29%) children in whom anti-asthmatic treatment was prescribed (inhaled corticosteroids in 4, montelukast in 3).

Prominent postinfectious cough (lasting less than 4 weeks) was reported by parents of 15 (63%) children in the first year after TM diagnosis and still reported in 12 (50%) in the last year preceding the survey (p = 0.38). Moreover, exertional dyspnea (exercise intolerance) was observed by parents in 10 (42%) children and post-exercise cough in 9 (38%). On the other hand, 7 (29%) children could manage strenuous physical activity without any disturbing respiratory symptoms.

In 22 (92%) children, parents described cough during respiratory infection as barking or unusual in sound. However, in 13 (54%), they reported the same characteristics of cough in periods outside of infections.

Conclusion:
Clinical symptoms of TM do not completely resolve with child's age. And until early school age, the most common persistent symptom is prominent postinfectious cough, which is characterized as barking or unusual in sound. In over one third of children with TM, exercise intolerance due to cough is also present. Respiratory tract infections diminish in frequency and severity with child age. Primary care physician should be aware of the evolution of TM symptoms to avoid unnecessary treatment.

We need further investigations in children with TM history in the area of pulmonary function testing, including considering exercise challenge testing.

D58 – Behind an "Uncontrolled Asthma" – Clinical Case of a Late Diagnosed Congenital Anomaly.

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According to WHO, asthma is the most common chronic disease among children. Therefore it is not surprising that if a child presents with a chronic respiratory symptoms to a physician, the latter’s first thought and probably therapeutic management would be about asthma.

We present a case of an 11-year-old girl referred to our clinic after being treated for asthma without success for more than 6 years and labeled as "difficult to treat, uncontrolled asthma". From the past medical history, the following findings were notable: breast-milk aspiration at the age of 1 day (confirmed hypventilation in the left lung), esophageal stricture surgically corrected at the age of 1 month, recurrent wheezing since infancy, food allergy and pet allergy. From the family history: elder brother with confirmed CF (the girl was born after pre-natal screening for CF and she was tested as carrier) and elder sister with epilepsy. At admission the notable findings were difference in both circumferences of the thorax (the left was larger than the right), diminished lung sounds on the right with crackles and rales. From the tests, we found negative bronchodilator response with predominant restriction on spirometry, right lung smaller in size compared to the left on X-ray of the lungs. CAT confirmed our suspected diagnosis – lung hypoplasia. The therapy was modified according the confirmed diagnosis and the asthma control medications were discontinued. For the following 6 months, no significant medical problems were noted, as well as no “asthma exacerbations”.

We present the case as an illustration that not all “difficult to treat asthma” patients are really stricken with asthma. The correct diagnosis requires a comprehensive investigation— including an in-depth history and physical examination, pulmonary function studies, X-rays, laboratory studies, endoscopy, and specialized studies (e.g. allergy testing, methacholine challenge, 24-hour pH probe)

D64 – Late Sequelae of Foreign Body Aspiration in the Bronchial Tree.

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Tracheobronchial foreign body aspiration is a common cause of pulmonary complications especially in toddlers. The delay in diagnosis is associated with increased incidence of complications with significant morbidity and mortality in the affected children.

We present a 3-year-old girl with chronic symptoms of daily spasmatic cough preceded by protracted pneumonia. The girl was non-atopic and had normal neurological development with negative family history. The parents reported that the child consumed whole nuts but emphatically declined any choking episode. The symptoms started a year ago prior to the admission in our department with roentgenological and clinical signs of infiltrative pneumonia in the right lower lobe. The CT-scan confirmed the clinical diagnosis without any suspicions for complications or foreign body aspiration. The aggressive and long-lasting antibiotic treatment led to temporary improvement followed by a two-month asymptomatic period. In the last nine months, the child had daily morning paroxysm of dry cough with expectoration of a low amount viscous mucoid sputum which was difficult to clear. The child was treated with antihistamines, LTRA, nasal corticosteroids, antibiotics without any improvement. Adenectomy was performed. In our Clinic, the child presented with clinical and roentgenological signs of right lower lobe pneumonia with suspected bronchiectasis and moderate elevated inflammatory markers. The sputum culture showed H. parainfluenzae, the Mantoux test and sweat test were negative, immune deficiency was excluded. The HRCT with contrast
demonstrated exacerbated chronic pneumonia in the middle and lower right lobe, zones of hypoventilation and atelectasis, bronchiectasis and visible foreign body in the right intermediary bronchus. Rigid and flexible bronchoscopy was performed and four small particles of whole sunflower seeds were extracted. After the foreign body extraction, complex conservative treatment for non-CF bronchiectasis and chronic wet cough was provided. The child is still being followed.

Tracheobronchial foreign-body aspiration in children is still considered as one of the most important diagnostic and therapeutic challenges for physicians. In cases without any history of choking incident, the early diagnosis is a state of art. The consumption of whole nuts in toddlers is one of the leading causes of foreign body aspirations in our geographical region and is often a missing clue pointing to the correct diagnosis. The delay in foreign body extraction could lead to non-reversible lung damage with chronic purulent inflammation.

D77 - An Unusual Cause for a Pulmonary Cavitary Lesion: Communicating Bronchopulmonary Foregut Malformation in a 9-Year-old Boy.

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Background: Communicating bronchopulmonary foregut malformations (CBPFM) are congenital anomalies characterized by a patent communication between a portion of the lung and the esophagus or stomach. The spectrum ranges from esophageal atresia with a communication between distal esophagus and the sequestrated lung (Type I), immature lung with a mass that is formed from the distal esophagus (Type II), a connection between the sequestered lung lobe and the esophagus or stomach (Type III), and a communication between the esophagus and the bronchial system (Type IV). CBPFM are rare and the majority of cases present with symptoms in infancy. We report a case of CBPFM with an unusual presentation of a pulmonary cavitary lesion in late childhood.

Case Report: A 9-year-old boy presented with hemoptysis for 3 days and prolonged cough for 3 months. There was no fever or constitutional symptoms such as loss of weight, loss of appetite or night sweats. There was no pulmonary tuberculosis contact.

Antenatal history was significant for maternal pre-eclampsia with severe fetal intrauterine growth retardation. He was born at 35 weeks of gestation, with birth weight of 1530 grams. There were no respiratory symptoms in the neonatal period.

This child also had a history of asthma and allergic rhinitis. His first wheezing episode was when he was a few months old, with subsequent wheezing episodes a few times a year. His wheezing episodes were preceded by fever and upper respiratory tract infection symptoms, and responsive to bronchodilators. He was asymptomatic in between the wheezing episodes. He was started on inhaled corticosteroids (ICS) from the age of 2 to 3 years old, after which he did not return for further review. He presented again after an admission for asthma exacerbation at 7 years old. Spirometry demonstrated mild bronchodilator response and he was restarted on ICS. Although non-adherent with his ICS, his wheezing episodes were infrequent. His grandfather has asthma and allergic rhinitis, and smokes at home.

Physical examination, including the respiratory system, was unremarkable. There was no digital clubbing, lymphadenopathy or abdominal organomegaly. Chest X-ray revealed a right upper lobe cavitary lesion, raising the concern of pulmonary tuberculosis. Blood and sputum investigations for bacterial, fungal and mycobacterial infections were negative. Mantoux test and human immunodeficiency virus screen were negative. Hypochromic, microcytic anemia (hemoglobin 7.3 g/DL) was noted, secondary to iron deficiency (low serum iron and ferritin, elevated serum transferrin). Occult blood was positive in his stools. Blood coagulation profile was normal.

He was treated empirically for cavitary pneumonia with a course of antibiotics. The follow-up chest X-ray showed persistence of the cavitary lesion. Computed tomography (CT) of the thorax revealed the lesion to be an area of consolidation with dilated air spaces. Of note, the medial end of the branching airways in the cavitary pneumonia did not show a connection with the trachea or right bronchus, but was instead directed towards the esophagus. The esophagus also showed a tubular out-pouching at its right lateral aspect, suspicious of a bronchopulmonary malformation with a communication to the esophagus. A water-soluble contrast swallow was performed, demonstrating the contrast opacifying a cranially angulated tubular branching structure arising from the right anterior aspect of the esophagus, consistent with a Type III CBPFM.

The child underwent resection of the CBPFM. Pre-operative flexible bronchoscopy showed absence of the right upper lobe bronchus. Esophagogastroduodenoscopy demonstrated an acutely angulated fistula on the right side of the mid esophagus. Purulent fluid was noted on entry into the esophagus. Open thoracotomy confirmed a Type III CBPFM with esophageal communication. The CBPFM was resected with no complications. Histology confirmed findings of CBPFM with presence of pneumonia, micro-abscess formation and bronchiectasis, and no signs of malignancy.

The child recovered well after the surgery, with resolution of the chronic cough.

Discussion: A wide spectrum of diseases ranging from infections, malignancies, chronic systemic diseases and congenital malformations such as CBPFM may cause cavitary lesions in the lung. This case highlights the pitfall of relying on “classical” chest X-ray finding and history in making the correct diagnosis. Pulmonary tuberculosis and malignancies would be the top differentials given the history of prolonged cough, hemoptysis and cavitary lesion on chest X-ray, but the cause turned out to be a rare condition.

Careful and unbiased history taking is important. A retrospective review of the case notes showed that the initial complaint was hematemesis at the Emergency Department triage. Retrospective clarification with the parents revealed that the prolonged cough was temporally related to feeding. These history findings would fit better with CBPFM.

While the chest X-ray suggested a cavitary lesion, the CT thorax revealed that it was severe bronchiectasis of the sequestered upper
Tuberculosis (TB) is a mycobacterial infectious disease that has a wide range of manifestations. Anemia is a commonly seen manifestation in patients with TB, however hemolytic anemia is a rare cause of tuberculosis-associated anemia. We report 4 cases of autoimmune hemolytic anemia (AIHA) in association with childhood disseminated tuberculosis.

**Methods:** Retrospective study including 4 cases of disseminated tuberculosis associated with autoimmune hemolytic anemia.

**Results:** A total of 4 cases of disseminated tuberculosis (DT) associated AIHA were hospitalized in our department during the year 2017. They were respectively aged 10, 8, 12 years, and 6 months. Two children had a history of DT (one child), and of lymph node TB (one child) one year before hospitalization. The initial presentation included fever, asthenia and pallor in all cases. The different localizations of TB were: pulmonary (3 patients), pericardial (3 patients), abdominal (3 patients), lymph nodes (4 patients) and meningitis (2 patients).

The initial laboratory tests showed hemoglobin levels between 6.6 and 8 g/dl, with direct Coombs test positive for IgG in all cases indicating warm AIHA. All children were transfused at least once, and two patients needed recurrent transfusions.

AIHA responded well to specific antibiotic treatment for two patients, and corticosteroid therapy was not necessary. For the two patients who had tubercular meningitis, they were started on anti-TB along with corticosteroids simultaneously, and AIHA responded well to this course of treatment. Direct Coombs test turned negative in all patients.

**Conclusion:** The association of AIHA with tuberculosis is extremely rare. Only 16 cases of AIHA in association with TB have been reported in the literature, 3 of which were pediatric cases. It is important to recognize this complication given its severe implications, and moreover, TB should be considered as a cause of AIHA, especially in areas where the disease is common.
Congenital lung anomalies comprise a group of anatomical abnormalities of the respiratory tree including congenital cystic malformations, bronchopulmonary sequestrations, bronchogenic cyst, bronchial atresia and congenital lobar emphysema. In this present study, we aimed to determine the types of congenital lung diseases (CLD) and each anomaly is discussed in terms of underlying etiology, clinical presentation, and imaging characterization with emphasis on the most up-to-date research and treatment in the pediatric patient group attended in our hospital. The obstetric and other patient groups were evaluated for CLD existence by various imaging techniques between 2003 – 2017. Patients with any type of CLD were evaluated retrospectively. In this 14-year time period, 23 patients were diagnosed with CLD. Seven patients were diagnosed with ultrasonography only, 2 patients with ultrasonography and magnetic resonance imaging in the prenatal period. Ten patients were diagnosed with computed tomography in the postnatal period. The early diagnosis and treatment of CLD is of most importance given its fatal progression in the prenatal and postnatal period.

Ten of the patients were operated, 3 were operated during the neonatal period, 4 during infancy, and 3 between 1 and 13 years of age. None of the patients developed any complications. Postoperative follow-up duration ranged between 1 month and 5 years of age. Only 5 patients had accompanying diseases, which were VSD, hemivertebra, pectus excavatus, PFO, IgA deficiency and milk allergy. These anomalies can be detected with increasing frequency by pre-natal sonography, but may also present for the first time with symptoms in childhood or later life. We believe intrauterine diagnosis and follow-up are important in these patients.

D169 – Keutel Syndrome with Partial IgA Deficiency: An Unusual Case in a Family with Keutel Syndrome.

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Introduction:

Keutel syndrome (KS) is an autosomal recessive hereditary syndrome caused by homozygous mutations in the MGP gene encoding the Matrix GlA protein. It is characterized by abnormal cartilage ossification/calciﬁcation, peripheral pulmonary stenoses (PPS), brachytelephalangia and inner ear deafness and patients generally have respiratory problems. Partial IgA deﬁciency has not been reported with KS previously.

We report a case with classic KS who also had partial IgA deﬁciency born in a family with six individuals with KS.

Case: The index case was a 15-year-old boy admitted to our clinic with chronic cough. He had brachytelephalangism, pulmonary stenosis, hypertension, mid facial retrusion, muffled voice and moderate hearing loss. Tracheobronchial calcifications were observed in chest X-ray and thorax computerized tomography. His mother, father, brother, sister and uncle had the same clinical and radiological features. All of the six individuals were diagnosed with KS after genetic analysis. His sister, a 12-year-old girl, also had recurrent sinusitis, otitis and pneumonia. Her immunological evaluation revealed partial IgA deﬁciency while peripheral lymphocyte subset analysis and lymphocyte activation test were normal. She was put on antibiotic prophylaxis. The infectious episodes decreased.

Conclusion: Although abnormal tracheobronchial cartilage calcification in Keutel syndrome can often cause asthma-like disease, however, recurrent upper and lower respiratory problems are not common. Therefore immune work-up should be performed in patients with KS.

D170 – Comparison of Clinical Presentation and Outcomes after Surgical Repair in Children with Aortic Arch Anomalies.

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Background: Aortic arch anomalies represent uncommon reasons for chronic respiratory and gastroesophageal symptoms in infants and young children. We sought to review our experience in infants and children with anatomically complete vascular rings, and compare clinical presentation and outcomes with those with double aortic arch (DAA) and right aortic arch with left ligamentum (RAA).

Patients and methods: Children with severe chronic respiratory and gastroesophageal symptoms and the above two aortic arch anomalies, detected by flexible bronchoscopy and chest CT scan, were evaluated. Age at symptom onset, at diagnosis and at surgery and symptoms frequency at diagnosis and after surgical correction were evaluated and compared in the two patient groups.

Results: Out of 35 children, 18 had a double aortic arc and 17 had a right aortic arc, 8 with right aortic and associated Kommerell diverticulum. In the whole population, the median age at symptom onset, at diagnosis and at surgery was 3.0 (3.0–36.0), 10.0 (1.0–72.0), and 36.0 (7.5–84.0) months old, respectively. Time intervals between age at symptom onset and diagnosis, age at symptom onset and surgery, and diagnosis and surgery were significantly lower in the DAA group than in the RAA group (p < 0.005, each comparison). In the whole population, the most prevalent manifestations at diagnosis were chronic cough (74%), dyspnea (37%), LRT infections (37%) and dysphagia/regurgitation (34%). Only the prevalence of dysphagia/regurgitation was different in the two groups, being higher in the DAA than in the RAA group (p < 0.05). Because of the severity of symptoms and the lack of response to medical treatment, all patients underwent surgical repair: a) resection of the lesser of the 2 aortic arches in DAA, and b) vascular ring release in RAA, with resection of the Kommerell diverticulum, when present, followed by transposition of the left subclavian artery to the left carotid artery. In addition, anterior aortopexy was performed in 4 patients. No major complications were
reported after surgical treatment in both groups, and morbidity was chiefly related to tracheomalacia or bronchomalacia, prolonging postoperative stay. At the follow-up evaluation [median: 10 (9–13) months] after surgery, a resolution of the gastroesophageal symptoms and an improvement in respiratory symptoms, as well as in patients with residual airway malacia, were reported in both groups.

Conclusion: In children with DAA and RAA, surgical treatment can be accomplished with low morbidity and essentially no mortality and good clinical outcomes.

D186 – Inflammatory Pseudotumor in Children.

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Introduction: Inflammatory lung pseudotumor is a rare benign neoplasm that usually manifests itself as a solitary pulmonary nodule. Endobronchial presentation is infrequent. Histologically, it is composed of lymphocytes, histiocytes, plasmaocytes and myofibroblasts. The treatment of choice remains conservative surgery and one should always seek to obtain free margins due to the possibility of local recurrence. The objective of this work is to report a case of inflammatory pseudotumor as a cause of persistent pulmonary images in children.

Case report: P.O.A, 9 years old, schoolboy, male, from RJ, Brazil, hospitalized at the Municipal Jesus Hospital, RJ, for investigation of persistent pulmonary imaging in HTE and recurrent pneumonia. The mother reported 10 days of fever and cough, with a treatment of amoxicillin given on an outpatient basis, with no improvement. The condition evolved with abdominal pain and vomiting. No weight loss or decline in general state of health was noted. He reported two previous hospitalizations for pneumonia, the first of which was 6 months ago, with left pleural effusion. Four months later, he presented a new pneumonia episode in the same location. All required immunizations had been given. There was a family history of tuberculosis (mother and maternal grandfather). He lives with his mother and grandfather in a home with good hygiene and sanitation.

Physical examination: eutrophic, eupneic (FR = 24irpm), good perfusion, acyanotic, hypocortical (+/- 4). Bronchial Murmur reduced in the left hemithorax, without adventitious noises. The remainder of the examination went without notable issues. Amoxicillin with clavulanate and symptomatic treatment was initiated. Complementary examinations demonstrated: anemia (ht = 28.8% and hb = 9.9g/dl), leukocytosis with left shunt 22000 (with 15 sticks and 65 segmented), HSV = 28 mm, PCR = 122 mg/l, normal biochemistry and two negative tuberculin tests. Amoxicillin was given for a short period. During evaluation in Pediatric Pulmonology at 3 months old, he presented a new episode of fever and cough, with a treatment of amoxicillin given on an outpatient basis, with no improvement. The condition evolved with abdominal pain and vomiting. No weight loss or decline in general state of health was noted. He reported two previous hospitalizations for pneumonia, the first of which was 6 months ago, with left pleural effusion. Four months later, he presented a new pneumonia episode in the same location. All required immunizations had been given. There was a family history of tuberculosis (mother and maternal grandfather). He lives with his mother and grandfather in a home with good hygiene and sanitation.

Physical examination: eutrophic, eupneic (FR = 24irpm), good perfusion, acyanotic, hypocortical (+/- 4). Bronchial Murmur reduced in the left hemithorax, without adventitious noises. The remainder of the examination went without notable issues. Amoxicillin with clavulanate and symptomatic treatment was initiated. Complementary examinations demonstrated: anemia (ht = 28.8% and hb = 9.9g/dl), leukocytosis with left shunt 22000 (with 15 sticks and 65 segmented), HSV = 28 mm, PCR = 122 mg/l, normal biochemistry and two negative tuberculin tests. Image exams: chest X-ray with hypotransparency in 2/3 lower HTE and left posterior opacity. Negative results for sputum smear microscopy were recorded. Chest tomography with contrast showed a left lung volume reduction, with discrete deviation of mediastinal structures and consolidation of heterogeneous impregnation of the left inferior lobe, compatible with mucoceles. Bronchoscopy: fragile endobronchial vegetative lesion in segment 6 of the left lower lobe bronchus. Biopsy: spindle cell proliferation, with low mitotic index, associated with mild lymphoplasmacytic inflammatory infiltrate, compatible with Inflammatory Pseudotumor. Favorable evolution, awaiting surgery.

Conclusion: In the case described, it is important to draw attention to the differential diagnosis of recurrent pneumonia cases of the same location. In the present case, due to the family history of tuberculosis, a high prevalence of the disease in Brazil, tuberculosis was investigated. However, the investigation was negative. Bronchoscopy examination with biopsy was decisive for the diagnosis. In young patients, those with well circumscribed lung mass and non-specific respiratory symptoms, the diagnosis of inflammatory pseudotumor (IPT) should be considered.

D208 – Neuroendocrine Cell Hyperplasia of Infancy Associated with Dermatofibrosarcoma Proteruberas: A Case Report.

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Introduction: Neuroendocrine cell hyperplasia of infancy (NEHI) is a rare form of childhood interstitial lung disease of undefined etiology. Infants affected tend to present with dyspnea, tachypnea, persistent cough, failure to thrive and hypoxemia. It is a poorly understood disease. Dermatofibrosarcoma protuberans (DFSP) is a rare low-grade skin malignancy with high probability of recurrence. Its origin is not well established. It presents as a firm lesion, on which nodes may arise. The disease prevails between the second and fifth decades of life, but there are reports of presentation in childhood and at birth. DFSP has surgical treatment.

Objective: To report a simultaneous occurrence of two rare diseases: NEHI and DFSP.

Case Report: Male patient, 5 years old, with hospitalization at 7 months of age with history of respiratory distress since birth, sporadic dry cough, failure to thrive and need for nocturnal supplemental oxygen for a short period. During evaluation in Pediatric Pulmonology at 8 months of age, physical examination revealed a weight lower than 3rd percentile of the standard growth chart, absence of toxemia, increased anteroposterior diameter of the chest and pectus carinatum, tachydyspnea at rest, with normal oxygen saturation in room air, and bibasilar crackles. Chest radiography showed lung hyperinflation. Chest HRCT scans showed ground-glass opacification in central regions of the middle lobe, the lingula, the lower lobes and upper lobes, and air trapping in the lower lobes and upper lobes (Images A and B). NEHI was confirmed based on clinical and tomographic findings.
During his follow-up, the child was referred to Dermatology to assess an abdominal macula with palpable subcutaneous nodules. His mother had noticed the lesion since birth. Histopathological and immunohistochemical examination with CD-34 antibody were consistent with DFSP (Images C and D). A tumor resection was performed. CT scans performed preoperatively did not show any metastases. Inguinal lymph node biopsy showed no signs of metastasis.

Discussion: It is important to report this case with an association of two rare pathologies to alert the possibility of a relationship between NEHI and the development of malignancy. A genetic basis is probably involved in these diseases due to the fact that both revealed clinical manifestations from birth.

5. FETAL AND NEONATAL RESPIRATORY DISORDERS

E4 – Case Description of Development of Diaphragm Eventration in a Three-Month-Old Infant with Goldenhar Syndrome Associated with a Severe Laryngomalacia.

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Introduction:

Eventration of diaphragm is a congenital disorder in which all or part of the diaphragmatic muscle is replaced by fibroelastic tissue. The weakened diaphragm may be displaced into the thorax and compromise the patient’s breathing. Complete eventration almost invariably occurs on the left side and is rarely on the right side. We present a premature female infant whose right-side diaphragm eventration was first noted at one month of age, although the previous CXR films showed normal bilateral diaphragmatic levels.

