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Procalcitonin Guidance to Reduce Antibiotic Treatment of Lower Respiratory Tract Infection in Children and Adolescents (ProPAED): A Randomized Controlled Trial.

Authors: G. Baer, P. Baumann, M. Buettcher, et al.
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3735552/
Comment: In adults with pneumonia, management based on procalcitonin (PCT) levels has been shown to be reduce the use of antibiotics without increasing morbidity. To date, there had been little evidence in children. This dual centre RCT is based in pediatric emergency departments in Switzerland, 337 previously healthy children (mean age 3.8 years (range 0.1-18) with LRTI were randomised to receive antibiotics either according to a PCT guidance algorithm established for adults or standard care clinical guidelines. There was no significant difference between groups for antibiotic prescribing rate (OR 1.26; 95% CI 0.81, 1.95) but the PCT guidance reduced the length of antibiotics used. In addition to the findings of the study, this RCT highlights, yet again, the inappropriateness of extrapolation of adult data to children without careful considerations.

Social Disadvantage and Asthma Control in Children.

Authors: L. S. Kopel, W. Phipatanakul, and J. M. Gaffin.
Comment: In this review, authors discuss the evidence and theories between poor asthma control and social disadvantage. They also present interventions designed to improve asthma morbidity in this vulnerable population. Social disadvantage include socioeconomic status, exposure to psychosocial stress and violence, minority affiliation, environmental exposures and pollution, and poverty in rural settings. Increasingly, biological mechanisms (such as increased caregiver stress during infancy are associated with heightened IgE expression and inflammatory markers) are described. This review is a timely reminder to clinicians to examine for, and if possible intervene, social disadvantage factors in children with poor asthma control.

New Impact factor and ranking for Respirology released July 2014

Edited By: Peter Eastwood

Impact Factor: 3.495
ISI Journal Citation Reports ©
Ranking:2013: 15/53 (Respiratory System)
Three Clinically Distinct Chronic Pediatric Airway Infections Share a Common Core Microbiota.

Authors: C. J. van der Gast, L. Cuthbertson, G. B. Rogers, et al.

Comment: Increasingly, microbiota in various human conditions in health and disease are described. In respiratory disease, this is the first study that have compared the microbiota in the same diseases in children and adult. Using bacterial 16S rRNA gene pyrosequencing, phylogenetic analysis, and ecological statistical tools, the authors describe that the three pediatric disease cohorts (cystic fibrosis, bronchiectasis and protracted bacterial bronchitis) shared similar core respiratory microbiota that was significantly different from adult CF and bronchiectasis microbiota. The most common species in pediatric disease cohort samples were also detected in those from healthy children. In contrast, in adults with CF and bronchiectasis, the microbiota differed from each other, suggesting common early infection airway microbiota that diverge by adulthood. Thus, the study suggest that irrespective of the underlying airway disease, the microbiota are similar in early disease and with increasing severity, the microbiota diverges. While only a longitudinal study on several different cohorts can definitely prove this, an ethical study is highly unlikely in the context of the requirement of recurrent bronchoalveolar specimens for infants and very young children.


Authors: P. C. Valery, P. S. Morris, C. A Byrnes, et al.

Comment: This is the first double-blinded RCT on the long term use of azithromycin in children with bronchiectasis unrelated to cystic fibrosis. This study also used azithromycin for the longest duration in a RCT in either children or adults with bronchiectasis. In this multi-centre RCT based in Australia and New Zealand, 89 Indigenous children were randomised to weekly azithromycin (30mg/kg/dose) or placebo for 12-24 months. Children who received azithromycin had a significant reduction in pulmonary exacerbations (incidence rate ratio 0.50; 95% CI 0.35-0.71) and increased weight z-score (mean difference 0.93 z-score, 95% CI 0.32-1.54). However, like the published studies on the use of macrolides in adults with bronchiectasis, higher carriage of azithromycin-resistant bacteria (19 of 41 children, 46%) were found in those on azithromycin compared to those receiving placebo (four of 37, 11%; p=0.002). Nevertheless, in a post-hoc analysis, children in azithromycin arm received significantly less other antibiotics for non-respiratory infections (IRR 0.50; 95% CI 0.31–0.81; p=0.005). Thus, the study supports the use of azithromycin for the reduction of pulmonary exacerbations in children with non-CF bronchiectasis (who do not have Pseudomonas). However, it remains uncertain who benefits the most, when azithromycin should be commenced and how long it should be used for.
**Prenatal vitamin D supplementation and child respiratory health: a randomised controlled trial.**

