

# APSR RESPIRATORY UPDATES



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## The obstructive sleep apnoea syndrome in adolescents

Authors: Marcus, CL et al.

Reference: Thorax 2017;72(8):720-9.

<http://thorax.bmj.com/content/72/8/720.long>

Obstructive sleep apnoea syndrome (OSAS) is prevalent and can lead to a variety of complications, namely cardiovascular, neurocognitive and metabolic disturbances. The syndrome results from a combination of neuromotor, structural and ventilatory factors, and in this study the relative contributions of these factors in the causation of adolescent OSAS were examined. Fourth-two obese adolescents with OSAS and 37 weight-matched controls underwent upper airway MRI, assessment of their upper airway critical closing pressure (Pcrit), genioglossal electromyography and ventilatory response to CO<sub>2</sub> during wakefulness and sleep. Multivariate analysis indicated that adenotonsillar volume (ATV), nasopharyngeal airway volume (NPAV), and activated Pcrit were independently associated with apnoea risk in this population of adolescents. This study highlights that OSAS in adolescents is mediated by a combination of anatomic (ATV, NPAV) and neuromotor factors (activated Pcrit), providing another piece of evidence as to why adenotonsillectomy alone does not lead to a complete cure in many of these cases.

## STAAR: a randomised controlled trial of electronic adherence monitoring with reminder alarms and feedback to improve clinical outcomes for children with asthma

Authors: Morton RW et al.

Reference: Thorax 2017;72(4):347-55.

<http://thorax.bmj.com/content/72/4/347.long>

Inhaled corticosteroids (ICS) remain the mainstay of treatment for childhood asthma. However, poor compliance to ICS is common and is associated with frequent disease exacerbations, reduced quality of life and even death. This study examined whether including feedback of electronically monitored adherence data in routine practice would result in improved clinical outcomes. Children 6-16 years with poorly controlled asthma and receiving ICS and long-acting  $\beta$ -agonists were randomised to active intervention (electronic adherence monitoring with daily reminder together with feedback at clinic visits) or to the usual care arm (adherence monitoring alone). All participants were seen in clinics every 3 months for 1 year, and the primary outcome was the Asthma Control Questionnaire (ACQ) score. Seventy-seven of 90 children completed the study (39 interventions, 38 controls). Adherence was greater in the intervention group (70% vs 49%,  $p \leq 0.001$ ). There was no significant difference in the change in ACQ, but children in the intervention group required fewer courses of oral steroids ( $p = 0.008$ ) and were

less likely to be hospitalised ( $p \leq 0.001$ ). This study suggests that electronic adherence monitoring with feedback is beneficial in the management of poorly controlled asthmatic subjects.

### **Protracted bacterial bronchitis in children - natural history and risk factors for bronchiectasis**

Authors: Wurzel DF et al.

Reference: Chest 2016;150(5):1101-8.

<http://www.sciencedirect.com/science/article/pii/S0012369216525914?via%3Dihub>

Protracted bacterial bronchitis (PBB) and bronchiectasis are two different conditions that share common clinical and laboratory features. It is suggested but remains to be proven that PBB precedes a diagnosis of bronchiectasis. In this study a cohort of children with PBB was longitudinally followed and the authors aimed to (1) determine the medium-term risk of bronchiectasis and (2) identify risk factors for bronchiectasis and recurrent episodes of PBB. One hundred sixty-one children with PBB and 25 control subjects were recruited and a subset of 106 children was followed for 2 years. Of 161 children with PBB (66% boys), 13 were diagnosed with bronchiectasis over the study period (8.1%). Almost one-half with PBB (43.5%) had recurrent attacks ( $> 3/y$ ). Risk factors for bronchiectasis included lower airway infection with *Haemophilus influenzae* (recovered in BAL fluid) ( $P = .013$ ) and recurrent episodes of PBB ( $P = .003$ ). Risk factors for recurrent PBB could not be identified. This study highlights potential risk factors for the subsequent development of bronchiectasis in children with PBB. Clinicians should take appropriate measures in those with such risk factors.

### **Feasibility and safety of substituting lung ultrasonography for chest radiography when diagnosing pneumonia in children - a randomized controlled trial**

Authors: Pardue Jones B et al.

Reference: Chest 2016;150(1):131-8.