Case report:

The 3-month-old female infant, with a history of symmetric SGA (bithym body weight 2400 g at 39 + 4 weeks of gestation) and multiple congenital anomalies, was referred to our hospital due to a deterioration of respiratory distress. She suffered from remarkable chest retractions at admission with a loud and high-pitch stridor sound. CXR showed increase infiltrations in bilateral lung field and a round-shape patch in the RLL area. Clinically, we provided support with nasal CPAP and chest physiotherapy, but the respiratory distress, stridor sound, and RLL patch persisted. Therefore, we arranged a bronchoscope study and noted a severe degree of laryngomalacia. We also examined the diaphragm movements with a fluoroscope, and found a remarkable eventration deformity of the right-side diaphragm at its posterior aspect by 3 rib spaces. (No paradoxical movement of the right diaphragm, and no herniation of abdominal contents into the thoracic cavity). Laser therapy to reconstruct the severe laryngomalacia and right diaphragm plication via abdominal approach to pull down the elevated diaphragm were undertaken. She improved in breathing and feeding and began to gain weight afterwards, and was discharged smoothly.

Discussion:

Although diaphragm eventration is a congenital defect, the case we present display a late development of right diaphragm eventration at one month of age. We suspect this to be a combination effect of both diaphragm muscle weakness of the right side and a high negative pleural pressure associated with the severe laryngomalacia. To date, we have not found any literature report mentioning this type of “late development of diaphragm eventration”.

E12 – Few Symptoms, Almost Normal Lung Function and Good Exercise Capacity in Adolescents Born Moderately Preterm: Findings from a Community-Based Cohort

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Introduction:

Pulmonary outcomes of moderately-preterm children (MP) in adolescence are unknown. The aim of this study was to determine the long-term effects of moderately preterm birth on respiratory health: that is, respiratory symptoms, allergic symptoms, lung function and exercise capacity. This is the first study on this topic.

Methods: This was a prospective cohort study. Outcome variables were prevalence of respiratory symptoms determined by ISAAC Questionnaires, Lung function parameters such as FEV1, FVC, LCI and exercise test parameters such as maximal workload, maximal VO2, breathing frequency, ventilatory reserve, and BORG score.

Results: 71 children participated in the measurements: 37 MP and 34 full-term (FT). Both groups were comparable in age, height, weight and exercise activities, but differed in gestational age (MP 34 ± 1 weeks, FT 39 ± 0.9 weeks) and birth weight (MP 2442 ± 539g, FT 3693 ± 393g). Participants did not report many symptoms, but MP adolescents reported more (dry) cough (MP 22% vs. FT 3%, p = 0.016) and hayfever (MP 32% vs. FT 9%, p = 0.015) than FT. MP did not report more wheeze, dyspnea, asthma or eczema during the last twelve months. Most lung function measurements including LCI were within the normal range for both groups, except PEF (MP 86% pred vs. FT 93% pred, p = 0.05) and MEF75, (MP 86% vs. FT 96%, p = 0.06) which were at the lower limit of normal in MP. We observed no differences between the groups in maximal workload, maximal VO2, breathing frequency, ventilatory reserve, and BORG score. (See also table 1).

Conclusion: Moderate preterm birth has little impact on respiratory health in adolescence. Adolescents born MP report few symptoms (but more than FTs), have only mild lung function abnormalities compared to FTs and do not differ in the maximal exercise test and in physical activity level.

Table 1: patient characteristics, results of symptoms mentioned in questionnaire, main lung function and exercise test parameters. *No results are shown if participants did not answer a specific question.
Background: The increased and earlier use of prenatal ultrasound has facilitated the detection of congenital thoracic malformations (CTMs). Our Pediatric Pulmonology Institute follows an increasing number of patients with CTMs. We sought to examine if the increased number of CTM reflects true higher incidence or the result of an increased early use of prenatal ultrasound.

Objectives: To evaluate prenatal sonography detection rates of CTM, and to estimate changes in detection rates over a period of 16 years.

Methods: A retrospective, cross-section analysis of prenatal ultrasound (US) screening tests carried out in a large community-based clinic, comparing two periods – 2001–2007 and 2007–2017.

Results: A total of 34,716 prenatal US were performed at a median (range) gestational age of 15.4 (11.6–23.9) and 15.7 (12–33.6) weeks in 2001–2007 and 2007–2017, respectively. In 2001–2007, 12,016 prenatal ultrasound tests detected 19 CTMs, compared to 30 CTMs out of 22,700 tests in 2007–2017. Twenty CTMs, mainly congenital diaphragmatic hernia (CDH) and congenital pleural effusion (CPE), were associated with other fetal lesions. Thirteen congenital pulmonary airway malformations (CPAM) were detected; none of the latter was associated with other malformations. Detection rates did not change (1.58/1000 in 2001–2007 vs. 1.32/1000 in 2007–2017, p = 0.64).

Conclusions: CTMs were diagnosed earlier than previously reported. CDH and CPE tend to appear with multiple lesions and warrant further attention. The incidence rates remained stable when comparing the last decade to previous years. Thus, the increased referral of CTM can be attributed to an increase in prenatal screening studies performed, rather than a change in detection rates.

6. CYSTIC FIBROSIS

F94 – Trends in Early Lung Disease in Infants and Children with Cystic Fibrosis.

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Improvements in survival are continuously accruing in people with cystic fibrosis (CF) and appear to be evident in sequential birth cohorts [1]. As accumulating evidence points to the importance of early lung disease in CF, we hypothesized whether such improvements are also reflected in early lung disease outcomes of pulmonary inflammation, lung function and lung structure in infants and preschool children with CF.

Pulmonary inflammation and infection, lung function, lung structure and hospital admissions were retrospectively assessed in infants and preschool children with CF from 0 to 3 years old included in the AREST-CF early surveillance program. Details about this program and its protocols have been published previously [2–4]. In our cross-sectional analysis, we compared patients treated between 2006 and 2010 (cohort 1) with patients treated between 2011 and 2015 (cohort 2). We analyzed patients at time of routine annual BAL, which was: 3 months, 1 year and 3 years. We included a control non-CF group which had BAL-samples and inflammation data available from 2006–2015. In our longitudinal analysis, we tested all early lung disease outcomes and used multivariate mixed effects models with random intercepts to account for repeat visits. All models were adjusted for age and test center.

Infants and preschool children had similar age, gender and genotype between cohort 1 and 2 for the analyzed age-groups. The proportion of patients with detectable neutrophil elastase (NE) in BAL fluid was significantly lower in our most recent cohort: 15.5% (95% confidence interval [CI], 4.7% – 26.3%; p = 0.005) difference for patients aged 3 months (n = 176), 15.3% (95% CI 6.1% – 24.5%; p = 0.001) for patients aged 1 year (n = 229) and 13.9% (95% CI 1.2% – 26.6%; p = 0.034) for patients aged 3 years (n = 191). The proportion of patients with detectable NE in our control non-CF group showed no significant difference between the cohorts: 10% vs. 0% (95% CI -8.5% – 28.6%; p = 0.184) for cohort 1 and 2 respectively in 1-year-olds (n = 27) and 16.7% vs. 11.1% (95% CI -30.6% – 41.7%; p = 0.756) in 3-year-olds (n = 15). Lung structure and lung function outcomes showed no significant changes for the two CF cohorts. The results from the longitudinal analysis were similar to those reported for the cross-sectional inflammation data, showing reduced inflammation outcomes in cohort 2. Being in the second cohort was associated with lower proportions of NE for all ages combined, with an odds-ratio (OR) of 0.44.

This is the first study to identify secular changes in early pulmonary inflammation during the first years of life in CF. This finding suggests that enhanced focus and surveillance of early lung disease over the past decade manifests as improvements in early disease outcomes. Alternatively, these trends may be arising due to improvements in treatment following diagnosis occurring generally and unrelated to increased surveillance. The finding of reduced inflammation has the potential to be associated with longer-term improvements and even enhanced survival. We report that the development of early CT-identified bronchiectasis has not yet shown a significant downward trend and it is therefore necessary to further evaluate the potential for reducing inflammation early in life and the subsequent development of bronchiectasis later in life.

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F148 – Relationship between the First Isolation of Pseudomonas Aeruginosa and the Preceding Viral Infection in Children with Cystic Fibrosis.

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Purpose of the study: Identifying a pattern between the first isolation of Pseudomonas aeruginosa (PA) from oropharyngeal swabs and the preceding viral infection in children with Cystic Fibrosis (CF). Children in the first five years of life acquire several episodes of viral upper and lower respiratory tract infections and can end up presenting to hospital for supportive treatment.

Methods: This was a retrospective study at the Royal Manchester Children’s Hospital, a tertiary center for cystic fibrosis. Children with CF up to the age of 5 years were included in the study. Data was collected using an electronic database from January 2012 until December 2016. A diagnosis of a first PA isolation was confirmed with cough / oropharyngeal swabs. A diagnosis of a viral infection was confirmed with viral PCR on the nasopharyngeal aspirate.

Results: 56 children were included in the study, out of which 24 acquired an initial PA infection in the first 5 years of life. 8 out of these 24 children had a preceding viral infection in the last 8 months. 1 child had a preceding viral infection in the last 2 years. This might be due to undiagnosed viral infections that occurred closer to the initial PA infection date. The length of time from the last viral infection to the first acquisition of PA infection varied from a few days to a few months. No temporal relationship was established between both variables. Common viral isolates were Rhino virus and RSV.

Conclusions: 9/24 is a significant number (p < 0.05) of preceding positive viral infections before first PA isolations. Nevertheless, it is difficult to find a causal correlation between viral infections and the initial acquisition of PA in the early years of CF patients. The earlier the acquisition of PA infection, the more severe the CF-associated lung disease and the worse the prognosis. Small numbers in this study made it difficult to identify a particular viral infection leading to increased likelihood of PA acquisition.

Discussion: Antibody titers against certain PA antigens can diagnose PA pulmonary infections 6−12 months before the organism is isolated from oropharyngeal cultures. Therefore, performing such titers after every viral infection, may better demonstrate a correlation between viral infections and the initial PA acquisition. In addition, it might provide information on the type of virus that is most likely paving the way for PA colonization and lung damage before respiratory symptoms appear. There might be a role of vaccines against some of these viruses in children with cystic fibrosis.

F160 – Galectin 9 Correlates with Lung Function Decline during Pulmonary Exacerbation in Cystic Fibrosis Pediatric Patients.

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Galectin 9 belongs to the family of glycoproteins interacting with glycoconjugates present at the cell surface that regulate proliferation and apoptosis. In the previous studies, enhanced galectin 9 breakdown by neutrophil elastase was observed during neutrophilic inflammation of the airways. We hypothesized that galectin 9 expression in the airways and in peripheral blood may be altered upon pulmonary exacerbation in cystic fibrosis.

We analyzed 31 CF patients and 20 healthy controls aged 6−18 years. Patients were assessed twice: during pulmonary exacerbation (PE) and during stable period. In all patients, we assessed lung function with several tests (FEV1, FVC, TLC, RV, R5, X5, Rf, AX), CBC, CRP, microbiological analysis of sputum culture and radiological analysis. Severity of symptoms was assessed using Shwachman − Kulczycki score. Galectin 9 mRNA expression was analyzed using real-time PCR method and protein concentration in serum and sputum supernatants was measured using ELISA kit.

We observed that Galectin 9 protein concentration was significantly higher in CF patients during exacerbation (9.74 ng/ul) and stable period (9.57 ng/ul) than in healthy control subjects (6.55 ng/ul) (both p values below 0.001). Concentration of Gal-9 was significantly higher in sputum than in blood (p < 0.0001). No significant correlation was observed between Gal-9 concentration and disease severity (SK score).

Gal-9 level correlated with disease progression (exacerbation within 3 months from inclusion in the study, changes in radiological picture, lung function); we observed a significant correlation with FVC decline (p = 0.025), but not with the other analyzed progression markers.

Galectin 9 seems to be related to airway inflammation in CF and may be a marker of lung function decline, mainly vital capacity reduction, and a marker of future exacerbations.

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7. RESPIRATORY MANIFESTATIONS OF EXTRAPULMONARY DISEASES (INCLUDING AIDS)

G5−Long-term Ventilation for Tracheobronchomalacia in Children with Hypophosphatasia.

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The work was supported by National Science Center, Poland, grant no. 2016/22/E/NZ5/00383.
Introduction:

Hypophosphatasia is a rare genetic condition causing abnormal development of bones and teeth due to mutations in tissue non-specific alkaline phosphatase (ALP) gene leading to low activity of the enzyme. There are six main forms with varying severity. The most severe form is perinatal (autosomal recessive) causing markedly impaired bone mineralization, skeletal malformation, nephrocalcinosis, cranial synostosis, chest wall deformities, underdeveloped lungs and airway malacia.

This is a potentially fatal condition for which termination was often previously offered. However there have been significant developments of new enzyme therapies along with the introduction of airway support which means these children can now survive.

Method and Results:

We present four cases treated by the endocrine department with enzyme replacement therapy (ERT) in the form of asfotase alpha in conjunction with the Respiratory, ENT and Intensive care teams. These additional teams facilitated tracheostomy and long-term ventilation in order to support their underdeveloped lungs and malacic airways in the initial phases of treatment. The children were recruited as part of a clinical trial for the ERT with one of the patients administered the treatment on compassionate grounds. In three patients, the malacia completely resolved in the first 24 months of life and airway support has been discontinued. One child continues on long term ventilation due to other comorbidities. Asfotase alpha has been shown to improve skeletal mineralization and may have a direct impact on airway malacia although this has not been fully investigated. We do know that it at least indirectly aids by supporting growth of the child and therefore the airway caliber and cartilage rigidity also improves with age.

Conclusion:

As demonstrated, our case series shows that these children now have a good prognosis. With timely, sometimes antenatal diagnosis and a multidisciplinary approach, novel therapies and airway support via long term ventilation mean that these children have been able to survive infancy and have their respiratory support removed as they have grown.

Objective: The purpose of this case report is to summarize the clinical characteristics, diagnostic workup and outcome of a patient affected by ROHHAD syndrome.
At age 9 he moved to Italy. He presented another respiratory failure associated with respiratory infection, needing higher levels of NIV support. Thermal dysregulation and abnormal sweating were noted, believed to be of central origin. A polysomnography was performed in the absence of NIV: it showed normal sleep architecture, without sleep disordered breathing, AHI of 3.2 and 5.2 in supine position, mean oxygen saturation 92%, lowest 86% only briefly. CO2 was not measured, sporadic central events (hypopneas and one apnea). Late onset congenital hypoventilation syndrome was suspected but PHOX2B gene mutation was negative. At this time, he was started on growth hormone (GH) because of GH deficiency and negative stimulation test. On follow-up, hypermotia with elevated plasma osmolality and elevated urine osmolality was noted, responding to fluid intake, but causing nocturnal enuresis which was distressing for the patient. Further hormone studies revealed central hypothyroidism, lower limit cortisol that responded to ACTH stimulation, and hyperprolactinemia. Hypothalamic dysfunction was diagnosed. A control brain and spinal cord MRI were performed and resulted normal. He was therefore treated with hormone replacement therapy: somatropin (GH), desmopressin, levothyroxine, and hydrocortisone in stress situations.

At age 10, he returned to Barcelona. A polysomnography showed a rapid (within one hour) and marked oxygen desaturation, mean 89% and lowest 78% following an obstructive respiratory event, peak CO2 was 59 mmHg, the study was deemed positive for severe hypoxemia with hypercarbia and he continued on NIV with normalization on usual home pressures (IPAP 21, EPAP 8).

At age 12, he moved to Germany. He presented another hypercapnic respiratory failure in the context of pneumonia which required intubation for two weeks. During that episode, he presented severe central and obstructive apneas that resulted in severe bradycardia with AV nodal escape rhythm and asystolia. An abnormally low heart rate was detected and a Holter study showed alternating sinus rhythm with low auricular rhythm, compatible with dysautonomia.

Nowadays, at age 14, he is being followed in our clinic again. He keeps presenting episodes of daytime sleepiness, fatigue, speech problems, and crises of palpebral pseudoptosis. His spirometry is normal (FEV1 84%, FVC 80%, FEV1/FVC 90, MEF 130%), and he keeps using home NIV for daytime naps and nocturnal sleep time. Holter monitoring shows normal sinus rhythm alternating with low auricular rhythm. Since atypical narcolepsy with low hypocretin levels in cerebrospinal fluid have been described, a lumbar puncture was performed but hypocretin levels were normal. An oncology screening protocol for neural cell tumors was negative. His stature is 155 cm (p21), weight 58.3 kg (p78), body mass index is 24.2 (p98), Bone age corresponds with chronological age, Tanner puberty stage P1G1, with both testes being 3 ml. Since puberty is delayed, he is started on testosterone. He is on hormone replacement therapy with GH, hydrocortisone, desmopressin, and levothyroxine. Neuropsychological study reveals normal intelligence quotient, but difficulties in planning, immediate visual memory, holding attention, orthography, and affective symptoms with difficulties establishing relationships.

Conclusion: ROHHAD syndrome is a clinical diagnosis, and lacks a known specific gene marker. It should be included in the differential diagnosis of hypoventilation syndromes (Congenital Central Hypoventilation Syndrome, Ondine’s syndrome, Prader Willi syndrome, neuromuscular diseases, structural or metabolic disorders) and especially suspected in patients with rapid-onset obesity or hypothalamic disorders. As has been published, not all the signs and symptoms appear at the same time and sleep-related breathing disorder can be the last one, hence endocrinologists should be aware of this feature and request sleep night studies regularly if ROHAAD syndrome is being suspected.

G159 – Non-Resolving Pneumonia: A Clinical Presentation of CVID.

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Introduction: Normal resolution of pneumonia is not easily defined and may vary depending upon the underlying cause and host response to pathogen. If clinical and radiographic indices are considered, it can be defined as slow resolution of radiographic infiltrates or clinical symptoms despite adequate antibiotic therapy. There are several components to successful resolution, including clinical improvement, radiographic resolution, and microbiological eradication. Improvement in vital parameters usually occurs in 2–3 days, and most patients note subjective improvement within 3–5 days of treatment. Radiographic resolution of pneumonia is estimated at 3–4 weeks and microbiological eradication is very variable and dependent on the infectious agent. If resolution of pneumonia is not appropriate, additional evaluation should be done. Considering the fact that non-resolving pneumonia is not a common condition, comorbid diseases and other host factors that can be associated with slower resolution of infiltrates should be investigated.

Case report: A 3.5-year-old boy was admitted to our hospital for diagnostic evaluation of recurrent pneumonias and bronchitis. Until the age of 3, he was already treated for 4 radiologically and clinically confirmed pneumonias, 3 of which were treated inpatient. By the time he was admitted for planned additional diagnostics, he had already had an adenoidectomy because of previously found adenoid hypertrophy. Allergy tests were conducted as well as 24-hour pH-metry of the esophagus with impedance and cardiac evaluation, which were all normal. Chest X-ray repeatedly showed bilateral infiltrations. Flexible bronchoscopy showed diffusely edematous bronchial mucosa with abundant turbid secretion, without any anatomical abnormalities or foreign bodies. Immunoelectrophoresis showed decreased levels of IgG (4.6 g/L) and IgM (0.3 g/L) with normal levels of IgA (0.7 g/L). Consequently, further immunological evaluation was performed. Lymphocyte flow cytometry immunophenotyping showed a decreased absolute number of CD4 + CD8- (T helper cells), while other subtypes...
were in normal range. Flow cytometry immunophenotyping of B lymphocyte subpopulations showed a decreased level of plasmablasts and double negative B lymphocytes. By assessing antibodies to hepatitis B surface antigen (antiHbs) titer, which were undetectable, inadequate antibody response to vaccines was confirmed. Considering the results of the diagnostic evaluation, the diagnosis of common variable immunodeficiency (CVID) was made and intravenous immunoglobulin replacement therapy was started. Since then, the boy has been receiving his therapy in monthly intervals and no new pneumonias were verified.

**Conclusion:** We present CVID in a boy who was initially diagnosed with non-resolving pneumonia. In children with non-resolving pneumonia, detailed immunological evaluation should be performed.

**Key words:** CVID, non-resolving pneumonia, children

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**G162 – Immunodeficiency and Respiratory Papillomatosis Coexistence.**

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We report on an association of immunodeficiency and juvenile laryngeal papillomatosis (JLP) in a pediatric-aged patient. A five-year-old female patient was referred from another center with suspicion of brochiectasis. Her tomography was reported as fibrotic changes due to necrotic pneumonia. She had an atypical facial appearance, bilateral rales and rhonchi on her physical examination. It was learned that she had recurrent upper respiratory airway infections frequently. Because of the medical history of recurrent lung infections, immunological investigations and flexible bronchoscopy under general anesthesia were performed, showing vocal cords and upper 1/3 trachea were normal. Papillovesicular lesions were extending from the trachea towards the right main bronchus. Part of the lesions was bundle. Swab sample and lavage were tested for HPV-6 and HPV-11. In immunological tests, there was a decrease in the number of cells recovered by bronchoalveolar lavage (BAL) was similar [0.78 (0.29–1.28) x 10^6 cells, and 1.05 (0.68–1.64) x 10^6 cells, respectively] (P = 0.22). A neutrophilic alveolitis and an elevated lipid-laden-macrophage (LLM) index were detected in both groups: no differences were found in neutrophils and lymphocyte percentages or in LLM index between WAR and AR children. In contrast, higher BAL epithelial cell proportions were seen in WAR [10.4 (4.85–23.45)], as compared to AR [2.5 (1.25–7.25)] children (P = 0.0045), suggesting greater airway damage in the former. In the whole patient population, a significant correlation was found between the proportions of BAL epithelial cells and the number of WAR events (r = 0.43; P < 0.037). Finally, elevated BAL concentrations of substance P and of pepsin were observed, not statistically different in the WAR and AR groups.

**Conclusions:** In this patient population, WAR events can be associated with a significant airway inflammation and injury that, because of the biochemical mechanisms involved, are likely not completely preventable and/or counteracted by anti-acid treatments.

**G172 – Airway Inflammation and Injury in Children with Prevalent Weakly Acidic Gastroesophageal Refluxes.**

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**Background:** In children with gastroesophageal reflux (GER), both acid refluxes (AR) and weakly acidic refluxes (WAR) can induce respiratory symptoms (RS).

**Methods:** In order to characterize the airway inflammation in children with more prevalent WAR or AR (defined according to a ROC curve analysis), we performed a 3-year retrospective review of the medical records of patients who underwent fiberoptic bronchoscopy for difficult-to-treat chronic/recurrent respiratory symptoms and who had a positive multiple intraluminal esophageal bronchoscopy (pH/MII) monitoring.

**Results:** In the 13 WAR and 11 AR children, the number of cells were in normal range. Flow cytometry immunophenotyping of B lymphocyte subpopulations showed a decreased level of plasmablasts and double negative B lymphocytes. By assessing antibodies to hepatitis B surface antigen (antiHbs) titer, which were undetectable, inadequate antibody response to vaccines was confirmed. Considering the results of the diagnostic evaluation, the diagnosis of common variable immunodeficiency (CVID) was made and intravenous immunoglobulin replacement therapy was started. Since then, the boy has been receiving his therapy in monthly intervals and no new pneumonias were verified.