**Authors:** S. T. Goldring, C. J. Griffiths, A. R. Martineau, et al.


**URL:** [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3691177/](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3691177/)

**Comment:** This double blind RCT randomized 180 pregnant women at 27 weeks gestation to either no vitamin D, 800 IU ergocalciferol daily until delivery or single oral bolus of 200,000 IU cholecalciferol. Children were assessed at 3 years of age (n=153 of the 180) and the supplemented groups were combined and compared to controls for analyses. The groups did not significantly differ in the primary outcome (wheeze ever) or any of the secondary outcomes: respiratory infections, atopy (assessed by skin prick test), eczema risk, lung function (impulse oscillometry) or exhaled nitric oxide levels. The later were performed only in a subset of children. Results is limited as there was only a modest increase in cord vitamin D level but results are consistent with systematic reviews showing little effect of vitamin D on respiratory outcomes in RCTs, which is in contrast to observational studies.

**Nasogastric hydration versus intravenous hydration for infants with bronchiolitis: a randomised trial.**

**Authors:** Oakley E, Borland M, Neutze J, et.al.

**Reference:** Lancet Respiratory Medicine 2103; 1(2): 113 – 120.


**Comment:** Children hospitalised with bronchiolitis sometimes require fluid support when their high work of breathing and/or respiratory rate impairs adequate or safe feeding. This is the first RCT that have examined the question of which hydration method is superior. In this multi-centre, open, randomised trial, based in Australia and New Zealand infants aged 2–12 months were randomised to nasogastric hydration (n=381) or intravenous hydration (n=378). Authors found no significant difference between groups for their primary outcome, duration of hospitalisation stay (nasogastric hydration: mean 86·6 hrs, SD 58·9 vs IV: 82·2, 58·8), absolute difference 4·5 h [95% CI –3·9 to 12·9]; p=0·30). There was also no difference between groups for rates of admission to intensive-care units, need for ventilatory support, and adverse events. This study is a welcomed contribution to evidence based practice in the field of bronchiolitis but is limited by a study designed for superiority, but equivalence between groups was found.

New online in Respirology:

*They said it was bronchiolitis; is it going to turn into asthma doctor?*

Gidaris D, Urquhart D, Anthracopoulos MB. Respirology, 2014,

DOI: 10.1111/resp.12371 Article first published online: 19 AUG 2014
**7% Hypertonic Saline in Acute Bronchiolitis: A Randomized Controlled Trial.**

**Authors:** Jacobs JD, Foster M, Wan J. Pershad J.  
**Reference:** Pediatrics 2014; 133:1 e8-e13.  
**URL:** [http://pediatrics.aappublications.org/content/133/1/e8.long](http://pediatrics.aappublications.org/content/133/1/e8.long)  
**Comment:** In some centers, 3% or 5% hypertonic saline (HS) is regularly used in children with bronchiolitis as some studies has been shown that HS improves clinical severity scores and reduce inpatient length of stay. In this uni-centre double-blind RCT, 101 infants with moderate to severe acute bronchiolitis were randomized to 7% HS (n=52) or placebo (n=49) in the emergency department. Trial medications were nebulized every 6 hours until discharge or 24 hours after the admission. There was no significant difference between groups for the primary outcome (bronchiolitis score) or secondary outcomes (proportion admitted, discharged at 23 hours after admission, or inpatient length of stay. Give the short duration of intervention, results of this study is not surprising but it does dispel the question of whether a higher HS concentration is efficacious in the emergency department setting.