<http://www.sciencedirect.com/science/article/pii/S0012369216012630?via%3Dihub>

Lung ultrasonography (LUS) is increasingly being used in respiratory medicine. This study examined the feasibility and safety of substituting LUS for chest radiography (CXR) in the evaluation of children suspected of having pneumonia. This randomized control study recruited 191 children from birth to 21 years of age and took place in an Accident and Emergency department. Patients allocated to the investigational arm underwent LUS. If there was clinical uncertainty after the procedure, the subjects could proceed to CXR. Patients in the control arm underwent sequential imaging with CXR followed by LUS. The primary outcome was the rate of CXR reduction. Chest radiography utilisation was reduced by 38.8% in the investigation group compared with no reduction in the control group. No cases of pneumonia were missed and there were no differences in adverse events or

subsequent unscheduled health-care visits between the two arms. The results suggest substituting LUS for CXR when evaluating children suspected of pneumonia is both feasible and safe.

### **Short- and long-term pulmonary outcome of Palivizumab in children born extremely prematurely**

Authors: Prais D et al.

Reference: Chest 2016; 149(3):801-8.

<http://www.sciencedirect.com/science/article/pii/S0012369215000021?via%3Dihub>

Palivizumab reduces disease severity and hospitalisation of respiratory syncytial virus (RSV) infection in premature infants. This study set out to evaluate the short- and long-term effects of palivizumab on respiratory morbidity and pulmonary function at school age in preterm children. Infants born before 29 weeks' gestation were examined at school age by parental questionnaire, hospital chart review, and lung function tests. Children born immediately before the introduction of routine palivizumab prophylaxis were compared with age-matched children who received palivizumab prophylaxis during the first RSV season. Sixty-three children (30 had received palivizumab) with a mean age of 8.9 years were included. The case and controls were similar in gestational age, birth weight, need for mechanical ventilation and oxygen supplementation. Fifty-three percent of the palivizumab group vs. 39% of the control group had bronchopulmonary dysplasia ( $P = .14$ ). Wheezing occurred in the first 2 years of life in 27% of the palivizumab group and in 70% of control subjects ( $P = .008$ ); respective hospitalization rates were 33% and 70% ( $P = .001$ ). At school age, rates of airway hyperresponsiveness, spirometry, lung volumes, diffusion and exhaled nitric oxide were within normal limits and comparable between groups. This study shows that Palivizumab prophylaxis lessens respiratory morbidity in the first 2 years but does not affect pulmonary outcome at school age.

### **Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice**

Authors: Benard B et al.

Reference: European Respiratory Journal 2017 50(2):1700148

<http://erj.ersjournals.com/content/50/2/1700148.long>

Montelukast is promoted as an alternative to inhaled corticosteroids (ICS) as first-line prophylaxis for children with asthma or recurrent wheezing disorder. It is usually well tolerated, taken once daily by the oral route. In this retrospective study involving asthmatic children aged 1-17 years, the authors determined the incidence of neuropsychiatric adverse drug effects (ADRs) leading to discontinuation of medication. Children initiated on montelukast as monotherapy or adjunct therapy to ICS were matched to those initiated on ICS monotherapy. Parental

interview served to ascertain the occurrence of any ADRs, circumstances related to and evolution of the event was carried out. Of the 106 participants initiated on montelukast, most were male (58%) with a median (interquartile range) age of 5 (3–8) years. The incidence of drug cessation due to neuropsychiatric ADRs was 16%, mostly occurring within 2 weeks. The common ADRs were irritability, aggressiveness and sleep disturbances. The relative risk of ADRs associated with montelukast vs. ICS was 12 (2–90). In this real-life study, children with asthma started on montelukast were at a notable risk of neuropsychiatric ADRs leading to drug cessation and such risk was significantly higher than that associated with ICS.

### **Breastfeeding, maternal asthma and wheezing in the first year of life: a longitudinal birth cohort study**

Authors: Azad MB et al.