**Conclusion:** We present CVID in a boy who was initially diagnosed with non-resolving pneumonia. In children with non-resolving pneumonia, detailed immunological evaluation should be performed.

**Key words:** CVID, non-resolving pneumonia, children

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**G175 – Tracheal Stenosis in Patients with Mucopolysaccharidoses: A Case Report and Literature Review.**

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**Introduction:** Mucopolysaccharidoses (MPS) are comprised of hereditary disorders of different lysosomal storage disorders, joined by errant degradation of glycosaminoglycans (GAGs). The main accumulated storage products include GAGs containing heparan, keratan, dermatan, and chondroitin sulfates. These substances are ubiquitous in connective tissues, hence the manifestations are broad and challenging, including upper and lower airways.
**Case Description:** A 5-year-old boy, with a history of MPS, indirect inguinal hernia, umbilical hernia. Four months before, he was admitted in a county hospital for surgery for indirect inguinal hernia repair. During anesthesia, asphyxia appeared. After emergency treatment, he recovered. The surgery was cancelled. He presented to the clinic department with a chief complaint of slight cough for 1-month history and fever for 2 days with no treatment. A chest X-ray film was obtained showing pneumonia. He was admitted to the pediatric pulmonology department. Physical examination revealed a short neck, growth delay and an abnormal facies. The three-dimensional reconstruction derived from the chest CT scans was performed, showing laryngotracheal stenosis. An electronic bronchofibroscopy was suggested for comprehensive evaluation of upper and lower airways and safe airway management. However, his parents rejected. Simultaneously, considering the risk of anesthesia, surgery was also rejected. Telephone follow-up was conducted every month. His parents noted that he had been in his usual state of health except for intermittent cough with difficult recovery.

**Discussion:** MPS, mainly MPS type I, II, and VI, are complicated by severe obstruction of the upper airways, tracheobronchial malacia, and/or stenosis of the lower airways resulting from the abnormal degradation of glycosaminoglycans which can result in severe, potentially fatal, difficulties during anesthetic procedures. Significant, multi-factorial airway compromise may occur already in early childhood. Airway obstructions may be localized in any of the physiological airways, from the nose to the peripheral bronchia. Insufficient understanding or insufficient emphasis will result in serious consequences, especially in grass-roots hospitals. Safe airway management necessitates a multidisciplinary approach and combined surgeries. 3D CT and bronchoscopy provide quantitative and morphological evaluation of airway stenosis, which is favorable to airway management in MPS children.

**Case Report:** A 6-month-old boy was admitted to evaluate failure to thrive after starting cow’s milk feeding at 4 months of age. On examination, he had tachypnea (75 breaths/min) and chest X-ray was abnormal with a diffuse interstitial pattern.

He was a full term newborn with no other previous history of interest apart from some choking on feedings and cough and cyanosis while crying. His mother, sister and grandmother were celiac. His mother suffered from diabetes and hypothyroidism.

He was then studied for sweat test, tuberculin skin test, echocardiography, abdominal ultrasound; all were normal. Erythrocyte sedimentation rate (ESR) was 71 mm/h, IgG was elevated (2100 mg/dl), and his chest CT showed diffuse ground-glass opacities and septal thickening. At bronchoalveolar lavage (BAL), 40% of lymphocytes and 20% of neutrophils were found. A 24-hour esophageal pH-metry showed severe gastroesophageal reflux, thus omeprazole was started.

A pulmonary biopsy at 8 months of age revealed septal widening with lymphocytic T and B aggregates in the interstitium and the airways.

Serum precipitating IgG antibodies to cow’s milk proteins were positive, and an initial tentative diagnosis of milk-induced hypersensitivity pulmonary disease was made. A cow’s milk-free diet was initiated, with an improvement in growth.

He was administered several boluses of high-dose steroids but no significant respiratory improvement was observed.

At the age of 14 months, he started having a macular rash on the cheeks and ear nodules that worsened with cold. During the following months, this rash extended and became purpuric-necrotic. A skin biopsy showed leukocytoclastic vasculitis and interface dermatitis. ESR was again high (64 mm/h) and transaminases were also increased (AST 110 IU/L, ALT 85 IU/L). Subsequent studies showed that some autoantibodies were positive: ANA (1/640), SMA (1/160), antiproteinase-3 lipin IgG>100, and anti-β2-glycoprotein G 131 U/ml. A suspicion of systemic lupus erythematosus was made.

Different treatments were tried with partial improvement of cutaneous lesions and transaminases: azathioprine, anakinra, hydroxychloroquine, mycophenolate, tacrolimus, and monthly administration of immunoglobulins.

During the first 3 years, he had mild tachypnea that subsequently resolved, with normal SaO2 and normal auscultation. Digital clubbing appeared. Respiratory auscultation and SaO2 were always normal and he never needed oxygen supplementation.

When he was 5 years old, Tocilizumab was started. There was a clear improvement both clinically and blood test-wise, nonetheless this treatment had to be stopped due to muscular toxicity after 4 months.

At six years of age in 2014 (after publication of this new entity: N Engl J Med 2014;371:507–18), this patient was found to have a mutation at the TMEM173 gen and SAVI syndrome was diagnosed.

Since the age of 3, he has been asymptomatic from the respiratory standpoint having only some dyspnea on heavy exercise. Currently he...
is 9 years old and has been following treatment with Ruxolitinib for two years now. There seems to be a good clinical response but ESR is still increased (112 mm/h). Interstitial disease on chest X-rays and CT has persisted. Spirometry shows an alteration compatible with mild restriction [FVC 0.67L (69.49%), FEV1 0.65L/s (75.79%), FEV1/FVC 113%, MMEF 1.78L/s (154%)].

Conclusion: SAVI syndrome is an autoinflammatory disease caused by gain-of-function mutations in TMEM173. It provokes interferon dysregulation that leads to persistent systemic inflammation and signs of peripheral vascular inflammation that starts in the first months of life. We describe the pulmonary anatomo-pathological features in a child with this disease.

It is important to include interferonopathies such as SAVI syndrome in the differential diagnosis of a child with interstitial lung disease, especially when associated with persistently increased acute-phase reactant levels and progressive skin damage.

8. NEUROMUSCULAR AND CHEST WALL DISEASES (INCLUDING SIDS)

H23 – Daily and Nocturnal Respiratory Monitoring in Patients with Duchenne Muscular Dystrophy and Left Ventricular Assistance Device.

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Background: Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder, characterized by progressive skeletal muscle weakness, loss of ambulation, and death secondary to cardiac or respiratory failure. Forced vital capacity (FVC) is an effective marker of respiratory failure evolution. FVC peaks between ages 9 and 16 and then decreases by 5–10% per year until ventilatory support is required for survival. Noninvasive ventilation (NIV) is an effective treatment for respiratory failure. End-stage dilated cardiomyopathy (DCM) is a frequent finding in DMD patients, but they are rarely candidates for cardiac transplantation, thus left ventricular assist devices (LVAD) can be used as a bridge-to-transplantation or as a destination therapy. The aim of our study was to analyze the diurnal and nocturnal respiratory assessment, survival, death rate and causes of death in DMD patients with LVAD.

Methods: FVC, polysomnography (PSG), nocturnal pulsoximetry, mean transcutaneous carbon dioxide (tcCO2) pre- and post-LVAD, survival and causes of death were recorded.

Results: Six DMD patients aged 15 years ± 0.5 at LVAD placement were enrolled. Mean FVC pre-LVAD, calculated on 5 patients at 14 ± 0.4 years, was 41.5% of predicted values. 3 patients had PSG pre-LVAD with normal outcome. Pulsoximetry and tcCO2 pre-LVAD performed in 4 patients showed normal range. After 2 years, the mean FVC of all 6 patients was 18.6% (minimum 6% and maximum 44%). 4 patients were treated with nocturnal NIV, introduced 4 months after LVAD, 1 patient did not need ventilation support (FVC 44%). All ventilated patients showed normal PSG, nocturnal pulsoximetry and tcCO2. Three patients died at 18 ± 0.2 years, at an average distance of 2 ± 0.5 years since LVAD placement. Causes of death were respectively brain hemorrhage during anticoagulant treatment, septic shock from lung infection and iatrogenic tracheal rupture in another hospital. Three patients are alive at 2 ± 0.3 years after surgery.

Conclusion: LVAD does not affect the natural decline of respiratory function in DMD patients, whom require NIV to treat the ventilatory failure and to ensure their survival.

H83 – An Unusual Cause of Atelectasis and Chronic Inflammation in the Lung.

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Case report: A 4-year-old girl presented with fever and pneumonia of the right middle lobe (RML). She was treated with antibiotics (cefuroxim) with a rapid clinical improvement, but with a persistent atelectasis of the RML, despite physiotherapy. A few weeks later, fever relapsed, demonstrating again pneumonia in the RML. A bronchoscopy was performed, showing mucus plugging in the RML, which was subsequently removed. No anatomical abnormalities were seen. Intrapulmonary percussion ventilation physiotherapy was started. However, a third episode of cough, wheezing and fever was seen after 2 weeks, showing again the same radiographic abnormalities. Biochemical markers of inflammation were low.

A second bronchoscopy showed inflamed mucosa with purulent secretions in the right bronchial tree, especially the right middle and upper lobe. A broncho-alveolar lavage revealed H. influenzae and M. catarrhalis. A CT scan was performed to exclude bronchiectasis. Instead, an important exostosis of the costal side of the anterolateral arch of the fourth right rib was observed, compressing a part of the RML. A 3D-reconstruction of the CT-images could precisely demonstrate the aspect of this shortened
and deformed rib. There was no history of thoracic trauma, suggesting this was a congenital rib malformation. To avoid further complications, endoscopic surgery for partial rib removal is planned in the near future.

**Conclusion:** Congenital rib malformations are a rare cause of compression atelectasis and subsequent chronic inflammation of the lung. This case emphasizes the importance of also considering extrapulmonary anatomical anomalies in cases of relapsing lung problems in the same lobe.

**H113 – Why Children with Pectus Excavatum Experience Exercise Intolerance? Cardiopulmonary Function at Rest and on Exercise in Children with Pectus Excavatum.**

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**Introduction:** Patients with pectus excavatum (PE) frequently experience shortness of breath and aerobic capacity limitation. However, it is unclear whether there is an objective limitation of the cardiorespiratory system. In the 1990’s, a minimally invasive procedure for PE repair (Nuss procedure) was introduced. The aims of the study were to assess whether there are cardiorespiratory limitations in these children at rest or during exercise.

**Methods:** A retrospective study. Demographic parameters, clinical symptoms and PE severity of all children assessed for PE at the Schneider Children’s Medical Center of Israel were extracted and evaluated.

Baseline pulmonary functions including volumes (total lung capacity-TLC, forced vital capacity-FVC and residual volume-RV), tidal volume-TV, flows (forced expiratory volume in one second-FEV1), maximal voluntary ventilation (MVV) and cardiopulmonary exercise testing were performed in all children.

**Results:** 140 children (111 boys, mean age 14.3 ± 3.6y) with PE were assessed in 2004-2015. Lung volumes at rest and flows were found to be normal with no difference between patients with chest pain or exercise intolerance and asymptomatic patients. However, severe PE was associated with lower lung volumes and lower tidal volume at rest. Dead space volume (VD) at rest was found to be higher in the moderate-severe group (VD/VT- 42 ± 7% vs. 37 ± 4%; p = 0.004).

Vo2max (O2 consumption at maximal exercise) was within normal range with large variability (94 ± 24% predicted). The maximal load achieved was 85 + 16% predicted and the ventilatory anaerobic threshold appeared earlier than expected (< 40% VO2max) in 53% of cases. Ventilatory breathing reserve was normal in most children (VE/ MVV- 66 ± 16%). O2 pulse was within normal range, but with large variability (O2 pulse- 86 + 21% predicted). No significant heart rhythm abnormalities were observed.

VD/VT at maximal exercise was 31 ± 5% and tidal volume at maximal exercise was increased to 0.44 ± 0.09Xvital capacity, both suggesting less efficient ventilation.

PE patients tended to be tachypneic at maximal exercise (respiratory rate- 118 + 29% predicted).

Pulmonary equivalents at maximal exercise were elevated, suggesting less effective gas exchange in these patients.

Severe PE was associated with lower maximal load, with no difference in VO2max and other ventilatory measurements.

Respiratory symptoms were associated with lower VO2max and higher respiratory equivalents compared to asymptomatic patients.

**Conclusions:** Children with PE have normal pulmonary functions at rest. However, they show maladaptation to exercise, suggesting compromised chest wall mechanics. These changes might have a role in the discomfort PE patients experience while exercising.

**H115 – Sleep Disordered Breathing in Children with Congenital Myasthenic Syndrome: Clinical Presentation and Management.**

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**Background:** Congenital myasthenic syndromes (CMS) are a heterogeneous group of inherited disorders affecting neuromuscular transmission, characterized by fatigable weakness that varies in severity, including respiratory failure. The presence and severity of sleep-disordered breathing (SDB) is poorly documented in this population.

**Objectives:** To describe the clinical presentation and the role of cardiorespiratory polygraphy (CRP), including capnography, in determining the presence of SDB and need for respiratory intervention, including ventilatory support.

**Methods:** Review of medical records and CRPs performed (Embla S4500; Software REMlogic ver 2) in all children with CMS referred to the Sleep Unit at Great Ormond Street Hospital (GOSH) 2003–2017.

**Results:** We identified 23 cases (15 girls) of CMS referred by neurologists to exclude SDB and/or hypoventilation. 4/23 children were established on ventilatory support before the referral and the CRP was performed on it. The median age at the first CRP was 8.3 years (range 0.3–16.8 years). The CRP was abnormal in 9/23 cases (39%). It showed six cases of SDB (five of them with hypventilation) with three of these showing symptoms of obstructive SDB at the time of referral. The other three cases had hypventilation without obstruction (all of whom were on Bi-Level pressure ventilation at the time of the study). We started positive pressure ventilatory support in 4 cases and optimized it in 4 patients (all of whom already established on ventilation).

**Conclusions:** The CRP with capnography has been useful in our study in order to determine the most appropriate time to commence long term ventilation or to optimize ventilation settings in patients already established on ventilatory support.
Although CRP may not predict a respiratory crisis in CMS, it is useful in the diagnosis of SDB even when there is a negative clinical history.

9. EPIDEMIOLOGY, ENVIRONMENTAL RISKS, PREVENTION, SOCIO-ECONOMIC COST, PUBLIC HEALTH RESOURCES

I29 – Are Pediatric Pulmonologists Adhering to Tobacco Prevention, Control, and Treatment Guidelines?

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Background: Tobacco use is the world’s leading preventable cause of death. Children exposed to second (SHSe) and third hand smoke (THSe) are at risk for smoke-related morbidity and have limited options for avoiding exposure. Tobacco smoke exposure increases the risk for sudden infant death syndrome, lower respiratory tract infections, middle ear disease, severe asthma, and slowed lung growth.1,2 Every possible effort should be made to decrease the burden of tobacco-related diseases.

The American Academy of Pediatrics (AAP)3, the American College of Chest Physicians (ACCP)4, and many international organizations have published guidelines to assist physicians in tobacco prevention, control, and treatment. The AAP recommends that pediatricians screen for tobacco smoke exposure at every visit and offer smoking parents counseling, treatment, and referral to quit lines5,6.

Unfortunately, pediatricians’ adherence to the guidelines remains low7,8,9. This may be attributed to lack of physician awareness and familiarity with published guidelines, as well as a lack of knowledge regarding available tools. It is essential that pediatric pulmonologists, who manage primarily diseases that are directly affected by SHSe, adhere to published guidelines.

Purpose of Study: Data regarding whether pediatric pulmonologists adhere to guidelines is lacking. We conducted a survey to assess pediatric pulmonologists’ practices with respect to SHSe screening, counseling, treatment, and referral to cessation services.

Methods: Survey questions included whether respondents used either the AAP Julius B. Richmond Center of Excellence Clinical Efforts Against Second Hand Smoke Exposure (CEASE) toolkit10 or the ACCP Smoking toolkit4. Participants were then queried whether they screened, counseled, treated, and referred caregivers to cessation services some of the time, always, or never. Confidence in smoking cessation promotion and willingness to attend a course if offered at a national meeting was asked. The questionnaire was posted on the pediatric pulmonology list server PedLung. PedLung reaches pediatric respiratory physicians around the globe. Survey Monkey was used to design and administer the questionnaire. Responses were anonymous. Results were compared with our previous data of general pediatricians7.

Results: Eighty responses were obtained. Only 1% stated they always use the AAP and ACCP clinical practice guidelines. Although respondents reported always screening (93%) and counseling (77%), only 27% referred caregivers. Zero percent responded to always prescribing nicotine replacement therapy (NRT), bupropion, and varenicline. Over 55% of respondents did not feel comfortable treating tobacco dependence in caregivers but only 41% responded that they would attend a cessation training course if offered at a national meeting.

Conclusion and Discussion: Compared to our cohort of general pediatricians, the rate of screening and counseling of the respondents was higher but the rate of treatment and referral was similar7. Despite the morbidity of SHSe in common pulmonary diseases like broncho-pulmonary dysplasia11, cystic fibrosis12, and asthma13, pediatric pulmonologists are not using available tools to assist smoking caregivers. It is imperative that physicians who treat children with respiratory disorders feel confident in treating caregivers’ tobacco dependence. A revision of pediatric pulmonary training programs’ curriculum is needed and should include tobacco cessation training to assure graduates are able to be actively involved and at the forefront of treating the tobacco epidemic.

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ABSTRACT

− B. Objective
nosocomial infection from occurring in the first place.
resources as well. It is important that we find other ways to prevent
economic burdens not just for the patient but for the hospital
disease state. Hospital-acquired infections generate substantial
length of stay far beyond what is expected based on the underlying
Nosocomial infections increase morbidity, mortality, and cost and
philippines
C. Significance of the Study
supplementation with arginine will have an effect on nosocomial
Philippines Pediatrics, University of the Philippines, Philippines General Hospital
Salise R. I57 − A Randomized Placebo-Controlled Trial on the Use of
Arginine Supplementation for the Prevention of
Nosocomial Infection in Critically Ill Patients.
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Introduction:
A. Rationale − Healthcare costs have increased through the years.
Nosocomial infections increase morbidity, mortality, and cost and
length of stay far beyond what is expected based on the underlying
disease state. Hospital-acquired infections generate substantial
economic burdens not just for the patient but for the hospital
resources as well. It is important that we find other ways to prevent
nosocomial infection from occurring in the first place.
B. Objective − The main objective of this study is to determine if
supplementation with arginine will have an effect on nosocomial
infection rate versus placebo in critically ill pediatric patients.
C. Significance of the Study − The efficacy of arginine supplementation
to prevent nosocomial infection among critically ill children has not
been well established. Various studies have yielded contradictory
conclusions and are mostly among adults.

Methodology:
A. Study design − Randomized, double blind, placebo-controlled
clinical study.
B. Study setting − This research was conducted in the UP Philippine
General Hospital Pediatric Emergency Room, Pediatric wards and
Pediatric Intensive Care Unit.
C. Study participants − Eligible patients aged 1–17 years old who are
critically ill and necessitate ICU admission were enrolled in the study
with the following inclusion criteria: critically ill patients who
necessitate ICU admission who will be admitted for at least 3 days,
able to tolerate oral feeding, no malabsorption diseases, have no
immunodeficiency, have no congestive heart failure, are well
nourished or are not severely malnourished, have no severe burns,
have no nosocomial infection during 1st day of admission from other
institution and are not allergic to arginine.
E. Statistical Analysis − Sample size was calculated using the Epi Info
software Version 7 based on the assumption that the use of arginine will
result in a 20% reduction in the occurrence of nosocomial infection. It
was estimated using a nosocomial infection rate of 44% and a
confidence interval of 90% with 80% power, we needed 22 children
per group to show a 20% difference. To allow for study withdrawal, a
total of 50 patients were recruited, 25 patients per arm. Data were
analyzed using Epi Info Version 7 software. A T-test was performed
comparing the difference between the means of 2 independent samples.
In comparing the distribution of discrete variables between two groups,
the chi-square test or Fisher’s exact test, when appropriate, was
performed. Bartlett’s test for homogeneity was used to determine if 2
groups were the same or not. All tests were performed at a significance
level at P < 0.05.

Results:
A total of 48 patients out of 50 predicted sample size of critically ill
patients were recruited for the study. Of the 50 patients recruited, 48
were discharged. 1 was withdrawn from the control group from the
study due to mortality and another was also withdrawn from the
arginine group due to mortality. Both patients died from their primary
disease of Pediatric Community Acquired Pneumonia D less than 48
hours after admission.

Baseline characteristics of both groups were not significantly
different from each other. Age, height, weight, sex, chief complaint and
primary diagnosis were statistically the same in both groups.

With regard to primary outcome of this research, it is interesting to
note that none of the patients in the arginine group developed nosocomial
infection as compared to the placebo group wherein 3 out of the 24
patients developed nosocomial infection, particularly a nosocomial
pneumonia. This showed a Relative Risk Reduction of 100% and an
Absolute Risk Reduction of 12.5% with number needed to treat at 8
patients. These are promising, however a result of 0.234 by Fisher’s Test
means that there was no statistical difference between the two groups.

Statistical analysis also showed that there was no statistical
difference in arginine levels between arginine group and the placebo
group, before and after supplementation, using the Bartlett’s Test, P
value 0.120 and 0.074 respectively and degrees of freedom 1. The lack
of statistical significance may be attributed to the dose given to our
subjects, which is a maximum of 3000 grams a day. In a review
performed by Wijands et al (20), several studies in arginine
supplementation used a higher dose of 3000–8000 grams a day, showing positive results.

There were no readmissions and no adverse effects noted.

Conclusion/ Recommendation:
Arginine supplementation has no effect in the prevention of
occurrence of nosocomial infection in patients that are critically ill.
However, further studies are highly recommended and use of a higher dose of arginine supplementation at 3000 grams –8000 grams is encouraged.

Reflections:
Even with the low dose of arginine that was used in this study, the results are promising. It is imperative that we perform further investigation using a high dose of arginine. Maybe with higher doses, the positive effect will be better demonstrated and a statistical difference will be achieved in the prevention of nosocomial infection.

I85 – Exposure to Radiation by Imaging in Severe Asthmatic Children, Hospital Concepcion, Chile

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Introduction: The effects of ionizing radiation occur up to a certain dose, the latter being measured in mSv. It can be instantaneous or occur over decades. Cancer has been identified as a possible manifestation years later. Human beings are exposed to radiation stemming from food, solar waves and certain equipment at home. It is measured as 3 mSv per year. This amount can increase with exposure to X-rays or computed tomography (CT). The age and type of irradiated tissue are important. Children are more sensitive and their life expectancy increases the possible long-term effects. Therefore, it is of vital importance to have the correct justification and optimization of these exams for diagnostic purposes in pediatrics.

Material and Method: 101 of 129 severe asthmatic children were included. They had been hospitalized in the Pediatric Service between October 2013 and July 2016. They were chosen because they were a well-identified group. Twenty-eight children were excluded due to incomplete data. Each child had a digital file in a program called Synapse. All files were reviewed with standard information on mSv from all X-rays and CT scans as a result of their complete medical files. All data were consolidated in Excel and statistical analysis with R-Project was performed.