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**Accuracy of Pulse Oximetry in Children.**

**Authors:** Ross PA, Newth CJL, Khemani RG.  
**Reference:** Pediatrics; 2014, 33(1); 22-29.  
**URL:** [http://pediatrics.aappublications.org/content/133/1/22.long](http://pediatrics.aappublications.org/content/133/1/22.long)  
**Comment:** The variable accuracy of pulse oximetry where SaO$_2$ are low are well known but have largely been based on small studies. Also, adult healthy volunteers breathing a hypoxic gas mixture are usually used to present data on the accuracy of pulse oximetry, a scenario very different to the clinical settings encountered in the field of paediatric pulmonology. This observational study undertaken in 5 PICUs aimed to “measure the accuracy of pulse oximetry in the saturations from pulse oximetry (SpO$_2$) range of 65% to 97%”. From 225 ventilated children, 1980 measurements of SpO$_2$ from pulse oximetry (Masimo and Nellcor) were compared to simultaneously obtained SaO$_2$ (measured from CO-oximetry) if the SpO$_2$ was <97%. The authors found that SpO$_2$ overestimates SaO$_2$ and described “significant variability in the bias, precision (SD) and accuracy of pulse oximetry as a function of SpO$_2$”. The bias was largest when SpO$_2$ was 81-85%. The importance of this paper for clinicians is the confirmation of the large variation found in SpO$_2$ when compared to SaO$_2$. As described by the authors, if the SpO$_2$ is measured at 85%, half “the time the SaO$_2$ would lie between 75% and 83%”. However, the range at 95% certainty, is between 64% and 89%.

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Watch Respirology video presenting the new review series on “Respiratory diseases: Using lung function measurements to greater advantages.”  
[https://www.youtube.com/watch?v=VulvdFlvhM0](https://www.youtube.com/watch?v=VulvdFlvhM0)
A cough algorithm for chronic cough in children: a multicentre, randomized controlled study.

Authors: A. B. Chang, C. F. Robertson, P. P. van Asperen, et al.
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2989328/

Comment: Using an evidence-based cough algorithm, this multicentre RCT conducted in Australia used a wait-list study design involving 272 children with chronic cough. These children who were newly referred to the study authors' clinical practice were randomised to early (2-weeks) vs. delayed (6-weeks) use of a cough algorithm. The RCT found that children in the early-arm (intervention group) had significantly better cough-specific quality of life and duration of cough (post randomisation) compared to the delayed-arm group (controls). In the intention to treat analyses, cough resolution (at week 6) was significantly more likely in the early-arm group (intervention group) compared with the delayed-arm (control) group (absolute risk reduction: 24.7%, 95% CI 13-35%). The median duration of cough pre-randomisation was 16 (IQR 8–28) in the early-arm group and 18 (10–42) weeks in the delayed-arm group. Once the cough algorithm was used, irrespective of whether it was applied early or delayed, the duration of cough was similar (early-arm: 4.4 weeks SD 5.2; delayed-arm (control): 4.2, SD 6.2). Thus, the study shows that management of children with chronic cough, in accordance with a standardized algorithm, improves clinical outcomes. Earlier application of the algorithm leads to earlier cough resolution and improved parental quality of life. However, whether this can be applied to primary care setting is yet to be determined.

Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments.

Authors: Jefferson T1, Jones M, Doshi P, Spencer EA, Onakpoya I, Heneghan CJ.
Reference: BMJ. 2014 Apr 9;348:g2545. doi: 10.1136/bmj.g2545.
URL: http://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24811411/

Comment: During the 2009/2010 H1N1 near-pandemic, governments, their Departments of Health and the WHO encouraged use of the oseltamivir when their 'expert committees' recommended it, leading to stock piling of the drug at considerable expense. Authors of this paper systematically reviewed published and unpublished RCTs on children and adults who had confirmed or suspected exposure to natural influenza. Authors found that treatment with oseltamivir had no effect in children with asthma an effect in otherwise healthy children (mean difference 29 hours, 95% confidence interval 12 to 47 hours, P=0.001). Limited data for prophylaxis in children found that oseltamivir did not significantly reduce unverified pneumonia in children. Further, oseltamivir causes nausea and vomiting and increases the risk of headaches and renal and psychiatric syndromes (the later in adults). This paper highlights (yet again) the importance of non-aligned researchers delving deeper into data not generally available and the extreme care required when interpreting pharmaceutical sponsored RCTs irrespective of which journal they are published in.