Reference: European Respiratory Journal 2017;49(5):1602019

<http://erj.ersjournals.com/content/49/5/1602019.long>

Breastfeeding is strongly encouraged by the World Health Organisation. However, the impact of breastfeeding on respiratory health remains unclear especially when the mother has asthma. In this study, the association of breastfeeding and wheezing in the first year of life was assessed. Two thousand plus infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort were studied. Caregivers were asked to report on the mode of infant feeding and wheezing episodes at 3, 6 and 12 months. Breastfeeding was categorised as exclusive, partial (supplemented with formula or complementary foods) or none. In the study population, 21% of mothers had asthma, 46% breastfed for at least 12 months and 21% of infants experienced wheezing. In mothers with asthma, breastfeeding was inversely associated with infant wheezing, independent of maternal smoking, education and other risk factors (adjusted rate ratio (aRR) 0.52; 95% CI 0.35–0.77 for  $\geq 12$  versus  $< 6$  months breastfeeding). Compared with no breastfeeding at 6 months, wheezing was reduced by 62% with exclusive breastfeeding (aRR 0.38; 95% CI 0.20–0.71) and by 37% with partial breastfeeding supplemented with complementary foods (aRR 0.63; 95% CI 0.43–0.93); however, breastfeeding was not significantly protective when supplemented with formula (aRR 0.89; 95% CI 0.61–1.30). Associations were not significant in the absence of maternal asthma (p-value for interaction  $< 0.01$ ). This study provides strong evidence that breastfeeding protects against wheezing in a dose-dependent manner amongst infants born to mothers with asthma.

### **Azithromycin for episodes with asthma-like symptoms in young children aged 1–3 years: a randomised, double-blind, placebo-controlled trial**

Authors: Stockholm J et al.

Reference: Lancet Respiratory Medicine 2016;4(1):19-26.

<http://www.sciencedirect.com/science/article/pii/S2213260015005007?via%3Dihub>

Bacteria and viruses are both advocated in causing acute episodes of asthma-like symptoms in young children. This study examined the effect of azithromycin on the duration of respiratory episodes in young children with recurrent asthma-like symptoms. In this randomised, double-blind, placebo-controlled trial, children aged 1–3 years, who were diagnosed with recurrent asthma-like symptoms were recruited. Each episode lasting at least 3 days was randomly allocated to a 3-day course of azithromycin oral solution of 10 mg/kg per day or placebo. The primary outcome was duration of the respiratory episode after treatment, verified by prospective daily diaries. One hundred and fifty-eight asthma-like episodes in 72 children were recorded and half were randomised to receive azithromycin. The mean duration of the episode after treatment was 3.4 days for cases and 7.7 days for children who received placebo. Azithromycin caused a significant shortening of the episode of 63.3% (95% CI 56.0–69.3;  $p < 0.0001$ ). The effect size increased with early initiation of treatment, showing a reduction in episode duration of 83% if treatment was initiated before day 6 of the episode compared with 36% if initiated on or after day 6 ( $p < 0.0001$ ). No differences in clinical adverse events between the two groups could be documented. This study shows that azithromycin could have a role in the acute management of asthma-like exacerbations.

### **Acetaminophen versus Ibuprofen in young children with mild persistent asthma**

Authors: William J. Sheehan, David T. Mauger, Ian M. Paul, et al.

Reference: N Engl J Med 2016; 375:619-30.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5085065/>

Physicians may recommend against the use of acetaminophen in children with asthma as some studies have suggested an association between frequent acetaminophen use and asthma-related complications. In this multicenter, prospective, randomised, double-blind, parallel-group study, 300 children (age range, 12 to 59 months) with mild persistent asthma were allocated to receive either acetaminophen or ibuprofen as needed for fever or pain relief over the course of 48 weeks. The primary outcome was the number of asthma exacerbations that led to treatment with systemic glucocorticoids. Children in both groups continued to receive standardized asthma-controller therapies. No significant between-group difference in the median number of study medication doses received ( $P=0.47$ ) could be found. The number of asthma exacerbations did not differ significantly between the two groups (relative rate of asthma exacerbations in the acetaminophen group vs. the ibuprofen group, 0.94; 95% confidence interval, 0.69 to 1.28;  $P=0.67$ ). The number of subjects having one or more exacerbations was similar in the two groups. In addition, no significant differences were detected between acetaminophen and ibuprofen with respect to the percentage of asthma-control days (85.8% and 86.8%, respectively;  $P=0.50$ ), use of an albuterol rescue inhaler (2.8 and 3.0 inhalations per week, respectively;  $P=0.69$ ), unscheduled health care utilisation for asthma (0.75 and 0.76 episodes per participant, respectively;  $P=0.94$ ), or adverse events. This study suggests that among young children with mild persistent asthma, as-needed use of acetaminophen is not associated with a higher incidence of asthma exacerbations or worse asthma control than was as-needed use of ibuprofen.



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