Results: The age of patients varied between 5 and 14 years with a median of 6.2 years. (Q1 = 4.94, Q3 = 8.4). A total of 430 radiological examinations were performed in the 101 patients corresponding to 95.8% for X-rays and 4.2% for CT scans. The most frequently irradiated areas were: 71.6% thorax, 12.5% limbs and 10% brain (skull). The standardized radiation received by patients in the period had a median of 0.56 mSv (Q1 = 0.28, Q3 = 2.31). Eight patients exceeded 10 mSv. One of them reached the value of 29.55 mSv.

Conclusions: Severe asthmatic children who have been hospitalized in Concepcion registered in their medical history that they have received a quantity of radiation stemming mainly from chest X-rays for which the median is equal to 17% of annual base radiation. Some patients must be followed over time in order to look for certain secondary effects of radiation exposure.

I96–Clinical Epidemiology Study on Mycoplasma pneumoniae Infection in Children

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Objective
Mycoplasma pneumoniae (M. pneumoniae) is an important pathogen causing respiratory tract infection in adults and children. It is one of the most common causes of community-acquired pneumonia (CAP). In recent years, epidemiological characteristics of M. pneumoniae infection have changed; in the last a few years macrolide-resistance M. pneumoniae strains have also become common. Further epidemiological studies are needed to find answers to this phenomenon.

Methods
(1) Study population: patients seen at fever clinic for on-site investigation of M. pneumoniae respiratory tract infections.
(2) The clinical data of the subjects were obtained by questionnaire, medical history collection, physical examination and assistant examination.
(3) Pharyngeal swab acquisition and DNA detection: after acquisition of pharyngeal throat swabs from subjects, we detected M. pneumoniae-DNA by real-time PCR method. For some objects, we conducted long-time monitoring for M. pneumoniae-DNA in pharyngeal swabs to observe the carrying duration of M. pneumoniae after infection and to observe its relationship with the progression of the disease.
(4) Culture and isolation of M. pneumoniae strains: throat swab was inoculated to M. pneumoniae solid medium, and the isolation, liquid culture and PCR validation were carried out.
(5) Drug resistance analysis and mutation detection of M. pneumoniae strains: isolated strains were detected and analyzed for macrolide-resistance, and the mutation points were confirmed.
(6) Molecular typing of M. pneumoniae strains: all isolates were detected by MLVA molecular genotyping. Parts of strains were also detected by P1 gene typing. The two types of molecular genotyping methods were compared. We also explored the significance of MLVA typing in molecular characters in M. pneumoniae infection.

Results
A total of 1025 patients were enrolled. Among these, 163 were M. pneumoniae-DNA positive, with a positive rate of 15.09%. We found that M. pneumoniae infection tended to occur in children over the age of 5 years, summer and autumn were epidemic seasons, and pneumonia was the most common form of M. pneumoniae infection. Multiple regression analysis found that M. pneumoniae infection was
positively correlated with age, severity of disease and multiple siblings, and was negatively correlated with runny nose, nasal symptoms, past history of pneumonia. *M. pneumoniae* carrying time varied according to different parts of *M. pneumoniae* infection: pneumonia was the longest, bronchitis the second, and URI the shortest. A total of 94 *M. pneumoniae* strains were isolated from *M. pneumoniae*-DNA positive patients, with an isolation rate of 57.7%. MLVA typing distinguished the strains into 8 types. Except for 2 strains, all the other 92 strains (97.9%) were macrolide-resistant strains. The 2 macrolide-sensitive strains had a special MLVA type.

**Conclusion**

*M. pneumoniae* infection tended to occur in children over the age of 5 years, summer and autumn were epidemic seasons, and pneumonia was the most common form of *M. pneumoniae* infection. Thus, *M. pneumoniae* is an important pathogen of CAP. Age, severity of disease and multiple siblings were risk factors of *M. pneumoniae* infection. Macrolide-resistant strains were predominant at present. MLVA genotyping may be a molecular epidemiological method of predicting macrolide-resistant strains of *M. pneumoniae* infection.

**Key words** Mycoplasma pneumoniae; surveillance; PCR real-time; outbreak; MLVA; genotyping

**I98 – Problematic Asthma: Risk Factors for the Persistence of Symptoms and Assessment of Features Distinguishing Difficult-to-Treat from Severe Asthma**

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**Introduction:** Problematic Asthma (PA) is characterized by an apparent resistance to therapy with high-dose inhaled corticosteroids (ICS) and other controllers. Although PA represents a small percentage of cases of asthma, the severity of its clinical manifestations affects the quality of life and has an economic impact on health care costs. In addition to confirming the diagnosis of asthma and excluding rare cases of steroid-resistant asthma, difficult-to-treat asthma (DA) must be distinguished from severe asthma (SA).

DA is the term that characterizes asthmatic patients with a poor control of symptoms depending on different factors: poor compliance, environmental triggers, presence of comorbidity.

SA is instead present when adequate control of asthma cannot be achieved by high-dose ICS and additional controllers (long-acting inhaled beta 2 agonists, montelukast and/or theophylline) or by oral corticosteroid treatment or is lost when the treatment is reduced.

The 2014 ATS / ERS Guidelines on SA underline the importance of discriminating the two entities for which the diagnostic and therapeutic approaches are different. During the first clinical evaluation, it is therefore important to identify severity markers that can suggest the diagnostic procedure to be undertaken.

**Methods:** We compared a group of patients with PA (*n* = 51) that were referred to our Broncopneumology clinic between November 2013 and October 2014 with a group of patients with well-controlled asthma (*n* = 62) that were referred in our clinic in 2015.

**Aim:** The aim of the study was to analyze the presence of risk factors determining the persistence of respiratory symptoms and identify anamnestic and instrumental data that allow an early identification of DA and SA, in order to optimize the therapy and direct more in-depth investigations only to those who warrant it.

**Results:** The PA group showed a significantly higher number of hospital admissions (*p* = 0.03), the presence of smoking parents (*p* = 0.03) and a compliance index in performing therapy statistically lower (*p* = 0.001).

The analysis of a subgroup of patients suffering from SA (*n* = 14) compared with the DA group (*n* = 37), showed that in the first group there was a higher frequency of hospital admissions (*p* = 0.04), the presence of food allergies from the first months of life (*p* = 0.0001) and a reduction in respiratory function, expressed by reduced values of Forced Expiratory Volume in 1 second (FEV1), at the limit of statistical significance (*p* = 0.06).

**Conclusions:** The identification of environmental, instrumental and anamnestic risk factors can reduce the number of more in-depth investigations that should be addressed to those cases that are warranted. By facilitating an early distinction between patients with DA and SA, therapy will be optimized, reducing the severity and recurrence of respiratory symptoms and consequently the need for additional medical care.

**I193 – Subgroups of Children with Severe Asthma: Clustering Data Mining Analysis.**

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**Introduction:** Asthma is a chronic respiratory manifestation including symptoms, genetic aspects, different response to treatment guidelines and is underdiagnosed in childhood. It produces missing days at school and a very expensive cost when it is undercontrolled. The prevalence is 15 to 18% and 4% will have severe asthma with a high risk of requiring emergency management and hospitalization. **Method:** Included were all children between 5 and 15 years old, hospitalized in the Pediatric Service at Hospital Regional Concepcion in Chile (HCRC) because of asthmatic crisis from October 2013 to July 2016. There were 129 children in this situation and their files were reviewed. Statistical analysis was made with clustering data mining. **Results:** The median value for age was 6 years old (5-15), with no differences regarding gender, cough 1 to 10 days (mean 2 days), fever 1 day or less (<38°C) (mean 1 day), 98% respiratory distress, initial O2 saturation 79 to 97% with digital equipment (mean 91%), white cell count from 7300 to 21790 (mean 13015), neutrophils from 46 to 96% (mean 88%), C-Reactive Protein (PCR) from 0.2 to 64 (normal < 10) (mean 11.35), days in pediatric service at hospital from 1 to 14 days (mean 3 days), oxygen requirement < 1 to 12 days (mean 2 days). The analysis separated all of these patients into 4 subgroups. Their characteristics were:
ABSTRACT

Subgroup I: This group was characterized by age 8 (Q1 = 6, Q3 = 10), urban address, without medical control, oxygen saturation 94% (Q1 = 92.25, Q3 = 95%), 3 days of cough, no fever, wheezing ++, no virus detectable with indirect immunofluorescence (Adenovirus, Influenzae, Respiratory syncytial virus, parainfluenzae, metapneumovirus), Polymerase Chain Reaction for mycoplasma negative, white cell count 28,000 (Q1 = 14500, Q3 = 39000), with 51% neutrophils (Q1 = 40.5, Q3 = 60), C-Reactive Protein (PCR) 21 (normal < 8) (Q1 = 4.1, Q3 = 38.15), need for oxygen 2 days (Q1 = 2, Q3 = 3), 4 days at hospital (Q1 = 3, Q3 = 5), chest X rays without pneumonia or atelectasis, pleural reaction 47.5 (Q1 = 33.75, Q3 = 66.75), 25% used clarithromycin.

Subgroup II: This group came from different areas, mean age 6.5 years (Q1 = 6, Q3 = 8.75), most of them under medical supervision, cough 6 days (Q1 = 3, Q3 = 8), fever < than 1 day (Q1 = 0, Q3 = 1), respiratory distress, wheezing ++, white cell count 23500 (Q1 = 18500, Q3 = 51750), neutrophils 48% (Q1 = 32.75, Q3 = 63), PCR 19.6 (Q1 = 15.32, Q3 = 24.5), oxygen supply 3 days (Q1 = 2, Q3 = 5), 6 days at hospital, chest X rays with hyperinsufflation.

Subgroup III: mean age 6 years (Q1 = 5, Q3 = 8), cough 6 days (Q1 = 3, Q3 = 6), without fever, with respiratory distress ++, wheezing ++, mean of oxygen saturation 92% (Q1 = 91, Q3 = 95), virus (~), mycoplasma (~), mean PCR 9.8 (Q1 = 3.7, Q3 = 17.8), oxygen supply 2 days (Q1 = 1, Q3 = 3), 4 days at hospital, without any abnormality at chest X-ray, mean of neutrophils 20%, mean of eosinophils 1440 (Q1 = 930, Q3 = 2560).

Subgroup IV: they came mainly from one area Chiguayante, age did not vary, most were under medical supervision with their family doctor, cough 4.5 days (Q1 = 3, Q3 = 6), without fever, without respiratory distress, oxygen saturation 92% (Q1 = 90, Q3 = 95), virus (~), mycoplasma (~), mean for neutrophils 52.5% (Q1 = 26.75, Q3 = 67.75), PCR 17.25 (Q1 = 7.3, Q3 = 32.33), oxygen supply 2 days (Q1 = 2, Q3 = 3), 4 days at hospital, azithromycin 40%, clarithromycin 30%, chest X-ray without pneumonia only inflammation signs, eosinophils 685 (Q1 = 495, Q3 = 1400).

Conclusion: Pediatric patients with severe asthma in crisis, hospitalized in Hospital de Concepción from 2013 to 2016, presented different characteristics forming 4 subgroups according to clustering data mining analysis.

10. INVESTIGATION AND DIAGNOSTIC TESTS

J14 – Polysonmography is an Important Method for Diagnosing the Pediatric Sleep Problem: Experience of One Children’s Hospital

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Background: Sleep problems in children are relatively fewer than in adults, but cannot be overlooked. Polysomnography (PSG) is an important method to diagnose sleep problems in adults, which could also be used for children. Here we collect the PSG data, analyze and share the experiences of PSG in children.

Methods: The results of a PSG study in children (< 18 years old) with sleep problems from April 2015 to May 2017 at the China Medical University Children’s Hospital were collected and analyzed retrospectively.

Results: A total of 310 patients (209 males and 101 females) undergoing PSG were collected. The apnea & hypopnea index (AHI) of these 310 patients was as follows: the AHI was 0–5 in 221 patients, 5.1–10 in 45 patients; and over 10.1 in 43 patients.

The final diagnoses in 209 male patients were as follows: 109 obstructive (52.2%), 65 snoring (31.1 %), 34 limb movement sleep disorder (16.3%), 11 insomnias (5.2 %), 9 parasomnias (4.3%), 8 hypersomnias (3.8%), 7 other sleep-related breathing disorder (3.3%), 6 central (2.9%), 3 narcolepsy (1.4%), 3 sleep terror (1.4%) and 1 sleep seizure 0.5%.

The final diagnoses in 101 female patients were as follows: 45 obstructive (44.6 %), 31 snoring (30.7%), 17 limb movement sleep disorder (16.8%), 13 other sleep-related breathing disorder (12.9%), 11 insomnias (5.3%), 7 central (3.3%), 7 parasomnias (3.3%), 4 hypersomnias (1.9%), 2 sleep seizure (0.9%) and 2 sleep terrors (0.9%).

Management of 270 patients (40 patients did not return to OPD for follow-up) was as follows: surgery with adenoidectomy and tonsillectomy in 19 patients (7.0%), continuous positive airway pressure (CPAP) in 2 patients (0.7%), and medical treatment or observation in 249 patients (92.2%).

Conclusion: The majority cause in children with sleep problems was obstructive sleep apnea syndrome (OSAS) (49.6%), while only 12.3% of pediatric OSAS underwent surgery in our study, which is underestimated since some children with OSAS underwent surgery without performing PSG. PSG may help detect significant sleep-related problems and application of PSG results is useful for therapeutic decisions in children; we suggest that children with sleep problems should accept a PSG study.

J19 – An Emerging Diagnostic and Therapeutic Procedure when Facing Lung Collapse in a Fontan Patient.

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A 10y old female with a history of complex congenital heart disease and Fontan physiology, presented to our institution with severe respiratory distress. She was diagnosed with plastic bronchitis and was treated with manual casts removal by rigid bronchoscopy. Due to her unstable condition, she was subsequently treated with high pressure ventilation, nitric oxide and inotropes. To facilitate potential cast resolution, she was also treated with tracheal installation of TPA as well as Alteplase and budesonide inhalations; however, her condition did not improve. A wide variety of imaging including chest X-ray, echocardiogram and cardiac catheterization failed to identify the etiology of her presentation.
Plastic bronchitis (PB) is a rare clinical disease, characterized by formation of casts that obstruct the airways and lead to asphyxia [Itkin MG et al.]. Plastic bronchitis can be associated with many conditions such as Congenital Heart Disease with Fontan physiology, lymphatic abnormalities, Allergy, Asthma, Cystic Fibrosis, Allergic Bronchopulmonary Aspergillosis, Tuberculosis, Influenza A virus infection, pneumonia, Sickle Cell Disease, neoplastic infiltrates and Rheumatoid Arthritis. Many cases are still labeled as idiopathic [Rubin BK]. A new recent diagnostic technique, DCMRL-Dynamic Contrast Magnetic Resonance Lymphangiography, has identified abnormal anatomic lymphatic variants as the cause for cast formation in many previous idiopathic cases [Dori Y]. This diagnostic technique improved our understanding of PB and enabled a new optimal therapeutic approach. The reasons why this new procedure has become our first-choice imaging technique are summarized in table 1.

Our patient's DCMRL showed markedly abnormal intrathoracic lymphatics. The thoracic duct (TD) was dilated and tortuous, coursing towards the innominate vein on the left. In addition, there was abnormal perfusion affecting mostly the right lung with largely sparing of the left lung. There was also an additional left-sided accessory thoracic duct supplying retrograde flow to the lungs. Last, there was flow into a large left-sided supraclavicular and axillary network. Following the diagnostic procedure, selective embolization of the lymphatic collaterals from distal TD and selective embolization of the left sided duct were performed. After the procedures her symptoms resolved, and she was able to wean from her medications.

Figure 3 DCMRL showing bilateral ducts (arrows) and bilateral abnormal pulmonary and mediastinal perfusion (arrow heads).

This case highlights the new approach to PB based on the role of lymphatic abnormalities in its etiology. DCMRL is a new technique to detect abnormal pulmonary lymphatics, and intervention radiology is a new way to treat it safely and successfully.

Table 1 Advantages and disadvantages of different lymphatic imaging procedures.

| Procedure               | Advantages                                                                 | Disadvantages                                      |
|-------------------------|---------------------------------------------------------------------------|----------------------------------------------------|
| MRI                     | 1) Good spatial and temporal resolution                                     | Cannot be performed in patients with certain metal implants |
| Lymphangiography        | 2) Minimally invasive                                                      |                                                    |
|                         | 3) Water-soluble contrast agent                                             |                                                    |
|                         | 4) Does not use ionizing radiation                                          |                                                    |
| Conventional Lymphangiography | 1) High spatial resolution                                              | 1) Invasive                                       |
|                         | 2) High temporal resolution                                                | 2) Require radiation                               |
| Lymphoscintigraphy      | 1) Minimally invasive                                                      | 3) uses oil contrast agent                         |
|                         | 2) Good temporal resolutions                                               | Poor spatial resolution                            |

Table 1: Advantages and disadvantages of different lymphatic imaging procedures.

J41 – Correlations of Six-minute Walk, Lung Clearance Index, and Quality of Life in Patients with Bronchiolitis Obliterans and Cystic Fibrosis.

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Background: Lung Clearance Index (LCI) is a global measurement of ventilation inhomogeneity, and it was recently suggested as an outcome measure for clinical trials in Cystic Fibrosis (CF). However, the test requires expensive equipment and expertise. Six-minute walk test (6MWT) is a simple non-invasive and inexpensive tool to predict outcome in pulmonary hypertension. Recently it has been used in CF to evaluate candidates for lung transplantation and to predict exacerbations. Both LCI and 6MWT were found as useful markers in Bronchiolits Obliterans (BO). In BO, 6MWT was found to have an important prognostic value and demonstrated a significant correlation with clinical scores and pulmonary function tests.

There are no studies in CF and post-infectious BO evaluating the correlation between the 6MWT results, LCI and Quality of Life (QOL). Such correlation may enable easy and non-expensive tests when resources are limited.

Objective: To evaluate the correlations between 6MWT, LCI, and quality of life in patients with BO and CF patients.

Methods: This is a prospective study including patients with BO and CF. Patients performed 6MWT, LCI test, spirometry, whole body plethysmography, MVV (minute ventilatory ventilation), and Quality of Life questionnaire – SF-36.

The primary outcome parameters were defined as 6MWT in both groups. Correlation of 6MWT to LCI, pulmonary function tests and
J46 – Lung Ultrasound in Bronchiolitis- Is it a Reliable Method?

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Background: Bronchiolitis is a diagnosis that is based on clinical criteria. The aim of the study is to evaluate the feasibility of ultrasound in the diagnosis of bronchiolitis.

Material and Methods: This was an observational study of 43 infants, 1 to 23 mo of age (average age 8.34), hospitalized in the “Alexandrovska” pediatric clinic with bronchiolitis for the period December 2016-March 2017. Ultrasound scans were performed in all patients in the first 24 hours of admission (linear transducer 5.3-11 MHz, with portable ultrasound) and chest X-ray in 35 children. Tests for respiratory viruses (PCR method) were undertaken in 32 patients.

Results: Lung ultrasound findings did not depend on the etiological agent, p = 0.5. Children without chest X-ray changes had normal ultrasound findings in 85% (11/13) of cases. In all patients with severe bronchiolitis, on oxygen treatment (8/8), ultrasonographic changes were recorded, p = 0.001. There was a correlation between the length of hospital stay and degree of ultrasound changes (p = 0.02). Lung ultrasound enabled the identification of infants with underlying radiological changes with a specificity of 84.6% (95% C: 54.5–98.3%) and sensitivity of 80% (95% CI: 59.3–93, 1%), a positive predictive value of 90.9% (95% CI: 72.2–97.1%) and a negative predictive value of 68.7 (95% CI: 49.2–83.3%).

Conclusions: Thoracic ultrasonography is a reliable tool and alternative to chest X-ray for infants with bronchiolitis, with some advantages: no risk of irradiation and the possibility of dynamic follow-up.

Keywords: lung ultrasound, bronchiolitis, infants.

J106 – The Study of the Expression of the Wnt-Related Signaling Pathway on the Development of Pulmonary Hypertension Secondary to Left Ventricular Dysfunction.

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Background: Pulmonary hypertension (PH) is a progressive pulmonary vascular disorder characterized by increased pulmonary vascular resistance and pulmonary arteriolar remodeling. Wnt signaling controls cellular functions during embryonic development and the injury of acquired tissues. β-catenin is a central mediator of the Wnt signaling pathway and controls the transcription of genes during both normal and malignant development. Recently, a gene expression analysis of pulmonary arterial resistance vessels revealed differentially regulated canonical and noncanonical WNT genes in PAH.

Aim: In this study, we attempted to investigate the altered expression of Wnt and Wnt-related proteins of lungs of rats with PH secondary to left ventricular dysfunction by aortic banding, so-called group II PH.

Materials and methods: Utilizing the PH rat model created by ascending aortic banding for 42 days (6 weeks), we studied altered expressions of β-catenin, mRNA and protein expression of canonical Wnt ligands (Wnt3a, Wnt 7a) and non-canonical Wnt ligands (Wnt5a and Wnt11) in lungs of 6-week-aorta-banded rats compared to sham-operated rats. In addition, the immunohistological staining of β-catenin of lungs was also performed in both groups.

Results: In lungs of aorta-banded rats, there were significantly increased protein expressions of Wnt5a, Wnt11 and Wnt5a, and significantly decreased protein expression of β-catenin. In contrast, there were increased mRNA expressions of Wnt 2, FZD5 and Ltb, and decreased mRNA expressions of Wnt3a, Wnt7a, Wif, sFRP1, sFRP2. Very interestingly, there was decreased β-catenin staining of endothelium in lungs of aorta-banded rats.

Discussion: In group II PH secondary to left ventricular dysfunction, the development of PH is closely related to the non-canonical Wnt pathway prominently, rather than the canonical Wnt pathway. The results are compatible with the up-regulated Rho expression of lungs of aorta-banded rats in our previous study.

J114 – Is It Possible to Predict Airway Basement Membrane Thickness by Non-invasive Parameters?

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Airway remodeling occurs in various chronic respiratory diseases. Basement membrane (BM) thickening is one of the most apparent signs of such changes. It can be found in different forms of chronic bronchitis and can be easily and objectively quantified. This makes it a convenient surrogate parameter of airway wall remodeling. However its clinical
use is hampered by an invasive procedure required to obtain a sample of endobronchial biopsy. Consequently the possibility to predict remodeling by non-invasive parameters would be of a great clinical value in the management of patients with chronic respiratory disease. In our work, we aimed to study the relationship between BM thickness and anthropometrical and/or functional parameters.

Between January 2014 and December 2016, we prospectively enrolled 47 patients with chronic bronchitis (CB group) including those with cystic fibrosis, primary ciliary dyskinesia and other forms of chronic bronchitis (e.g. related to primary immunodeficiency), who underwent clinically indicated flexible bronchoscopy. Additionally 20 controls (Co group) – that is, patients with bronchoscopy for acute non-inflammatory conditions (foreign body aspiration, stridor) and no chronic respiratory pathology – were enrolled. The age of our patients ranged from 1 to 18 years (median 8.6 years). At first, all patients underwent lung function testing using nitrogen multiple breath washout test (N2-MBW) and tidal breath analysis. All relevant international recommendations were adhered to. Patients older than 4 years performed the testing in full consciousness and with active cooperation. In younger children, lung function testing was performed during tidal breathing under intravenous anesthesia (propofol) immediately before the bronchoscopy. Flexible bronchoscopy with endobronchial forceps biopsy was performed in the same session after addition of inhaled anesthesia (sevoflurane). The samples were processed for light microscopy and stained by hematoxylin-eosin. BM width was measured by one investigator (VK) using computer image analysis software (NIS Elements). The two study groups were compared using the Welch t test. The relationship between non-invasive parameters (anthropometrical and functional) and BM width was analyzed in the whole study group (CB + Co group). At first, Spearman’s correlation coefficient was used to evaluate the relationship of each single non-invasive parameter with BM width. Next, more advanced approaches (principal component analysis, least angle regression method) enabling analysis of multiple predictors simultaneously were employed to evaluate the possibility of making BM width predictions using more non-invasive parameters at the same time.

There were no differences in age and z-scores relative to weight, height or BMI of patients enrolled in the CB and Co groups. Complete lung function and morphological data were available in 43 patients (64.2%). Patients in the CB group had significantly greater BM width (ΔBM width = 1.13 µm, P < 0.001) and worse lung function compared to controls. When analyzed separately, none of the anthropometrical parameters alone (weight, height, BMI and their z-scores) correlated significantly with BM width. When more anthropometrical parameters were taken into account simultaneously, a small but significant part of BM width variability (R2 = 0.111, p = 0.036) could be explained. Only a few lung function parameters individually were significantly correlated with BM width: LCI2.5 - r = 0.42, p = 0.008; Scond - r = 0.51, p < 0.001 and tPTEF/TE - r = -0.39, p = 0.013. Simultaneous analysis of more functional parameters increased the predictive power and allowed to explain 30.8% of BM width variability (p = 0.003). If anthropometrical and functional parameters were combined together, the predictive power of such model was clearly increased (R2 = 0.621, P < 0.001).

Our work focused on BM width, as a sign of airway wall remodeling. In a wide age spectrum group of patients, we investigated its relationship to anthropometrical and lung function parameters, which may be its determinants (measured non-invasively). Our data showed a clear correlation of airway wall remodeling with lung function and anthropometrical parameters. This finding is in contrast with several previous studies. Hilliard et al (Thorax, 2007) found significant relationship between lung function (measured by spirometry) and inflammation occurring in airway lumen (assessed by bronchoalveolar lavage fluid). On the other hand, changes occurring in airway wall (BM width) were not reflected by spirometry. Contrarily to this, we proved a significant relationship between ventilation inhomogeneity (as assessed by N2-MBW) and BM width. This discrepancy may be partly explained by the higher sensitivity of N2-MBW to the early stages of chronic respiratory diseases. Similarly, previous works addressing anthropometrical parameters as determinants of BM width did not reveal any relationship. Our approach, however, studied additional anthropometrical parameters as BM width determinants simultaneously, and indeed we were able to explain a small but significant part of BM width variability in this way. We hypothesize that this relationship is too complex to be described by just one determinant. Consequently, we combined both anthropometrical and functional parameters in one predictive model which further increased the predictive power of this model for BM width variability – reaching 62.1%. In our opinion, such predictive power is sufficiently high to be considered clinically relevant. However there still remains significant variability to be explained by other parameters (e.g. diagnosis itself). This finding requires further research before it can be implemented into routine care of patients with chronic bronchitis.

J116 – Impulse Oscillometry at Preschool Age Is a Strong Predictor of Lung Function by Flow-Volume Spirometry in Adolescence.

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Background: The transition from early childhood wheezing to persistent asthma is linked to lung function impairment over time. Little is known how the methods used to study lung function at different ages correlate longitudinally.

Methods: Sixty-four children with a history of hospitalization for bronchiolitis before six months of age were prospectively studied with impulse oscillometry (IOS) at the mean age of 6.3 years and these preschool IOS results were compared with flow-volume spirometry (FVS) measurements at mean age of 11.4 years.
Results: The baseline respiratory system resistance at 5 Hz (Rrs5) showed a modest statistically significant correlation with all baseline FVS parameters except FVC. The post-bronchodilator (post-BD) Rrs5 showed a modest statistically significant correlation with post-BD FEV1 and FEV1/FVC. The bronchodilator-induced increase in Rrs5 showed a modest statistically significant correlation with baseline and post-BD FVS parameters except post-BD FEV1/FVC, respectively, and post-BD Xrs5 showed even a strong correlation with post-BD FVC (ρ = 0.61) and post-BD FEV1 (ρ = 0.59). In adjusted linear regression, preschool Xrs5 remained as a statistically independent predictor of FVS parameters in adolescence; the one-unit decrease in the Z-score of preschool post-BD Xrs5 predicted 9.6% lower post-BD FEV1, 9.3% lower post-BD FVC and 9.7% lower post-BD MEF50 when expressed as %-predicted parameters.

Conclusion: Persistent post-BD small airway impairment in children with a history of bronchiolitis detected with IOS at preschool age predicted FVS results measured in early adolescence.

Introduction: Flexible bronchoscopy is widely recognized as an important diagnostic and therapeutic procedure utilized by pulmonologists worldwide, allowing the physician to perform a wide range of interventions including obtaining samples from a broncho-alveolar lavage (BAL). The flexible bronchoscopy is relatively safe but procedural complications reported in the literature include the standard risks of anesthesia, oxygen desaturations, airway bleeding and cough. (1) The role of bronchoscopy and BAL in pediatric oncology is not well established in the literature. We looked at 5-year data at a large tertiary center in the United Kingdom.

Methods: We retrospectively looked at all flexible bronchoscopies conducted on cancer patients with persistent fever at a pediatric tertiary care facility over a five-year period. We looked at the results of the BAL and determined if there were modifications in clinical management attributable to the bronchoscopy.

Results: A total of 21 patients were identified with 26 corresponding flexible bronchoscopies with BAL. Diagnosis of these children were as follows: 7 with Acute Lymphoblastic Leukemia (ALL), 7 with Acute Myeloid Leukemia (AML), 1 Chronic Myeloid Leukemia, 1 T-Cell Lymphoblastic Non-Hodgkin's Lymphoma, 1 B-Cell Lymphoblastic (Burkitt's like) Lymphoma, 1 Ewing's Sarcoma, 1 Neuroblastoma, 1 Pontine Brainstem Tumor, and 1 Ewing’s Sarcoma. Seven of these patients had a stem cell transplantation.

Out of the 26 bronchoscopies, 5 were repeat bronchoscopies. Treatments were modified in 6 out of 26 bronchoscopies (23%), none of which were repeat bronchoscopies. All patients who had their treatment modified were either diagnosed with ALL or AML. Two of these patients had a bone marrow or stem cell transplant. The organisms identified on BAL were as follows: Pneumocystis jirovecii in 2 cases, Mycoplasma pneumoniae in 1 case, Adenovirus in 1 case, Influenza A in 1 case. A negative BAL ruled out fungal infection in 1 patient enabling a high dose systemic steroid therapy.

Conclusion: Our single-center study shows that bronchoscopies in oncologic pediatric patients are useful and yield a change in the clinical management in a significant portion of a population (23%). Children with common cancers such as ALL and AML end up receiving more interventional procedures for persistent fever. There was no clear association with treatment modification and bone marrow or stem cell transplant patients, as only 2 of the 7 bone marrow or stem cell transplants had their treatment modified (28.5%). Further multi-center research with a larger sample size is warranted to fully evaluate the role of bronchoscopies in future management.

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J138 – Clinical Value of Functional Parameters in the Determination of the Genesis of Prolonged and Chronic Children’s Cough

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Aim: to investigate the clinical significance of the functional parameters of the microcirculation, vegetative nervous (VNS) and respiratory systems for the differential diagnosis in children with prolonged and chronic cough.

Patients and Methods: 272 children aged from 2 to 17 years with cough during more than 4 weeks were examined. All patients were divided into six groups (Gr) according to diseases: 68 patients with postnasal drip syndrome (PNDS) of infectious genesis (Gr1); 39 patients with allergic rhinitis (AR) (Gr2); 12 patients with lower respiratory tract infection without wheezing (Gr3); 20 patients with acute wheezing (Gr4); 20 patients with postinfectious cough (PIC) (Gr5); 78 patients with mild persistent bronchial asthma (BA) in exacerbation and incomplete remission (Gr6). Catamnesis lasted from 6 to 17 months. The control Gr (C) included 60 healthy children.

From this study were excluded patients with a diagnosis of chronic bronchitis (n = 13); whooping cough (n = 13); psychogenic and...
neurogenic cough (n = 4); gastroesophageal reflux disease (n = 2); foreign body airway obstruction (n = 1); epilepsy (n = 1). All patients underwent history, examination; computer capillaroscopy of the nail bed; evaluation of heart rate variability (HRV) ("Cardiovizer-65", "MCS", Russia) and computerized bronchophonography (MEI, Russia).

Results: The morphological changes in the capillaries had a similar directionality in all children with a cough during more than 4 weeks. But patients with cough due to allergic diseases of the respiratory tract (Gr2, 6) were characterized by significant deformation of the arterial part of the capillaries and an increase in the length of the perivascular areas (L) compared with children with infectious genesis of cough (Gr1,3,4,5), in whom changes were often observed in the parameters of the venous part of the capillaries (p < 0.05). This may indicate a persistence of the chronic allergic inflammation in patients with AR (Gr2) and BA (Gr6). A more pronounced increase of L was observed in children with BA under 7 years old compared with patients older than 7 years (P < 0.05).

Gr2 and Gr6 were characterized by the prevalence of parasympathetic activity (at HRV analysis): increase in RMSSD, pNN50% and SDNN compared with Gr1,3,4,5, C (p < 0.05). A more pronounced imbalance of autonomic regulation was found in patients with BA (Gr6): increase in VLF and reduction in HF, LF compared with Gr2 (p < 0.05).

HRV parameters of Gr1,3,4,5 had a similar orientation as the predominance tone of the sympathetic (SNS): reduction in RMSSD, pNN50%, HF and increase in VLF and LF compared with Gr2, 6, C (p < 0.05). The Gr5 was characterized by more pronounced activity of the SNS (P < 0.05). This may indicate a high degree of tension in the adaptive mechanisms of the VNS in children with PIC (Gr5).

Patients with acute wheezing (Gr4) and BA (Gr6) showed a higher level of the coefficient of acoustic component of the work of breathing in the high frequency zone (5.0–12.6 kHz) (ϕ3), compared with Gr1,2,3,5, C (P < 0.05). Test with standard dose of salbutamol was positive in both Gr, although a more pronounced decrease in ϕ3 (26–72%) was typical for BA (Gr6) (P < 0.01).

Based on the data obtained, the clinical and functional parameters of the microcirculation and VNS for differential diagnosis of the allergic and infectious genesis of coughs during more than 4 weeks in patients with PNDS were determined: a rise in body temperature above 37.5°C; increased cough during exercise; a level of total IgE in blood serum; L and the coefficient of tortuosity of the arterial part of the capillaries; SDNN. As additional criteria for diagnosing BA in children with a cough during more than 4 weeks, the following clinical and functional parameters are proposed: degree of the allergenic condition of the patient; L; the unevenness of the caliber of capillaries; HF; LF; ϕ3.

Conclusion: These results showed that the functional parameters of the microcirculation, VNS and respiratory system can be used as additional criteria for the differential diagnosis of the allergic or infectious genesis of prolonged and chronic cough in children. It can be important in relation to early diagnostics of BA in children.

J157 – Noninvasive Hemoglobin (SpHb) with Spo2 Measurement as a New Monitoring Device for Pulmonary and Hemodynamic Condition in Neonates or Infants below three Kg.

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Introduction: A new technology, Pulse CO-Oximetry, provides a continuous and noninvasive estimate of both hemoglobin concentration and Spo2 from a sensor placed on the extremity. In other words, it may be possible to measure pulmonary and hemodynamic condition without collection of blood at the same time in a noninvasive method as usual. Neonates often undergo a significant decrease in hemoglobin (Hb) due to immaturity of hematopoietic function and frequently undergo blood tests, when medical intervention is required. Because neonates and infants below 3 kg have relatively small circulating blood volume, it is easy for them to develop an iatrogenic anemia resulting from the collection of blood. Therefore noninvasive methods of detecting blood Hb levels may help reduce iatrogenic anemia and pain caused by taking blood. Currently available noninvasive hemoglobin (SpHb) devices are aimed at children above 3 kg. However their feasibility for neonates or infants below 3 kg is not known. The purpose of this study is to clarify whether use of SpHb devices appears feasible for neonates or infants below 3 kg.

Methods: Subjects: Newborn infants who were scheduled to have a blood test including Hb measurement by blood sampling in NICU of St. Luke's International Hospital. Equipment: A prototype SpHb device and a finger sensor, which have the routine function for Spo2 monitoring, (Masimo Radical-7 ver. 1.1.4.8, sensor 25L rev. K) were used. A sensor was attached to a lower extremity in the same manner as a pulse oximeter sensor with appropriate light shielding. Measurement: SpHb measurement with recording was started about 30 minutes prior to scheduled usual blood sampling (not heel cut). After observing at least 10 minutes of infant stabilization and confirming the stability of SpHb values (±1 g/dL) for over 5 minutes, venous blood sampling (about 1 ml depending on other concomitant blood tests) were performed by neonatologists, while routine Spo2 monitoring was continued routinely throughout these procedure. The specimens were immediately taken for accurate measurement to our hospital laboratory. Analysis: The difference between sampled Hb and SpHb was evaluated on linear regression and Bland–Altman analysis.

Results: Thirty-three infants aged 5 days to 112 days (median 15 days) with body weights ranging from 956 to 3.160 grams (median 2.195 grams) were studied and 44 samples were analyzed. Eleven infants underwent a second sampling after an interval of more than 2 weeks due to medical necessity. In all cases, there were no adverse events due to measurement of SpHb and blood sampling in this study. The difference between sampled Hb and SpHb levels fell mostly within the ±2 g/dL range with a fair correlation (R = 0.73). The Bland and Altman Plot indicated that this prototype system tended to show relatively high SpHb values when sampled Hb levels were
The correlation between SpHb and sampled Hb levels is below almost 13.0 g/dL, and 95% limits of agreement were from 4.046 to 3.077.

Discussion: The correlation between SpHb and sampled Hb levels is good. SpHb device appeared feasible, even if the device was used for neonates or infants below 3 kg at a wide range of Hb levels. By attaching this SpHb device in neonates or infants below 3 kg, it is possible to detect an anemia faster and to reduce unnecessary blood tests. Furthermore, pulmonary edema and circulation failure caused by excess blood transfusion may be prevented. Erythropoietin therapy is given to anemia of prematurity below Hb 12g/dL. In infants weighing less than 3 kg, SpHb tended to exhibit higher values than sampled Hb when the latter levels were below almost 13.0 g/dL. Therefore SpHb could underestimate an anemia. When SpHb was measured on a lower extremity and the sampled blood Hb was taken from an upper extremity, there was almost no difference in these values. From this fact, it is considered that the measurement location can be anywhere. It is more likely that the bioengineering factors in measurement play a significant role in this data skewing, although we do not currently have access to the information needed.

Conclusion: Application of a prototype SpHb device appeared feasible for neonates or infants below 3 kg at a wide range of Hb levels. It may be possible to measure pulmonary and hemodynamic conditions without collection of blood at the same time with a noninvasive method. However, at this time, with the SpHb device, there is still room for improving the accuracy when levels were below almost 13.0 g/dL. Data obtained in this study should be used as a reference for future improvement.

J168 – Radiation Doses from Pediatric Chest Computed Tomography Scans Performed at a Tertiary Care Hospital.

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The purpose of this study was to evaluate the radiation doses to which children from 0 to <18 years of age undergoing chest computed tomography (CT) examinations in the radiology department of a tertiary care hospital are being exposed.

We performed a retrospective study of all consecutive pediatric patients (age <18 years) who underwent a CT of the chest between October 2015 and October 2016. Only inspiratory chest CTs with a single acquisition (single phase) and without contrast-media injection were included. Data on radiation exposure (tube current, tube voltage, CT dose volume [CTDI], dose length product [DLP] and size-specific dose estimate [SSDE]), as well as demographic and clinical data, were recorded from 193 chest CTs (median age: 12.6 years [IQR: 9.2 – 15.5], 107 males [55%]) from which the dose estimates were calculated using a 32 cm phantom. Size-specific dose estimates (SSDE) were generated for each patient and results were compared to CTDI. Patients were grouped into 5 categories based on mean effective diameter of the chest (square-root of the anteroposterior times latero-lateral chest diameters), as follows: group 1: 15 cm; group 2: 15 – 19 cm; group 3: 20 – 24 cm; group 4: 25 – 29 cm, and group 5: >30 cm. Factors associated with higher radiation doses were assessed using multiple linear regression analysis. Statistical analyses were performed using Statistical Package for Social Sciences, version 20.0. This study was approved by the local research ethics committee.

Median and interquartile range (25th and 75th percentiles) in groups 1 to 5 for SSDE (mGy) (p < 0.001) were 8.1 (5.0 – 21.9 [group 1]), 6.4 (4.6 – 9.9 [group 2]), 7.5 (5.5 – 9.1 [group 3]), 9.5 (6.9 – 13.3 [group 4]) and 13.5 (8.9 – 14.7 [group 5]); for CTDI, they were 3.4 (2.3 – 9.6 [group 1]), 3.4 (2.5 – 5.2 [group 2]), 4.6 (3.5 – 5.8 [group 3]), 7.0 (5.0 – 9.4 [group 4]) and 12.0 (7.4 – 13.8 [group 5]); and for DLP, they were 67.3 (45.8 – 169.2 [group 1]), 84.2 (55.1 – 100.9 [group 2]), 125.1 (92.8 – 166.2 [group 3]), 209.0 (153.1 – 275.4 [group 4]) and 403.0 (249.6 – 471.2 [group 5]). CTDI systematically underestimated radiation dose in relation to SSDE. Median and interquartile range for each patient group (25th and 75th percentiles) of the percentage of how much the CTDI underestimated SSDE were 55% (53%–56% [group 1]), 48% (46%–49% [group 2]), 39% (35%–42% [group 3]), 27% (24%–30% [group 4]) and 12% (9%–16% [group 5]). CTDI dose parameters (tube current and tube voltage), age, weight and the mean effective diameter were the variables associated with higher radiation doses.

We demonstrate the feasibility of performing an evaluation of pediatric CT radiation doses in a tertiary care hospital. Our results demonstrate the need for continuous monitoring of pediatric radiation doses in CT, as evidenced by the high doses detected. In addition, CTDI systematically underestimated radiation dose in comparison to SSDE in pediatric patients and should not be used as the primary parameter to monitor CT protocols.

11. THERAPEUTIC PROCEDURES

K55 – Management of Empyema by Video-Assisted Thoracoscopic Surgery (VATS) vs Chest Drain with Fibrinolysis (CDF): A Systematic Review and Meta-analysis

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Purpose of the study: The ideal surgical approach for empyema in children (<18 years) remains controversial. Both VATS and CDF are accepted methods. The aim of this study was to clarify which technique provides the best outcome.

Materials & methods: A systematic review and meta-analysis (1997–2017) was conducted according to the PRISMA guidelines. Selected studies included randomized controlled trials (RCT), retrospective and prospective comparative studies (CS). Studies containing children and adults with no clear distinction were excluded. The meta-analysis was conducted with Comprehensive Meta-Analysis 2. We used the random-effect model to produce risk ratio (RR) for categorical
variables, and standard difference in means (SDM) for continuous
variables, along with 95% confidence intervals [CI]. I2 value was used
to assess heterogeneity: I2>50% was considered to have substantial
heterogeneity between studies. Egger’s regression test was used to
assess publication biases. P values < 0.05 were considered significant.

Results: We identified 707 studies: 506 duplicates were removed, 193
did not meet the inclusion criteria, 8 studies (4 RCT and 4 CS) were
included. Results of the meta-analysis are reported in Figures 1, 2 and
3. The incidence of total peri-operative complications was not
different between the two groups (RR 1.09 [CI: 0.42–2.8]; p = 0.8;
I2 = 44%; Figure 1); post-operative length of hospital stay was
significantly shorter in the VATS group (SDM −0.6 [CI: −1.1–−0.05];
p = 0.03; I2 = 53%; Figure 2); need for re-intervention was significantly
lower in the VATS group (RR 0.6 [CI: 0.4–0.9]; p = 0.04; I2 = 22%;
Figure 3). Egger’s regression test did not identify significant biases
between studies [p>0.3 for all outcomes].

Conclusion: Current evidence suggests that VATS and CDF for
empyema have similar incidence of peri-operative complications.
However, VATS is associated with shorter post-operative hospital stay
and a reduced need for re-interventions. In centers with minimally
invasive surgery expertise, VATS should be considered the treatment
of choice in the surgical management of empyema.

Of the children who are brought to the emergency department,
respiratory issues are often the cause. As Ueda et al. reported, Biphasic
Cuirass Ventilation (BCV) is comfortable, fits easily and the expression
of the effect is early. Therefore, we use BCV first to patients with
respiratory distress as much as possible. Recently, in patients with
respiratory distress, we utilized BCV using the built-in battery, in order
to continue medical treatment without interruption during transpor-
tation of the sick children from the emergency department to the
pediatric ward. Through the early intervention of BCV for respiratory
distress in children, it is possible to start the treatment immediately and
continue treatment without interruption during transportation be-
tween wards.

In our institution, on the 14 cases in which Continuous Negative
Mode of BCV was started from the emergency department, their
symptoms were improved shortly in all cases. Respiratory rate and heart
rate were improved in 30 minutes after starting Continuous Negative
Mode of BCV, and hypercapnia was improved in less than 1 hours. In all
cases, BCV worked smoothly and the respiratory condition was improved.

For children with respiratory distress who breathe spontaneously and
do not need artificial respiration, it is difficult to maintain airway
pressure using bag-mask ventilation. In such cases, bag-mask
ventilation is unstable as treatment. On the other hand, BCV does
not require sedation and has greater mobility due to its battery power.
We can continue the same treatment after hospitalization.

We suggest that starting the treatment with BCV in the emergency
department and continuing the treatment without interruption during
the transportation of the patients to the ward are feasible and safe.
Furthermore, the treatment conducted by loading the battery with the
BCV does not require gas piping, such as oxygen or air. In other words,
this treatment is available under the situation in which there is difficulty
in gas supply at the time of a disaster. In our country, we experienced
certain large-scale disasters and all utilities including electricity and gas
supply were thus cut off. BCV can be run only on the battery power
supply and can also work under the situation without gas piping, and it is
considered to be an effective means even as an acute respiratory
management method at the time of disaster.

We can use BCV with built-in battery as not only an early intervention
in the emergency department, but also as an effective means during
transportation and disasters.

K84 – Use of Inhaled Antibiotics (IAb) in Non-CF Chronic
Lower Respiratory Infections.

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Introduction: Based on the experience in CF, there is a growing interest in the use of IAb in non-CF lower respiratory tract infections. Studies have been performed mostly in adults with non-CF bronchiectasis, ventilator-associated pneumonia, COPD, mycobacterial disease and other infections; applying Ab formulations for inhalation as well as “off-label” use of injectable Ab for inhalation. Also, the use of IAb for eradicating organisms such as P. aeruginosa in non-CF bronchiectasis is under investigation.

Aim: To investigate tolerance and efficacy of IAb treated non-CF infants and children.

Method: Retrospective review of data of all IAb treatment courses in young non-CF subjects in our pediatric department.

Results: Eight non-CF subjects (2 boys), age 0–15 years (median 71 months), with chronic colonization of pseudomonas or other resistant species were included. Underlying medical condition: extreme prematurity (GA 24–25 weeks) with O2 dependent BPD (3, including 2 with pulmonary hypertension, 1 with a tracheocanula and 2 on CPAP or BiPap), Down syndrome with GA 34 weeks, severe pulmonary hypertension, O2 dependency and tracheocanula (1), congenital esophageal atresia with tracheal fistula and recurrent aspiration pneumonias with bronchiectasis (1), poly-malformative syndrome with mental retardation and intractable respiratory infection (2 adolescents), bronchiectasis after PCP pneumonia in T-cell lymphoma (1 adolescent).

Reasons for starting IAb were: absence of response to repetitive IV antibiotic courses, practical issues with IV access, increased ventilatory conditions, recurrent acute exacerbations. Seventy-five percent of treatments were started in hospital; 2 adolescents started IAb in outpatient consultation. Age at start of IAb varied from 4 months to 15 years of age; duration of treatment was from 14 days to several months.

IAb utilized were colomycin, amikacin, gentamycin, ceftazidim, in mono or bitherapy, based on sensitivity testing. Doses and preparation were extrapolated from CF guidelines, including use of salbutamol before IAb to avoid bronchial hyperreactivity. Inhalation was well tolerated and safe. Eradication was successful and resulted in clinical improvement, decreased ventilator conditions and less acute exacerbation during a 4 to several months follow-up.

Conclusion: Data on the use of IAb in prematures and young children are scarce. These pilot data show that treatment with IAb in selected non-CF subjects with severe respiratory condition is safe and effective. It is feasible in non-hospitalized children and avoids the need for parenteral administration. IAb in non-CF is currently not formally indicated and more scientific evidence from ongoing clinical trials is awaited.

K142 – Open Lung Biopsy for Chronic Pulmonary Disease in Children.

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Introduction: This study aimed to evaluate the efficacy of open lung biopsy in children with chronic lung disease.

Methods: Patients who underwent open lung biopsy in 2006–2017 at the Hacettepe University Department of Pediatric Pulmonology were examined retrospectively.

Results: Twelve patients (6 boys, 6 girls) underwent open lung biopsy for diagnostic purposes. The mean age of the patients was 8.5 years (4 months–15.1 years). Four patients were followed-up with immune deficiency. The diagnoses of these patients were chronic granulomatous disease (n: 1), CVID (n: 1) and hypogammaglobulinemia (n: 2). None of the patients had any malignancy. The mean time between the onset of respiratory symptoms and the open lung biopsies was 6 months (range 1 to 36 months). None of the patients developed acute respiratory failure on follow-up. Nine of the patients (75%) required mechanical ventilation in the first 24 hours postoperatively. The mean chest tube withdrawal time in patients was 4.2 days (2 days to 7 days). Three patients were diagnosed with hypersensitivity pneumonitis, 1 patient with SPC deficiency, 2 patients with interstitial pneumonia. 1 patient with granulomatous lymphocytic interstitial lung disease, 1 patient with cryptogenic organizing pneumonia, 1 patient with follicular bronchiolitis, 1 patient with pulmonary hemosiderosis, 1 patient with giant air cyst and 1 patient with granulomatosis inflammation. Ten patients underwent a treatment change after biopsy results. According to biopsy results, steroid treatment was started for all of these patients, 1 patient was given mycophenolate mofetil and 1 patient was given hydroxychloroquine treatment.

Conclusion: Our results suggest that open lung biopsy is both safe and guiding for diagnosis in children with chronic lung disease.

12. CELLULAR AND MOLECULAR BIOLOGY

L40 – TIPE2 Regulates Type I Interferon Production in Antiviral Innate Immunity.

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Objective: Acute respiratory tract infection (ARTI) is the most common type of infectious disease in children. Virus infection can account for as many as 90% of ARTI and the majority of viruses are RNA viruses. In addition to the influenza virus, there is no effective treatment for RNA virus infection. Thus, we attempted to explore the regulating mechanisms of RNA virus infection, which might help to find a new approach to treatment of RNA virus infection in the future. Tumor necrosis factor-α-induced protein 8-like 2 (TIPE2), a member of the tumor necrosis factor-α-induced protein-8 (TNFAIP8) family is a negative regulator of immune response, and could prevent
hyperresponsiveness and maintain immune homeostasis. However, the regulatory role of TIPE2 in RNA virus infection and the effect of TIPE2 in the signaling pathway after RNA virus infection are poorly clarified. This study aims to investigate the effect and underlying mechanisms of TIPE2 on RNA virus infection.

Methods: We collected peripheral blood mononuclear cells from 154 children infected with Respiratory Syncytial Virus (RSV) (the most common virus in children) and 66 control healthy children, and detected the expression of TIPE2. We also detected the levels of TIPE2 in macrophages in vitro after VSV (the common virus used in research) infection. Meanwhile, we aimed to explore the effect and underlying mechanisms of TIPE2 in regulating RNA virus response through gain and loss of function.

Results: In our study, we detected a significant decrease in TIPE2 mRNA in peripheral blood mononuclear cells (PBMCs) from 154 cases of children infected with RSV compared to that in PBMCs from 66 control healthy children. In vitro, we also found that the expression of TIPE2 was down-regulated after VSV infection. It implied that TIPE2 might play a critical role in anti-RNA viral immunity. Furthermore, we observed that TIPE2-/- macrophages were more susceptible to vesicular stomatitis virus (VSV) infection and showed increased levels of VSV-G mRNA after VSV infection in vitro. In addition, the deficiency in TIPE2 was found to enhance type-I IFNs and inflammatory cytokine production by macrophages; moreover, overexpression of TIPE2 dampened the capacity of macrophages to produce type-I IFNs and inflammatory cytokines. Furthermore, TIPE2 could restrain the activation of TBK1 and IRF3 signaling pathways, thus inhibiting the production of type I interferon and inflammatory cytokines.

Conclusions: Taken together, our results suggest that TIPE2 could suppress type-I interferon and inflammatory cytokine production induced by RNA virus by inhibiting the activation of TBK1, IRF3 signaling pathways. This research uncovered an important negative role of TIPE2 in regulating innate antiviral immunity, and may help to provide new strategies for the treatment of viral infection clinically.

13. PEDIATRIC PULMONOLOGY IN DEVELOPING COUNTRIES

M22 – Vascular Ring Abnormalities: A Retrospective Study of 50 Cases.

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Introduction: Vascular ring abnormalities (VRA) are a rare condition where clinical presentation is essentially related to the degree of compression of the trachea and esophagus. VRA is often mistaken for bronchial asthma, knowing how to evoke it on simple elements will avoid delay in diagnosis.

Materials and methods: This is a retrospective study over a period of 25 years (1992 to 2017) covering all cases of VRA collected in a Pediatric Pulmonology clinic. We analyzed clinical data, all radiological and biological investigations as well as surgical reports and post-surgical evolution.

Results: A total of 50 children were included in the study, all of whom were explored as outpatients. A male predominance was noted with a M/ F sex ratio of 1.36. The age varied from 30 days to 15 years. The onset of clinical signs was in the first month of life for 90% of our patients. All children presented with a stridor that often started from the first month of life, it was more important and earlier in the double aortic arch. Cough was present in all cases in early life, in relation to tracheal malacia and congestion, it was hoarse and worsened with effort. Wheezing was present in more than 60% of patients. Digestive signs were mainly vomiting (26% of our patients) and dysphagia (20% of our patients) which was complicated by an esophageal food bolus obstruction that required extraction in 9% of patients. Patients were hospitalized at least once in 34% of cases, 36% were treated as bronchial asthma often considered difficult to control, 15% as chronic obstructive bronchopathy and 20% as chronic cough. Chest X-rays showed a right tracheal imprint with a right deviation in 44% of cases and a right aorta in 48% of cases. Barium swallow performed in more than 50% of patients showed esophagus impressions. The type of VRA confirmed in all our patients by a CT scan was distributed as follows: arteria lusoria 16 cases (32%), Neuhauser anomaly 15 cases (30%), double aortic arch (DAA) 8 cases (16%), innominate artery 7 cases (14%), circumflex artery 2 cases (4%), retrotracheal left pulmonary artery 2 cases (4%), right aortic arch with mirror-image branching 1 case (2%). Pulmonary function testing (PFT) guided the diagnosis in 8 cases. Bronchoscopy was only performed in 10 patients confirming tracheal malacia. Congenital heart diseases were rare in our series. Surgery was performed in only 13 patients: 5 cases of DAA, 6 cases of Neuhauser anomaly, 1 case of retrotracheal left pulmonary artery and 1 case of Arteria Lusoria. Eight patients are waiting for surgery, Parents refused surgery in 4 cases and there was no surgical indication for the other patients. Postoperative complications were infectious in 3 cases, high blood pressure in 1 case, laryngeal paralysis in 1 case and persistent mild tracheomalacia in 3 cases.

Conclusion: VRA is a rare condition although deserves to be known by the pediatrician, the gynecologist (no prenatal diagnosis in our series) and the radiologist to be diagnosed in time. The explorations must take into account the level of irradiation, barium swallow must be abandoned and MRI must take its place in radiological exploration. PFT have an important place in the diagnosis. Surgical indications must be studied on a case by case basis. Total improvement is not always observed, it remains dependent on the degree of tracheomalacia.

M49 – Congenital Cystic Adenomatoid Malformation: Report of Two Cases.

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Congenital cystic adenomatoid malformations (CCAM) are the most common malformations of the lower respiratory tract, and represent 20% of the pulmonary malformations. Diagnosis is increasingly made by antenatal ultrasonography. Chest infections can compromise vital prognosis and pulmonary function. We report here two cases of children with CCAM.

Case 1: an 8-year-old girl with a history of recurrent bacterial pneumonia in the right lower lobe since the age of 6 years. Radiological investigations, in particular CT angiography, showed the presence of large cysts and pulmonary condensation located in the apical segment of the lower lobe without signs of pulmonary sequestration. Bronchoscopy did not find any foreign body, granuloma or hydatid cyst membrane retention, the hydatid serologies were negative. The immunological profile did not show any primary or acquired immune deficiency, exploration by pulmonary scintigraphy showed a hypoperfusion of the right lower lobe, pulmonary function testing was normal, no associated cardiac or renal malformation.

Regarding all these elements, the diagnosis of CCAM was retained and the child was operated, she underwent a lower right lobectomy with good postoperative evolution. Pathology confirmed CCAM type 1 with large cysts according to the Stoker classification.

Case 2: a 26-month-old girl with a history of recurrent chest infections in the right lower lobe since the age of 18 months with respiratory distress that required more than five hospitalizations. The CT scan confirmed the presence of cystic lesions of the right lower lobe and two small cystic lesions of the apical segment of the left lower lobe, with no systemic vessel which eliminated a sequestration. Bronchoscopy was normal as well as hydatid cyst serology, no associated renal or cardiac malformations. The diagnosis of CCAM being retained, the patient was referred to the surgeon for right inferior lobectomy; during surgery it was decided to limit the ablation to the right ventral and paracardial segments, the immediate surgical evolution was good and pathology confirmed the diagnosis of CCAM type 1. Four months later, the child presented a chest infection in the right inflamed lobe, the CT confirmed the presence of cystic lesions of the inferior lobe; however, the left lesions disappeared. A second surgery was performed and an inferior lobectomy was carried out with a good follow-up.

Conclusion: None of our two patients was diagnosed at the antenatal period despite ultrasound monitoring during pregnancy. We noticed an important delay in the diagnosis despite clinical and radiological evidence, selective surgery in the second patient failed. Any recurrent chest infections must evoke a CCAM, surgery in this situation is the rule and the only possible treatment.

M54 – An Unusual Repetition of Anti-Tuberculosis Drug-Induced Hepatotoxicity in Indonesian Children.

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Background: Anti-tuberculosis drug induced hepatotoxicity (ADIH) is one of the serious adverse effects ascribed to anti-tuberculosis (TB) drugs which causes an increase in serum aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) and total bilirubin. ADIH is uncommonly reported in children, particularly recurrent or repeated ADIH. It requires stopping all the potential hepatotoxic anti-tuberculosis drugs with a systematic and regular monitoring of liver enzymes. Even though there are available British Thoracic Society (BTS) and the American Thoracic Society (ATS) guidelines for reintroduction regimens for treating ADIH in adults, there are no guidelines adopted officially in Indonesia. We aimed to report an unusual repetition of ADIH in Indonesian children.

Case Reports: Six cases (3 TB meningitis, 1 miliary TB and 2 pulmonary TB), age range 18–60 months, of experienced repeated ADIH were reported. The four severe TB cases received daily 4-drug anti-TB therapy comprising isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA) and ethambutol which planned to be continued for a period of 2 months, followed by INH and RIF for a period of 10 months, whereas two pulmonary TB cases received 3 drugs (INH, RIF, PZA) for a period of 2 months and continued for a period of 4 months with INH and RIF. All patients had an increased serum AST, ALT and total bilirubin, while hepatitis markers showed negative results. No abnormalities were identified in hepatobiliar ultrasonography. When ADIH occurred, anti-TB drugs were stopped immediately without considering the severity of ADIH. Most ADIH occurred during the intensive phase of TB regimen, although one during the continuation phase. However, all cases experienced repeated ADIH when they were on INH reintroduction. Two cases experienced repeated ADIH three times, while the others experienced ADIH two times. We managed ADIH cases by modifying ATS guidelines treated individually. One TB meningitis case received levofloxacin and RIF when treating the third instance of ADIH. At present, all patients are in continuous phase and managed with full doses of INH and RIF. Good clinical responses were noted in all of them. Acetylator status of all ADIH cases was not studied.

Conclusions: Diagnosis of ADIH is still conducted by clinical and laboratory examinations. The reintroduction of anti-TB drugs after ADIH is to be taken with care and should be treated individually. There are no official guidelines to treat ADIH in Indonesian children and these challenges made us create our own proposed guideline for ADIH which is based on ATS guidelines.

Keywords: Anti-tuberculosis drug-induced hepatotoxicity, children

M71 – A Retrospective Study on the Diagnostic Accuracy of TB PCR vs Culture in Diagnosing Children Aged 3 Months to 18 Years at a Tertiary Care Center.

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Introduction: Tuberculosis (TB) is both a preventable and treatable illness. In children, it is infrequently confirmed bacteriologically due to the lack of effective diagnostic tools. Early identification of TB is very important, as it can help in the initiation of adequate treatment for patients and in prevention of further spread of drug-resistant strains.
Objectives: This study aims to establish the diagnostic accuracy of TB PCR versus TB culture and rifampicin resistance by PCR versus conventional susceptibility testing of body fluid in all inpatient and outpatient Filipino children aged 3 months to 18 years with suspected tuberculous disease seen in a tertiary care center.

Methods: This is a retrospective analytical study of out-patients and in-patients seen at a tertiary care center between January 1, 2012 to May 31, 2017. During the study period, all patients with clinical features, radiographic, tomographic, imaging and hematological findings suggestive of tuberculosis and who had diagnostic TB sampling of body fluids were recruited into the study.

Results: Among 159 patients suspected with TB, 46 (28%) were found positive by PCR, of which one was rifampicin-resistant. Forty (25%) were TB culture-positive, four (2%) of whom were PCR-negative. Overall rifampicin resistance was 1.8%. The sensitivity, specificity, positive predictive value and negative predictive values of TB PCR, using TB culture as the gold standard, were 90%, 91.6%, 78.3%, and 96.5% respectively. The sensitivity, specificity, positive predictive value, and negative predictive values of TB PCR rifampicin resistance detection, using TB culture susceptibility as the gold standard, were 33%, 100%, 100% and 95%, respectively. Overall, the accuracy of TB PCR in detecting TB disease was 91.2% and the accuracy of TB PCR in detecting rifampicin resistance was 95%.

Conclusion: The findings in our study suggest that TB PCR plays an important role in TB disease diagnosis, but clinical and radiological assessment continue to be essential in the diagnosis of childhood tuberculosis. The high accuracy of TB PCR and detection of rifampicin resistance allows a rapid presumptive diagnosis of TB disease, allowing prompt institution of therapy. However, conventional culture is still needed to detect resistance to drugs other than rifampicin.

Keywords: TB PCR, tuberculosis, Filipino, pediatrics, accuracy

M79 – Is Hypertonic Saline Nebulization Prior to Chest Physiotherapy Effective in Children with Non-CF Bronchiectasis.

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Introduction: Though cystic fibrosis (CF) is the commonest cause of bronchiectasis in the Western world, non-CF bronchiectasis is the major contributor to the burden of chronic respiratory morbidity in developing countries. Failure to expectorate collected mucus results in plugging of the airways, thus creating a vicious cycle of progressive airway damage. Therefore, airway clearance techniques play an important role in the management of non-CF bronchiectasis. Although multiple airway clearance techniques have been introduced, none of the latter have been validated. Usage of a method would depend on effectiveness, convenience, compliance, and cost. Hypertonic saline nebulization prior to airway clearance is a well-established method in managing CF and non-CF bronchiectatic adults. Hence we planned to assess the effectiveness of hypertonic saline nebulizations over conventional physiotherapy in children with non-CF bronchiectasis.

Aims: To evaluate the effectiveness of hypertonic saline nebulization prior to physiotherapy in improving lung functions in children with non-CF bronchiectasis.

Materials and Methods: All 5 – 15 year old children with non-CF bronchiectasis, attending a tertiary care hospital in Colombo, Sri Lanka from August 1st to December 1st 2017 were included in the study. Inability to comply with regular follow up, use of regular hypertonic saline nebulization during the preceding one year, chronic colonization of Pseudomonas in the respiratory tract, those who had frequent exacerbations, presence of typical extra pulmonary features of CF and children who were unable to perform spirometry test due to poor effort were excluded.

A baseline spirometry was performed on all selected patients. They were treated according to the airway clearance technique, which was prescribed by the treating physician. One group of children received hypertonic saline nebulizations followed by inhaled bronchodilators prior to chest physiotherapy and the other group received only inhaled bronchodilators prior to chest physiotherapy. The technique used to deliver bronchodilators was a metered dose inhaler with spacer device in both groups. Use of a home nebulizer was taught to parents in order to deliver the saline. An adequate training on chest physiotherapy was given to the parents in two sessions by a physiotherapist. A physiotherapy session of 20–30 min was recommended and 2 sessions were performed each day. The number of exacerbations during the 2-month period was documented and spirometric assessment was done at the completion of the two months of therapy.

Data were processed with Microsoft Excel; independent t test and Mann-Whitney U test were used to examine the statistical significance. Statistical significance was established as p value less than 0.05. Descriptive statistics are presented as mean ± SD

Results: A total of 27 children were evaluated in the study. Fifteen children received hypertonic saline nebulizations prior to the use of bronchodilator and chest physiotherapy while 12 were given bronchodilators and chest physiotherapy only. The demographic and baseline measurements were comparable between the two groups. The most common etiology was suggested to be post infective bronchiectasis in 18 children. The mean improvement in percentage predicted FEV1 was significantly higher (p = 0.002) in the hypertonic saline nebulized group (11.3 ± 2.7) than in the non saline group −(3.5 ± 8.9). The hypertonic saline group showed a statistically significantly higher mean improvement in predicted FVC in saline group (9 ± 5.9) compared to the non saline group (2.2 ± 5.7)(P < 0.012). A significant improvement in PEFR was demonstrated in the hypertonic saline 11.3 (7.4) than conventional group −4.2(6.2)
2014. ON1 genotype was the only genotype of subtype A during the two epidemic seasons (2010/2011, 2011/2012). 52 strains of subtype A and B, respectively. Subgroup A types were predominant during the first two epidemic seasons, followed by ON1 genotype (10/52, 19%), which was the predominant form in the first four popular seasons, followed by ON1 genotype (10/52, 19%), which were first verified in December 2011, and totally 9 strains in 2013/2014. ON1 genotype was the only genotype of subtype A during the season of 2013/2014. There were some different variations in the second hypervariable region at the carboxyl-terminal of the G gene. The rates of homology between prototype strain A2 and the 52 strains of subtype A RSV were 80.7% to 89.3% at the nucleotide level and 74.4% to 82.6% at the amino acid level. On comparison of strains among the sequenced subgroup A RSV, the rates of homology were 81.5% to 100% at the nucleotide level and 80.2% to 100% at the amino acid level. G protein variants included substitution, insertion and repeat, and the N- glycosylation sites mutation was obvious. There were several variations in the 24 amino acid sequence that inserted into the ON1 genotype.

Conclusions: NA1 is the predominant genotypes of subtype A RSV during 4 consecutive epidemic seasons from 2009 to 2013 in Eastern China. The variation in the nucleotide and amino acid sequence of G protein is obvious. There were various transmission chains of RSV caused by different genotypes during the 5 consecutive seasons.

M82 – The Molecular Epidemiological Characteristics of Subtype A Respiratory Syncytial Virus in Eastern China from 2009 to 2014.

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Objective: To investigate the epidemiological characteristics of respiratory syncytial virus (RSV) subtypes and genotypes in Eastern China from 2009 to 2014, and to explore the genetic variability of the attachment (G) protein gene among subtype A RSV strains.

Method: Nasopharyngeal secretions (NPS) from children under 5 years of age who were hospitalized with lower respiratory tract infection (LRTI) in three tertiary hospitals during 5 consecutive seasons from July, 2009 to June, 2014 were collected. RSV antigen was determined using direct immunofluorescence. 200 samples with RSV antigen positive were randomly selected from each epidemic season. RNA was extracted and identified as subtype A or B by using RT-polymerase chain reaction (RT-PCR), and randomly selected subtype A strains of the nearly full-length attachment (G) protein were amplified by PCR and sequenced. Result A total of 25,449 specimens were collected from patients during 5 consecutive epidemic periods, and 6416 (25.21%) were positive for RSV. Among 1000 randomly selected samples, 462 (46.2%) and 538(53.8%) samples were identified assubtype A and B, respectively. Subgroup A types were predominant during two epidemic seasons (2010/2011, 2011/2012). 52 strains of complete sequences of G genes were obtained, including four group A genotypes NA1, NA4, GA2 and ON1. NA1 genotype was the most (39/52, 75%) common one, and was the predominant form in the first four popular seasons, followed by ON1 genotype (10/52, 19%), which were first verified in December 2011, and totally 9 strains in 2013/2014. ON1 genotype was the only genotype of subtype A during the season of 2013/2014. There were some different variations in the second hypervariable region at the carboxyl-terminal of the G gene. The rates of homology between prototype strain A2 and the 52 strains of subtype A RSV were 80.7% to 89.3% at the nucleotide level and 74.4% to 82.6% at the amino acid level. On comparison of strains among the sequenced subgroup A RSV, the rates of homology were 81.5% to 100% at the nucleotide level and 80.2% to 100% at the amino acid level. G protein variants included substitution, insertion and repeat, and the N- glycosylation sites mutation was obvious. There were several variations in the 24 amino acid sequence that inserted into the ON1 genotype.

Conclusions: NA1 is the predominant genotypes of subtype A RSV during 4 consecutive epidemic seasons from 2009 to 2013 in Eastern China. The variation in the nucleotide and amino acid sequence of G protein is obvious. There were various transmission chains of RSV caused by different genotypes during the 5 consecutive seasons.

M93 – Rupture of a Massive Pulmonary Hydatid Cyst in an 8-Year-old Girl. A Case Report

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Morbidity by Hydatid cyst in children is not uncommon in some portions of world still. Our country (as has been reported in Lancet 2003; 362: 1295–1304, Echinococcosis) is located in a hyper endemic area. In alveolar hydatidosis, if surgical removal is unsuccessful, the mortality rate after 10 years is more than 90%.

Case presentation: An 8-year-old girl referred to our hospital with productive cough and intermittent decrease of consciousness level on September 17 2017. Mild tachypnea was the only positive finding on first physical examination. A chest X-ray was ordered that showed surprisingly, right side massive pleural effusion and concurrent pneumothorax which shifted the mediastina to the opposite side. A consultation with the surgery department was performed for the patient, and additional clinical imaging showed bronchiectasis in upper lobe of the right lung. Water Lily-specific signs in thoracic-abdominal CT made our preliminary initial diagnosis as Echinococcus of the lung. After ultimately starting Albendazole 15 mg/kg treatment, surgery was performed in an equipped hospital. After right posterolateral thoracotomy, lung empyema from a ruptured hydatid cyst, pleural adhesion and inter-thoracic fibrin was reported and finally wide decortication was performed. The patient was discharged after 6 days post-operation hospitalization with good condition and administration of Albendazole continued and parents advised for referral to pediatrics infectious disease clinic for serial observations. She had good performance in school and was well on November 10 as of our last recall date. Rupture may occur during therapy or percutaneous aspiration and trauma can lead to severe complications, such as massive hemoptysis and tension pneumothorax, lung abscess and asphyxia.
Prevalence of Allergic Rhinitis and Atopic Eczema among Schoolchildren in Jordan.

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Background: The prevalence rate of allergic diseases, such as asthma, allergic rhinitis and atopic eczema are increasing worldwide among children.

Objective: This part of the International Study of Asthma and Allergies in Childhood (ISAAC) Phase III was to determine the prevalence of asthma, allergic rhinitis and atopic eczema among schoolchildren age 6–7 years and 13–14 years.

Methods: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase III questionnaires were administered to 3000 children from both age groups. The questionnaires were collected after having been completed by the parents.

Results: The total number of students included in both studied groups was 5045. The response rate was 84% for schoolchildren. Physician-diagnosed asthma was found in 9.5%. Primary school children aged 6–7 years had significant wheezing ever (27.2%) compared with older children (25.2%); P < 0.05. Asthma was more common in males. The prevalence of allergic rhinitis ever was 23.6% and 26.6% in primary schoolchildren and older children respectively (P< 0.014). Current symptoms of AR were 70.9% and 75.5% in primary schoolchildren and older children respectively (P < 0.08). Physician-diagnosed hay fever was 5.5% in primary school children compared to 7.9% in older children aged 13–14 years old (P < 0.000). The prevalence of eczema ever was 15.6% and 13.5% in primary schoolchildren and in older children respectively (P < 0.03).

Conclusion: This is the first study on the prevalence of most allergic diseases in Jordan. Asthma is increasing and other allergic diseases are not an uncommon problem in our area. Allergic rhinitis is more common in older children. Females more commonly have allergic rhinitis and eczema.

Contribution of Oxygen Therapy at High Flow in the Management of Severe Bronchiolitis in a General Pediatric Ward.

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Purpose: The aim of our study was to describe the contribution of HFNC in the management and evolution of severe bronchiolitis.

Methods: We retrospectively studied cases of severe bronchiolitis for three months (November 1, 2015 – January 31, 2016). We compared two groups: a first group including the cases of severe bronchiolitis in which HFNC was used, and a second group including patients who were not placed under HFNC due to lack of availability.
Results: Eighty cases of severe bronchiolitis were collected, of which 35 (43.8%) were placed on HFNC. The average age was 60 days (11–180 days). A history of prematurity was found in 22.5% of cases, hypotrophy in 10% of cases, neonatal mechanical ventilation in 10% of cases and congenital heart disease in 3% of cases. Viral contagion was found in 70% of cases. In all cases, HFNC was used in the first 72 hours of hospitalization, and in the first 24 hours in 38% of cases. The average duration of HFNC was 2.62 days (1–17 days). The mean total hospital stay was 6.3 days in the HFNC group versus 9.8 days in the other group, with a statistically significant difference (p = 0.028). A transfer to the intensive care unit was indicated in 13/35 of the cases (37%) in the group using HFNC versus 19/45 cases (42.2%) in the second group.

Conclusion: HFNC appears to be really effective in severe bronchiolitis, with a decrease in the use of invasive ventilation, especially in children under 3 months of age. HFNC is available in a general pediatric ward and is easy to use, improving the prognosis of patients and reducing pressure on the pediatric intensive care unit.

M125 – Vitamin D Supplementation and Tuberculin Skin Test Conversion among Healthy Under-Five Children with Tuberculosis Contact.

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Background: Tuberculosis (TB) contact increases the risk of TB infection among under-five children, whose immune systems are not fully developed. Vitamin D is known to affect innate and adaptive immunity, inhibit bacterial invasion, therefore will protect from developing TB infection indicated by TST conversion.

Objective: To evaluate the effects of vitamin D supplementation among healthy under-five children with tuberculosis contact to develop TST conversion.

Methods: We conducted a randomized, double-blind, controlled trial in 66 under-five children who had tuberculosis contact but whose tuberculin skin tests (TST) were negative (healthy). We administered a high single dose of vitamin D3 supplementation twice, at an interval of 6 weeks. After 12 weeks, we performed a 2nd TST, with positive TST (diameter>10 mm) indicating TST conversion. Ethics approval was obtained from the Ethics Committee from Faculty of Medicine, Universitas Andalas.

Results: There were no difference in TST conversion between intervention (12.9%) and placebo groups (11.4%) with a p value = 0.855. Baseline characteristics showed mean levels of vitamin D <30 ng / ml, vitamin D supplementation significantly increased vitamin D level in the intervention groups (24.32 ± 7.50 vs. 28.47 ± 7.19, p = 0.003) compared to the placebo groups (26.93 ± 8.60 vs. 27.67 ± 9.02, p = 0.508).

Conclusion: There were no differences in TST conversion between intervention and placebo groups after vitamin D supplementation twice over 12 weeks among under-five healthy children with TB contacts, although increased vitamin D serum levels.

M158 – Study of Bacterial Agents of Pneumoniae in Children and Detection of Antibiogram Patterns in Hamadan, West of Iran.

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Background and aims: Bacterial pneumoniae is still one of the most dangerous infectious diseases and causes serious complications and mortalities in children. The aim of the present study was to identify the most common bacterial agents causing pneumoniae in children less than 12 years old and detection of their resistance to current antibiotics in Hamadan.

Methods: Overall, 542 children suspected of pneumoniae were investigated for results of pleural fluid cultures and antibiogram patterns. Frequency of age, sex and seasons of patients were also studied from 1999 to 2003. The data were gathered through a questionnaire and analyzed using Epı6 system. The species were identified by biochemical and serological methods. Antibiogram tests were also performed using the Kirby-Bauer method.

Results: Out of 542 children suspected of pneumoniae, 72 cases (13.2%) had positive bacterial culture of which 54.4% were gram-negative and 43.6% were also gram-positive bacteria. The most common species were: Staphylococcus aureus 18.6%, Streptococcus pneumoniae 16.9%, Klebsiella aerazenae 12.3%, Pseudomonas aeruginosa 11.8%, Haemophilus influenzae 9.4%, Bacteroides species 7.8%, Streptococcus β-haemolyticus 6.1%, E. coli 4.9%, Neisseria meningitidis 4.5%, Acinetobacter species 3.2% and other gram-negative bacteria 23.3%. The most positive cultures were observed in children 1–4 year age group (31.3%), male (52.4%) and during winter (41.8%). The results of antibiograms showed that the most effective antibiotics were ceftaxime, ceftriaxone, gentamycin, ciprofloxacin for both gram positive- and gram-negative bacteria, but they showed high resistance to tetracycline, amoxicillin and ampicillin.

Conclusions: The present study showed that some gram-positive bacteria, in particular Staphylococcus aureus and Streptococcus pneumoniae, are predominant causes of bacterial pneumoniae in children less than 12 years old in these regions. Most species showed high resistance to routine antibiotics such as tetracycline, amoxicillin and ampicillin.

M166 – The Correspondence of Client Statistics Referred to our Clinic with the Rate of Airborne Particle Pollution.

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Zanjan city is located in the country of Iran, in the Middle East continent (or region). DMS latitude longitude coordinates for Zanjan are: 36°40'24.96"N, 48°28'43.32"E. Zanjan (48° 28' longitude and 36° 40' latitude) (Figure 1).

In recent few years, our country’s climate was threatened by four main Dust Particle Focuses through our Western neighbors of which the most significant (23 cases of forty airborne particle flows in last years) was the North-West of Iraq and the East of Syria Countries.

As our recorded documents in environmental organization shows, these known hotspots have been activated around March to September annually in past years and we had school closures and work shut downs for a few days in 2017. As we know, airborne particles not only can play an important role in dysfunction of the pulmonary system but can also trigger an attack in known cases of asthmatic children. In the present study, we will try to show the relationship between the number of patients referred to the Zanjan solitary pediatrics asthma and allergy clinic and the rate of airborne particles that was recorded by the Department of Environment in Zanjan branch. Airborne particles are divided into two classifications: coarse, or those particles larger than 2.5 microns in diameter, and fine, those particles 2.5 microns or less in diameter. Air monitoring in Zanjan is conducted by a local environmental organization which provides air pollution data regarding ozone and particulate matter (PM2.5) as has been recommended in Air Quality System (AQS) which contains data from approximately 6 monitoring stations in the city center and around the area, mainly in urban areas. We have collected only the data of the city center station.

Client statistics in our clinic correspond to the rate of airborne particle pollution that is recorded in the city center station. The negative effects of air pollutants on pulmonary function place children at a greater risk of air pollutant-induced exacerbation of asthma for the duration of their lives. All studies reviewed indicate that outdoor air pollution affects the appearance and exacerbation of asthma in children. (J Asthma. 2011 Jun; 48(5):470–81. doi: 10.3109/02770903.2011.570407. Epub 2011 Apr 13. Outdoor air pollution and asthma in children. Tzivian L.). According to “AQI”, when air pollution is even in moderate range, children with asthma should limit their time outdoors; especially from 10 a.m. to 8 p.m. Most of all, do not exercise outdoors. In such conditions, we recommend that, because of its morbidity, despite schools being open, students with a history of asthma should be exempted from school.

"AQI" in Zanjan City Center Station Day/Month:

| Quality/Months | Good | Unhealthy for sensitive groups | Unhealthy | Very unhealthy | Hazardous |
|----------------|------|--------------------------------|-----------|----------------|-----------|
| March          | 11   | 3                              | 15        | 3              | 7         |
| April          | 16   | 5                              | 14        | 11             | 7         |
| May            | 12   | -                              | 14        | 11             | 7         |
| June           | -    | -                              | -         | -              | 3         |
| July           | 9    | -                              | 11        | 8              | 7         |
| August         | 8    | -                              | -         | -              | 3         |
| September      | -    | -                              | -         | -              | 3         |
| October        | -    | -                              | -         | -              | 3         |
| November       | 10   | -                              | 18        | 22             | 3         |
| December       | 22   | -                              | 3         | 8              | 7         |
| January        | 8    | -                              | -         | -              | 76        |
difficult, such that the tuberculin test (TST) and interferon gamma release assay [IGRA, QuantiFERON®-TB Gold In-Tube (QFT-GIT)] are expected to be accurate for diagnosis of TB infection in HIV infected children. Reports on QFT-GIT accuracy in children with HIV infection still vary.

**Objective:** To evaluate the accuracy of QFT-GIT and TST to diagnose TB in HIV infected children.

**Method:** A cross-sectional study was conducted in 48 HIV infected children with suspected TB aged 1 month to 15 years old. Data which included history taking, physical examination, thorax radiology, TST, QFT-GIT, and bacteriological examination (Xpert MTB/RIF and MGIT culture) were collected.

**Result:** The prevalence of TB in HIV-infected children is 20.9% (confirmed TB 4.2% and clinical TB 18.7%). The clinical symptoms of HIV-infected children with TB are: chronic cough (90%), body weight decrement (80%), reduction of activity (80%), lymph node enlargement (60%), and prolonged fever (50%). The sensitivity of QFT-GIT towards clinical TB in HIV-infected children is 38% (CI 95%: 12.77%), specificity 100% (CI 95%: 98.100%), and NPV 88% (CI 95%: 76.94%). The sensitivity of tuberculin test towards clinical TB is 29% (CI 95%: 8.64%), specificity 97% (CI 95%: 87.100%), PPV 67% (CI 95%: 21.94), and NPV 88% (CI 95%: 76.95%). The sensitivity of QFT-GIT towards bacteriological examination is 50% (CI 95%: 9.91%), specificity 96% (CI 95%: 85.99%), PPV 33% (CI 95%: 6.79%), and NPV 98% (CI 95%: 88.100%). Accurancy towards bacteriological examination and tuberculin test could not be evaluated.

**Conclusion:** Both QFT and TST showed high specificity but low sensitivity to diagnose TB. The accuracy of QFT-GIT to detect TB in HIV infected children is slightly superior than TST. Therefore, these two methods could be a choice depending on its availability and patient comfort.

**ABSTRACT**

To describe the clinical profile, etiology, specific management and outcome in children with non-cystic fibrosis bronchiectasis attending a tertiary care hospital in Colombo, Sri Lanka.

**Methods:** Twenty-seven children with an HRCT scan-based diagnosis of bronchiectasis, presenting to the Professorial Pediatric Unit, Lady Ridgeway Hospital, Colombo during the period of September 2016 to December 2017, were selected for the review. Absence of typical clinical features and having two negative sweat tests performed at a minimum of 6 months apart were taken to exclude cystic fibrosis. A detailed chart review of children diagnosed with non-cystic fibrosis bronchiectasis was done.

**Results:** The majority of the patients with non-CF bronchiectasis were females 18 (66%) and the mean age of the study sample was 7.4 years (SD =3.24). The mean age at the diagnosis of bronchiectasis was 5.2 years (SD = 2.50) and the indication to perform an HRCT in the majority (19 children) was the combination of recurrent respiratory tract infections with persistent crepitations on examination. Mean duration of symptoms /medical concerns prior to the diagnosis/HRCT was 3.8 years (SD = 1.54). Bilateral involvement was seen in 9 (33%) patients. Only 6 (22%) patients were referred to the center by a pediatrician or a general practitioner with the suspicion of bronchiectasis and the rest (21) were diagnosed when admitted with an exacerbation, with the background of recurrent respiratory tract infections. Twelve (44%) children showed a weight for height or a BMI centile for age less than –2SD. Mean number of episodes of exacerbations per year was 6. Spirometry was done in 22 patients at the analysis of the clinical profile. Best FEV1/FVC (Forced Expiratory Volume in 1 second/Forced Vital Capacity) ratio was >80% in 16 (72%) and <80% only in 6 (28%). FVC was reduced with a predicted value >80% in the majority (12 patients, 44%). FVC was > 60–80% in 7 patients and < 60% in 3 patients who were on home oxygen therapy. Predicted FEV1 was more than 80% in 14 (63 %) and less than 80% in 8 children. Analysis of etiology revealed one patient each with common variable immune deficiency (14 years), with a past history of tuberculosis (15 years), intralobar sequestration (13 years) and late diagnosis of severe gastroesophageal reflux disease (3 years).

The commonest etiology was post infectious where 14 (51%) had one or more episodes of severe pneumonia needing respiratory support during infancy with other common etiologies being excluded. Nine...
(33%) children had no identifiable etiology. Diagnostic facilities for Primary Ciliary Dyskinesia (PCD) were not available but there were no patients with a typical clinical profile of PCD. Satisfactory postural drainage was followed by 15 (55%) and the rest had deficiencies in the technique. Pneumococcal vaccination was given for 24 patients (85%) outside of the Expanded Program of Immunization. Only 20 (74%) patients had complied with regular follow-up. Three patients had undergone lobectomy. Out of the sample, 3 children are on home oxygen therapy and were dependent on parents for activities of daily living.

**Conclusion:** The commonest cause of non-CF bronchiectasis in the above group is post infection. There is a significant delay in the diagnosis despite children being symptomatic. A high degree of suspicion is needed for the early diagnosis especially in children with a history of severe respiratory infections in early childhood. There is a need to create awareness about the importance of early diagnosis of bronchiectasis and the importance of correct postural drainage techniques and follow-up as it would lead to less complications and better prognosis.

**14. MISCELLANEOUS**

**N13 – Pleuropulmonary Blastoma in Congenital Pulmonary Airway Malformation: Challenging Diagnosis of an Asymptomatic Child**

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**Introduction:** Congenital pulmonary airway malformation (CPAM) is an abnormality of lung development and cannot be distinguished radiologically or clinically from rare primary tumors such as Pleuropulmonary Blastoma (PPB). We report a rare case of CPAM and PPB overlap in a 2-year-old absolutely asymptomatic girl with a huge cystic lesion.

**Case Presentation:** A 2-year-old girl was referred to our hospital for a giant cystic pulmonary lesion with a large and solid mass. This lesion had undergone a huge increase in 18 months since it was first discovered by a pediatrician during a random chest X-ray performed because of a flu. The initial clinical examination revealed a very good condition. The pulmonary auscultation was absolutely normal despite the dramatic appearance of the radiological findings. There were no reported anomalies on the antenatal ultrasound or neonatal complications. Good birth weight (w: 3000g; h: 49 cm) and development. She had no episodes of respiratory distress or pneumonia whatsoever. The first chest X-ray performed when she was 6 months old showed a cystic lesion in her right hemithorax with a round-shaped white shadow at the bottom of the lesion (Image1). CT scan showed the cystic lesion contained a few thin internal septations with a consolidated area (Image2). The last images performed 18 months later on X-ray and CT scan demonstrated an important increase in the cystic lesion and the round-shaped opacity (Image 3). The child underwent a right thoracotomy through the fifth intercostal space. A multiloculated giant cystic lesion was found occupying the entire hemithorax and compressed all right lower lobes which was the solid round mass. During the mechanical ventilation, this lobe got insufflated recovering its functions normally. The anatomy of the affected lobe appeared normal. The removal of the cystic mass was performed simultaneously with the posterior apical segment of the lower lobe where the lesion was fixed. Grossly, the diameter of the cystic mass was 8.0 cm. Histopathologically, the cystic epithelial layer was composed predominantly of flattened cells and at the subepithelial layer, there were foci of spindle cells with an atypical appearance. Moreover, the parenchyma showed normal microscopic characteristics. Immunohistochemical analysis detected positivity for Desmin, an intracellular intermediate filament found in muscle tissue and demonstrated in some atypical stromal cells, indicating sarcomatous differentiation characteristic of pleuropulmonary blastoma (image 5). The patient did not receive chemotherapy. She is in her first postoperative year and is being followed closely, presenting a very good condition.

Image 1. Chest X-ray showing a cystic lesion with round-shaped shadow (red arrow).

Image 2. CT scan showing a more defined multiloculated cystic lesion (red arrow) and the round mass (a).
Discussion: Congenital Pulmonary Airway Malformation (CPAM), formerly known as Congenital Cystic Adenomatoid Malformation (CCAM) consists in multicystic masses of segmental lung tissue with abnormal bronchial proliferation. It accounts for approximately 95% of all congenital cystic lung diseases and 10% of pediatric lung cancers have a history of CPAM. There are five subtypes classified mainly according to cystic size: Type I: large cysts, Type II: cysts less than 2 cm in diameter. Type III: microcysts that involve an entire lobe, Type IV: unlined cysts that typically affect a single lobe that it is indistinguishable from Type I on imaging and Type 0: very rare and lethal postnatally.

PPB is a very rare intrathoracic malignant neoplasm that originates during lung development and can arise from the lung, pleura or both. It
was described by Manivel et al. in 1988 and was later subdivided into three types on the basis of the morphological pattern: Type I: multicellular cysts containing primitive small mesenchymal cells within the cyst wall, Type II: cystic and solid components (mixed) and Type III: exclusively solid tumors, in order of increasing and malignancy. Priest et al. in 1996 reported that type I is most observed in patients in the first years of life compared to type II and III that are found in older patients – between 3 and 4 years of age. Type 1 is different from the rest because of its subtle malignant changes and good prognosis. The clinical presentation may be asymptomatic or have secondary symptoms due to the expansion or infection of the cyst, infection sometimes being recurrent. The most frequent findings on chest X-ray are: cystic lesions, hyperinflation, mediastinal shift and pneumothorax. Usually there is no adjacent rib erosion or calcification. CT scan remains the most sensitive technique including the largest cyst size, the nature of the cyst (septated or containing solid components) and the presence of a systemic vascular supply. The incidence of PPB among apparently benign lesions is 4%. Several studies have suggested that these two entities can be indistinguishable.

The precise relationship between CPAM and malignancy, especially Pleuropulmonary Blastoma (PPB) remains unknown. Some studies indicate that the PPB etiology may originate from previously existing CPAM in the lung – about 31% – but nothing has been proven to date. There are cases that correlate these two pathologies, because they present very similar histological types. Generally the diagnosis is made through the microscopic analysis of Hematoxylin & Eosin (HE), but sometimes it is necessary to perform immunohistochemistry in some conflicting cases. Biomarkers: Ki-67, Desmin and Myogenin may be observed in these borderline cases. According to Hill et al., in order to distinguish PPB from other pathologies it is necessary to observe the presence of multicellular cystic areas, a well circumscribed tumor with normal parenchyma, presence of small foci of primitive cells and an epithelial layer with flat cells which was noticed in our case.

Conclusion: Congenital Pulmonary Airway Malformation (CPAM) and type 1 Pleuropulmonary Blastoma (PPB) are indistinguishable by clinical and radiological presentation. Therefore, children with asymptomatic cystic lesion should be assessed thoroughly and the lesion resected early to avoid later complications such as its malignization. Careful histological examination of the resection specimen is mandatory to identify occult malignancy, thereby to manage the treatment properly and reach the best prognosis.

N51 – Validation of GLI-2012 Spirometry Reference Values in Italian Preschool Children

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Rationale: The Global Lung Initiative (GLI-2012) spirometry reference values are a potentially valuable tool for the interpretation of spirometry worldwide [1]. Although their validity has been proven in many countries, doubts remain for some populations. The aim of this study was to assess the validity of the GLI-2012 reference values in preschool Italian children.

Methods: Healthy children were recruited from randomly selected kindergartens in or around Florence, Italy. The subject’s history of respiratory symptoms was assessed using a standardized questionnaire (ISAAC modified), translated into Italian [2]. Children born at less than 36 weeks of gestational age or who had received oxygen at birth for more than 30 days were excluded. Children with no more than 3 episodes of wheezing ever, but no episodes of wheezing during the previous 12 months, were included. All children had no respiratory symptoms or signs at the time of testing. Spirometry was performed with the “Spiro Cosmed” spirometer (Cosmed, Rome, Italy) according to ATS/ERS spirometry recommendations for preschoolers [3]. Z-scores for forced vital capacity (FVC), forced expiratory volume in 0.75 s (FEV0.75) and in 1 s (FEV1), and forced expiratory flow between 25% and 75% of FVC (FEF25-75) were calculated using GLI-2012. Absolute Z-score values larger than 0.5 were considered to have a clinical significance.

Analysis: The results of questionnaires and spirometry were transformed into numeric values and reported in an Excel table and subsequently analyzed using Stata/SE v.12 for Windows. The analysis was performed using the paired t-test. The t-test is a type of parametric statistical test which allows verifying if the average value of a distribution differs significantly from a certain reference value. The mean values of the spirometric parameters FVC, FEV0.75, FEV1 and forced expiratory flow 25−75% of FVC (FEF25-75%) obtained from the examined sample were compared with the predicted values for the same spirometric parameters derived from the 2012 GLI reference equations. The values with a P < 0.05 and a Z-score > 0.5 were considered statistically and clinically significant [4].

Results: A total of 109 healthy children [57 female and 52 male, age range 3.2–6.3 yr, mean age (SD) 5.1 (0.8) yr, mean height 109.7 (8.1) cm, mean weight 19 (3.9) kg] performed acceptable and reproducible spirometry maneuvers (feasibility 85%). A total of 100 (78.1%) children had>2 reproducible maneuvers and 70 (54.7%) had>3 reproducible maneuvers. Mean (SD) measured spirometry indices and predicted values using GLI-2012 are reported. A paired t-test showed that measured values were not significantly different from predicted values. The mean Z-scores of the measured values were smaller than 0.5, showing that the difference was not clinically significant.

Potential Study Limitation: The number of subjects enrolled in the study, to confirm the validity of these reference equations (GLI-2012), was less than the 300 local “healthy” controls (150 males and 150 females) that would be needed to validate published reference equations with any degree of certainty, since with smaller sample size differences of up to 0.5 z-scores may occur purely by chance [4]. Furthermore, this relative inclusion flexibility has been used to select a sample closer to the reality of the population, to avoid selecting “abnormally normal” children, which would distort the study, resulting in an overestimation of the results; this is still a topic of many discussions regarding what would be the “normal” parameters necessary to be considered [5].
Conclusions: This is the first study with the aim to assess the validity of the GLI-2012 reference values in preschool Italian children. These data so far suggest that the difference between measured and predicted values using GLI-2012 is neither statistically nor clinically significant in healthy Italian preschoolers.

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ABSTRACT

N69 – Sleep Habits of Lower Primary School Children in Singapore.

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Background/Objectives: Sleep is essential for optimal body functioning. The National Sleep Foundation recommends that primary school children get 9–11 hours of sleep per day. A previous study in Singapore showed that sleep duration is significantly lower in preschool children when compared to Western populations. There is little published data on the sleep habits of primary school children in Singapore. Our study aims to investigate sleep practices amongst lower primary school age children in Singapore.

Methods: This was a questionnaire survey of parents with children aged between 6 and 9 years old attending primary schools in Singapore.

Results: A total of 307 questionnaires out of 721 given out were completed (response rate 42.6%). 115 children (37.5%) felt sleepy during the day for at least 2 days per week, with 52 children (17%) falling asleep while watching television at least 2 days per week. 177 children (57.7%) slept less than the recommended 9 hours on a school day. On a non-school day, 58 children (18.9%) got less than 9 hours sleep. 106 children (34.6%) of children did not have a regular bedtime routine at least 5 nights a week. The most popular activity in the hour before bedtime was watching television; 229 children (74.6%) regularly engaged in watching television at night. 143 children (46.6%) used smartphones for games in the hour before bedtime. 52 children (6.9%) used computers to watch videos during the hour before bedtime. Despite this, 273 of 307 parents surveyed (88.9%) felt that their child did not have a sleep problem. Amongst parents, the most popular activity in the hour before bedtime was watching television (218 parents, 71.0%). 159 parents (51.8%) use smartphones for social media in the hour before bedtime.

Conclusion: Daytime sleepiness was present in a third of children. Most children surveyed were not getting the recommended duration of sleep. Some lacked regular bedtime routine and most used televisions and smartphones before bedtime (which is known to negatively affect sleep quality). However, most parents did not think their child had a sleep problem. Parental role-modeling is challenging due to parents’ own suboptimal sleep habits including a high rate of digital device use amongst themselves. Parental education is needed to ensure their children get the right quality and quantity of sleep.

N110 – Sleep-Disordered Breathing and Behavioral Symptoms in Children in a South-East Nigerian City.

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Background: Sleep-disordered breathing (SDB) comprises sleep-associated breathing difficulties which can lead to significant morbidity in children. It can be assessed with validated questionnaires as screening tools, where polysomnography (PSG) is not available. Data is scarce on these disorders in black children.

Aim: The study aims to determine the prevalence of SDB, its behavioral manifestations and associated risk factors for poor score in children in a South-Eastern Nigerian city.

Methods: A community-based descriptive study was conducted using the child sleep questionnaire (SRBD subscale-070129). Children aged 1 month to 18 years from consenting households were recruited.

Results: Three hundred and ninety nine proxy-reports were analyzed. The mean age was 70 ± 43 months, with a male to female ratio of 1:1. Up to 193 (48.4%) of these children belonged to families of the middle socio-economic status. SDB problems were present in 12.7%. Sleep habits were age-related. Significantly prevalent symptoms included difficulty in waking up from sleep among children aged 1 to <5 years (p = 0.035), and easy distractibility (p = 0.010) and disruptiveness (p = 0.005) among children aged 5 to 10 years old. SDB was highly correlated with the assessed components, with the exception of restlessness (r = 0.019, p = 0.737), easy distractibility (r = -0.085,
N124 – Pulmonary Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma and Epstein-Barr Virus Many Years after Cardiac Transplant.

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Introduction: Primary lung lymphoma is a rare lung disorder, mostly presenting as mucosa-associated lymphoid tissue (MALT) lymphoma; a type of extranodal low-grade B-cell lymphoma. It is a rare pathology in children, with the median age at diagnosis being 50–60 years. Lung location represents 15% of cases and gastrointestinal (GI) tract involvement is the predominant primary location for MALT lymphoma. Unlike the case of GI, MALT lymphoma of the lung has no established association with microbial infections. We present a case of a 16-year-old girl who underwent orthotopic cardiac transplant in infancy and presented with signs and symptoms concerning for post-transplant lymphoproliferative disorder (PTLD). Following recurrent pneumothoraces, she underwent lung biopsy that revealed MALT lymphoma and Epstein-Barr Virus (EBV).

Case Report: 16-year-old female with history of idiopathic dilated cardiomyopathy status post orthotopic cardiac transplant at 1 year of age. Patient had a relatively uncomplicated course until age 15, when persistent cough and declining spirometry triggered a computed tomography (CT) of the chest and abdomen that revealed diffuse lymphadenopathy concerning for PTLD. Laparoscopic mesenteric lymph node biopsy resulted positive for EBV and infectious mononucleosis-like lesion and was followed by mediastinal lymph node biopsy due to uncertainty regarding PTLD, and resulted inconclusive as well. Cough, weight loss and significant decrease in pulmonary function test eventually culminated by recurrent left-sided pneumothoraces, leading to lung biopsy that established MALT lymphoma of the lung as well as infection with EBV.

Discussion: Primary lung lymphoma is a rare disorder and represents only 0.3% of all primary pulmonary malignancies. MALT lymphoma is the most frequent subset of primary pulmonary lymphomas. It may present with pulmonary symptoms such as dyspnea, cough, chest pain, or constitutional symptoms. Our patient developed cough, weight loss and recurrent pneumothoraces; the latter, while an unusual presentation, pointed us to a serious morbidity requiring lung biopsy for diagnosis.

PTLD is a well-recognized and relatively common complication of prolonged immunosuppression in recipients of both solid organ and bone marrow transplants, often associated with EBV. MALT lymphoma has not been classified as an entity within the spectrum of PTLD, and is infrequently associated to EBV. This report raises the question of such link in this patient with pulmonary MALT lymphoma after orthotopic cardiac transplant and in association to EBV.

N129 – Study on Bacterial Contamination of Neonatal Intensive Care Units (NICU) in a Pediatric Hospital in Hamadan, West of Iran.

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Background and aim: Bacterial contamination in hospitals is one of the major problems in hospitals that cause serious damage to humans and society. One of the major causes of the increase in bacterial contamination is misuse of disinfectants and an increase in antibiotics resistance in hospitals. The aims of this study were the evaluation of bacterial contamination of intensive care units (NICU) and determination of antibiotics resistance patterns in isolated bacteria in a Fatemih hospital, west of Iran.

Material and Methods: This was a cross-sectional study in which 100 samples were randomly collected from environments and apparatus of neonatal intensive care units including washing sink, ward floors, patient beds, phototherapy, oxygen mask, incubator, infant scale, suction and staff fingers. The samples were inoculated into EMB and Blood agar by sterile wet swabs and transferred to the medical laboratory for identification. Strains were tested for antibiogram by NCCLS protocol. The antibiotics disks consisted of: ampicillin, imipenem, ceftriaxone, ceftizoxime, erythromycin, vancomycin, gentamicin, cephalaxin, cefepime and ciprofloxacin. Data were gathered through a questionnaire and analyzed using SPSS 13 software.

Results: The average rate of bacterial contamination of NICU of was 73%. The most contaminated areas were washing sink (98%), suction (74%) and the lowest was phototherapy (35%) and oxygen mask (44%), respectively. The most frequent bacteria isolated were as follows: *Staphylococcus epidermidis* (17%), *Bacillus subtilis* (12.5%), *Acinetobacter baumannii* (11.3%) and *E. coli* (8.2%). Most of the isolates (60%–90%) were sensitive against imipenem, ceftriaxone, vancomycin, gentamicin, cephalaxin, cefepime and ciprofloxacin, whereas most of them were resistant to ampicillin, gentamicin, erythromycin and cephalexine.

Conclusion: Our results showed the considerable bacterial contamination (73%) of NICU in particular with *Acinetobacter baumannii* and the high drug resistance in strains isolated from hospital; it seems that sterilization and disinfection methods in hospitals were not performed...
N144 – Cautionary Tales of Tachypneic Infants in the Bronchiolitis Season.

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Abstract: Although the diagnosis of bronchiolitis is usually straightforward, cardiac, metabolic, musculoskeletal and hematological conditions may present in a similar way and therefore, should not be overlooked.

Methods: We describe four cases presenting with increased work of breathing that were treated initially as bronchiolitis. However, the progressive clinical course of these cases and further investigations revealed an alternative diagnosis.

Results: The first case was a 36-week baby boy who presented with symptoms of bronchiolitis and was treated accordingly. A slow response to treatment and a subsequent CT scan revealed the diagnosis of congenital lobar emphysema, which needed resection. Another 7-month-old child with similar clinical presentation, was found to have a white cell count of 1032 × 10⁹/l, Hemoglobin 34g/l; platelets of 30 × 10⁹/l. The blood film confirmed the diagnosis of Acute Lymphocytic Leukemia. A third case of a 9-week baby girl showed persistent tachypnea and intermittent grunting out of proportion to her chest signs. Her blood gas revealed metabolic acidosis, urine was persistently alkaline and renal ultrasound showed nephrocalcinosis leading to the diagnosis of distal renal tubular acidosis. Finally, we had 4-week-old boy presenting with symptoms suggestive of bronchiolitis, that was subsequently confirmed to be pulmonary vein stenosis.

Conclusion: This case series demonstrated that rare respiratory and non-respiratory conditions can mimic the presentation of common conditions such as bronchiolitis. This highlights the importance of a detailed history and examination in infants presenting with increased work of breathing. When atypical findings are present or there is a delay in response to standard treatment, seeking senior or specialist review and thinking out of the box, is vital.

N153 – Correlation between Doppler Echocardiography of the Main Pulmonary Arteries and Ventilation/Perfusion Scintigraphy in a Case of Swyer-James Syndrome.

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Introduction: Swyer-James syndrome (SJS) is an infrequent entity sometimes diagnosed as a casual finding on a chest radiograph of a hyperlucent lung or lung lobe. Clinically, patients may have productive cough, shortness of breath, and dyspnea on exertion, sometimes with hemoptysis. Some patients, who have little or no associated sequelae are not diagnosed until they are adults. In the appropriate clinical setting, radiography and CT usually are sufficient to diagnose the condition. Ventilation-perfusion scintigraphy scans may contribute to diagnosis by showing the displayed characteristic pattern of a matched ventilation and perfusion defect. We have recently observed in patients with complicated pneumonia, by Doppler echocardiography of the pulmonary main arteries, that pulmonary artery blood supply is markedly decreased in the affected lung. Ventilation-perfusion scintigraphy was compared with Doppler echocardiography of the pulmonary main arteries in a 2-year-old patient recently diagnosed with this syndrome.

Case Report: A 2-year-old boy underwent chest radiography in the context of acute bronchitis. Complete atelectasis of the left lower lobe (LLL) and lingula with bronchiectasis, and hyperinflation of the left upper lobe (LUL) with ipsilateral deviation of the mediastinum were observed. He was a healthy child with wheezing episodes triggered by upper respiratory tract infections. There was no history of cough, expectoration, choking, pneumonia or other significant bacterial infections. He was a well-nourished boy without respiratory distress. Lung auscultation showed hypoventilation and crackles in the left hemithorax. No changes in chest X-rays were observed after an oral course of amoxycillin-clavulanate. A pulmonary CT scan showed atelectasis of the entire LLL with bronchiectasis and hypoattenuation of the rest of the lung segments due to air trapping, thickening of the bronchial tree, bronchiectasis in LUL and retention of secretions. In addition, a decreased size of the left pulmonary artery and decreased vasculature of the left lung were observed. The child underwent fiberoptic bronchoscopy, discarding the presence of a foreign body, intrabronchial lesion or abnormalities of segmentation. A sample of respiratory secretions was collected, with growing of Haemophilus influenzae. Other studies (tuberculin test, sweat test and immune system evaluation) rendered normal results. Doppler echocardiography showed a clear flow asymmetry between the main pulmonary arteries with a markedly decreased blood flow in the left pulmonary artery. The ratio between the right and the left pulmonary artery flow was estimated at 6.9/1. Ventilation-perfusion scintigraphy showed a matched severe deterioration of ventilation and perfusion of the left lung (perfusion ratio between right and left lungs 9/1). A diagnosis of SJS was established, and recommendations were made to receive respiratory physiotherapy, anti-flu and pneumococcal vaccination, and early antibiotherapy in case of respiratory exacerbations.

Discussion: SJS is considered to be a relatively uncommon and complex disease characterized by unilateral hyperlucent of a part of
or the entire lung, with decreased vascularization and air trapping, being currently considered as a form of bronchiolitis obliterans. The syndrome may emerge after an episode of viral pneumonia or bronchiolitis-bronchitis, with progression to a fibrous obliteration of the bronchiolar lumen that leads to emphysema and a component of vasculitis obliterans, with the consequent alteration of pulmonary perfusion. It is a diagnosis of exclusion, discarding other causes of pulmonary hyperlucency such as pneumothorax, emphysema, endobronchial obstruction, hypoplastic lung, pulmonary embolism or agenesis of the pectoralis major muscle. Pulmonary CT is the test of choice for diagnosis, showing destruction of the affected lung parenchyma, with or without bronchiectasis, in addition to an ipsilateral pulmonary artery with diminished caliber. Ventilation-perfusion scintigraphy scans may contribute to diagnosis. In our patient, a non-invasive and accessible test such as Doppler echocardiography revealed a decrease in pulmonary artery flow on the affected side, which correlated with the degree of pulmonary hypoperfusion observed in the ventilation-perfusion scintigraphy. This finding suggests that Doppler echocardiography of the main pulmonary arteries could be a simple method to verify the degree of pulmonary hypoperfusion in SJS and other unilateral or asymmetric pulmonary disorders.

In children with a diagnosis of OSA, poor compliance with prescribed therapy was described (43% never use night-time CPAP). Compliance and perception of benefit were directly related to each other. This has an immediate and long term impact. However, those that wear CPAP report a clear benefit as most describe treatment as moderately or extremely successful.

One quarter of parents reported recurrent chest infections. One third reported concerns regarding swallow.

Implications: This is the largest survey of its kind conducted internationally with parents of children with Down Syndrome reporting significant respiratory morbidity. There is a high prevalence of OSA with variability in perceived benefit of treatments and in compliance with CPAP. A significant proportion of children have recurrent infections of prolonged duration. This survey highlights the need for increased awareness and services for children with DS who are at a higher risk of developing respiratory disorders. There are significant clinical, service provision and economic implications needed to address these findings. The authors are considering these in the context of what matters to our patients.

**N192 – Sleep Study in the Pediatric Population of Castilla La Mancha. Do We Have Good Tools at The Present Time?**

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**Objective:** The objective of the project is to analyze sleep in the pediatric population of Castilla la Mancha to produce a representative percentile graph of our population with the aim of comparing it with those used at the present time.

**Method:** Observational, retrospective study of the children who were attended at the healthy child's review in our clinic for 9 months. The number of hours of sleep was recorded, including the difference between day and night hours. Each patient was associated with a percentile according to graphs currently used as a reference (Iglowstein, 2003). The data were analyzed bearing in mind the different age ranges for the elaboration of a representative percentile chart of our population.

**Results:** A total of 311 children were analyzed in a 9-month period: 51 children of 6 months, 56 children of 12 months, 63 children of 2 years, 46 children of 4 years, 57 children of 6 years and 38 children of 12 years. The results show a clear difference between the percentiles of our sample and those currently used as a reference. Two clear examples would be the following (our graph VS reference graph):

1- Infant of 3 months who sleeps 13 hours a day: 50th percentile vs. 25th percentile
2- Infant of 3 months who sleeps 10.5 hours a day: 10th percentile vs. 2nd percentile.
3- Infant of 3 months that sleeps 8 hours a day: percentile 3 vs percentile 5.1.
4- A 12-year-old boy who sleeps 9 hours a day: 50th percentile vs. 25th percentile.
5- A 12-year-old boy who sleeps 7 hours a day: percentile 3 vs. percentile 1.1.

Conclusions: The graphs currently used as a reference for sleep are not representative of our population because there are cultural and geographical differences.

Sleep percentiles obtained from the analysis of our population clearly differ from those currently used as a reference. The percentile ranges obtained after the analysis of our population are clearly lower than those currently used as a reference.

Reflections: Sleep disorders are very prevalent and a frequent reason for consultation. There is evidence of the inversely proportional association of sleep duration and various pathologies, mainly overweight and obesity.

Percentiles of sleep duration are a fundamental tool for detecting children at risk of developing sleep problems.

The current graphs emerge from a sample of 493 subjects from Zurich in 2003 and are not representative of our population.

The use of the graphs originated after the study of our population would allow us to identify more effectively those patients with sleep deprivation and therefore at risk of developing secondary problems to this sleep deprivation.

N197 - A rare case of hemoptysis: mucoepidermoid carcinoma of the lung in a 12-year-old boy.

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Introduction: We present a case of a 12-year-old boy with a 12-month history of chronic cough and hemoptysis.

Case report: A 12-year-old boy with poorly controlled asthma, who was treated with inhaled steroids during exacerbations, presents with a year-long history of predominant nocturnal, productive cough, associated with two episodes of hemoptysis. There were no other relevant respiratory symptoms. A chest X-ray was performed and revealed a right upper lobe collapse and consolidation, leading to his referral to our institution for a thorough diagnostic workup. There was no history of foreign body aspiration, fever, night sweats or weight loss. He underwent an initial flexible bronchoscopy that showed an endobronchial exophytic nodular lesion at the right upper lobe (see figure 1). Given his longstanding history of respiratory symptoms and the area from which he was referred, our initial diagnosis presumption was endobronchial tuberculosis. Nevertheless, his tuberculin skin test was 0 mm and both Ziehl Nielsen stain and polymerase chain reaction (PCR) in the bronchoalveolar lavage (BAL) sample and bronchial brushing were negative for Mycobacterium tuberculosis. This sample was positive for Streptococcus pneumoniae; therefore, he was commenced on IV antibiotics, but he persisted with hemoptysis. A high resolution computerized tomography scan (HRCT scan) of the chest was performed looking for malignancy or vascular abnormalities. This study revealed a nearly complete atelectasis of the right upper lobe plus an endobronchial lesion that obliterated the right upper lobe bronchi. It also showed cylindrical bronchiectasis and some intraparenchymal cavities. A second bronchoscopy was performed showing similar findings, therefore an endobronchial biopsy of the exophytic lesion was performed. Bronchial biopsy was characterized by mucus-secreting cells with abundant fluffy cytoplasm and large mucin vacuoles, compatible with a Mucoepidermoid Carcinoma (MEC).

The child underwent a lobectomy of the right upper lobe, guided by flexible bronchoscopy. Given that worldwide reports suggest surgery rather than chemotherapy or radiotherapy, our patient did not receive any of these therapies and underwent surgical removal. The tumor was completely resected and its histopathological analysis was consistent with a well differentiated MEC (0.6 × 0.3 × 0.8 cm), stage T1N1M0 with metastasis to 1 of 39 lymph nodes without extracapsular extension.

Currently, the patient continues under routine surveillance, he is thriving well, asymptomatic and his lung function remains stable.

Conclusion: Among the rare causes of hemoptysis which the pediatric pulmonologist can expect to encounter, tumors such as pulmonary adenomas or carcinomas may be present, particularly in older children. Therefore, malignancy must be always considered as part of the differential diagnosis of persistent hemoptysis in children with no underlying chronic lung disease.

Mucoepidermoid carcinoma is a rare disease that accounts for less than 1% of primary malignant lung tumors. They are derived from epithelial and mucous secretory cells with a common origin in the salivary glands. These tumors do not have a characteristic trait that differentiates them from other benign or malignant lesions. MEC generally occurs in the central bronchial region. In our patient, the tumor was arising from the right upper bronchus. The common clinical symptoms and signs include cough, hemoptysis, bronchitis, wheezing and sometimes fever; therefore, the clinical picture of MEC is similar to other common entities such as asthma, lower respiratory tract infections or pneumonia. Tumors are usually small, ranging from 0.5 to 6 cm. They are usually soft, polypoid and pink-tan in color. Their diagnosis is based solely in the histopathology report. There is no standardized treatment and their prognosis depends on the histological grade of the tumor.

MEC is a rare entity that pediatric pulmonologists should encounter and keep in mind.
Figure:
Figure 1. Exophytic endobronchial lesion with hemoptysis in right upper lobe.

Below: macroscopic and microscopic picture of the lesion.

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