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Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids

Authors: Lemanske RF Jr et al.


**Comment:** This triple-crossover trial involved 182 children (6-17 years of age) with uncontrolled asthma, despite being on 100 μg of fluticasone twice daily. Each child received the following step-up therapies in random order for 16 weeks: 250 μg of fluticasone twice daily (ICS step-up), 100 μg fluticasone plus 50 μg of long-acting beta-agonist twice daily (LABA step-up), or 100 μg of fluticasone twice daily plus 5 or 10 mg of leukotriene receptor antagonist daily (LTRA step-up). Although LABA step-up was significantly more likely to provide the best response compared with either the ICS or LTRA step-ups, the children showed differential responses to each of the step-up therapies. While the effect of wash out periods remains unknown, the study basically confirmed what many vigilant clinicians currently do in clinical practice, i.e. monitor and appropriately adjust each child's asthma therapy. The study confirmed that response to therapies is not universal. Interestingly, the study showed that being a ‘white patient’ predicted a better response to the LABA step-up, whereas ‘black patients’ were least likely to show the best response to the LTRA step-up ($P = 0.005$).
Effect of azithromycin on pulmonary function in patients with cystic fibrosis uninfected with Pseudomonas aeruginosa: a randomized controlled trial

Authors: Saiman L et al.
URL: http://jama.ama-assn.org/cgi/content/full/303/17/1707

Comment: In this multicentre, randomized, double-blind placebo-controlled trial performed at 40 CF centres in the United States and Canada, 260 children (aged 6-18 years), with negative cultures for *Pseudomonas aeruginosa* for at least 1 year, were randomised to azithromycin [250 mg (weight 18-35.9 kg) or 500 mg (weight ≥ 36 kg)] or placebo, three days per week for 168 days. While there was no difference between the groups for the main outcome (change in FEV₁), there were significant differences in other important clinical outcomes: pulmonary exacerbations [50% reduction in exacerbations (95% CI 31-79%)], body weight [increase of 0.58 kg (95% CI 0.14-1.02)] and improvement in cough, in the azithromycin group compared with the placebo group. However, there were no significant differences between the groups in the use of intravenous or inhaled antibiotics, or hospitalizations. Participants in the azithromycin group did not have an increased risk of adverse events. While further evidence is required, particularly with respect to longer term clinical or microbiological outcomes, the study suggests that azithromycin should be considered as an adjunct therapy even in children without *Pseudomonas* infection, but who have chronic cough and/or frequent exacerbations. The relevance of this study for non-CF bronchiectasis remains unknown.

Longitudinal growth and lung function in pediatric non-cystic fibrosis bronchiectasis: what influences lung function stability?

Authors: Kapur N et al.
Reference: Chest 2010; 138: 158-64.
URL: http://chestjournal.chestpubs.org/content/138/1/158.long

Comment: This study adds to two others on longitudinal cohorts of children with non-CF bronchiectasis. The London study (Thorax 2009; 64: 246-51) showed that with intensive treatment lung function improved, but did not necessarily normalize. In contrast, the Auckland study (Thorax 2006; 61: 414-18) showed a decline in FEV₁ of 1.9% per year. This new Brisbane study showed that spirometry improved in children who had a low FEV₁ (<80% of predicted) and remained stable over a 3-5 year period. This study also examined the influences on lung function decline. Age, gender and the underlying aetiology of bronchiectasis did not influence longitudinal spirometry values. Frequency of hospitalization for exacerbations was a significant predictor of decline in FEV₁%. FEV₁% predicted declined by 1.95 points for each exacerbation (P = 0.048). In addition, the decline in FEV₁ % predicted was large (but not significant) for each additional year of age at diagnosis. This study confirmed the need for early diagnosis, monitoring and aggressive management to improve long term outcomes in children with non-CF bronchiectasis, irrespective of aetiology. Interventions to reduce exacerbations are required as there is currently little data. It is possible that children predisposed to more rapid decline are more likely to have severe exacerbations. However, given the evidence that intensive therapy reduces exacerbations, the data is in keeping with that for adult COPD in suggesting that exacerbations contribute to decline in FEV₁. It is highly unlikely that a sufficiently large long term RCT (to evaluate treatment vs. non-treatment) will ever be performed, and hence vigilance, close monitoring and aggressive treatment are advocated in children with non-CF bronchiectasis.
Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial

Authors: Schuh S et al.
URL: http://www.jpeds.com/article/PIIS0022347609005538/fulltext
Comment: In this randomized, double-blind, double-dummy non-inferiority trial, 130 children (aged 2-17 years) with mild to moderate acute asthma, received five daily treatments with either prednisolone or montelukast, after stabilization of the exacerbation with prednisolone in the emergency department. Treatment failure within eight days, i.e. an unscheduled asthma-related visit, hospitalization, or the need for additional systemic corticosteroids, was significantly greater in the montelukast group (22.4%) compared with the prednisolone group (7.9%). Thus, while montelukast is an attractive option, especially for children with virus induced asthma, this study confirmed that standard oral corticosteroids remain the mainstay of therapy for non-hospitalised children with asthma exacerbations. However, five days of oral corticosteroid therapy is unlikely to be necessary, as previous RCTs have shown that three days of oral corticosteroids is sufficient in this group of children (Med J Aust 2008; 189: 306-10). It remains unknown whether the addition of montelukast to oral corticosteroids reduces morbidity in children with asthma exacerbations.

The transient value of classifying preschool wheeze into episodic viral wheeze and multiple trigger wheeze

Authors: Schultz A et al.
Comment: This study determined whether recently proposed phenotypes of pre-school wheeze (e.g. viral wheeze, multi-trigger wheeze) are stable over time. Clinicians are already well aware of the clinical limitations of these phenotypes. This study demonstrated the non-stability of these phenotypes (54% change in 12 months), and confirmed their limited value, clinically, as well as for research purposes.

The influence of neonatal lung function on rhinovirus associated wheeze

Authors: van der Zalm MM et al.
URL: http://ajrccm.atsjournals.org/cgi/reprint/200905-0716OCv1
Comment: This was a prospective birth cohort study, in which infants were followed from birth through the first year of life, with daily questionnaires about respiratory symptoms. This is yet another study showing that wheeze in infancy is associated with altered lung function. In this study infants with increased airway resistance, as measured by the single occlusion technique performed within the first two months of life, had a greater risk of wheeze associated with the detection of human rhinovirus (HRV). Maternal smoking during pregnancy was the only other factor independently associated with wheeze (OR 4.42, CI 1.27-15.5). However, it is unlikely that lung function is the only contributor to wheeze or HRV infection in young children, as long-term follow-up studies have shown that deficits in interferon gamma responses in the first year of life are also associated with recurrent episodes of wheezing during the pre-school years.
**Controlled trial of cycled antibiotic prophylaxis to prevent initial Pseudomonas aeruginosa infection in children with cystic fibrosis**

Authors: Tramper-Stranders GA et al.


URL: http://thorax.bmj.com/content/early/2010/08/19/thx.2009.126128.long

Comment: Given that *Pseudomonas aeruginosa* colonisation is associated with poorer respiratory outcomes in CF and non-CF bronchiectasis, interventions that can delay *P. aeruginosa* colonisation are attractive. In this RCT involving three-monthly, three-week treatments with oral ciprofloxacin and inhaled colistin, or both placebo controls for three years, there was no difference in the acquisition of *P. aeruginosa* infection between the control and treatment groups. Decline in pulmonary function and other clinical outcomes also did not differ between the two groups. Thus three-monthly cycled anti-*P. aeruginosa* prophylaxis did not reduce the risk of initial and chronic infection in *P. aeruginosa*-negative children of all ages with CF, and this therapy should not be used. As children with CF are substantially more likely to acquire *P. aeruginosa* than those with non-CF bronchiectasis, the results are also applicable to the management of children with non-CF bronchiectasis.

**Multicenter, double-blind, randomized, placebo-controlled trial assessing the efficacy and safety of proton pump inhibitor lansoprazole in infants with symptoms of gastroesophageal reflux disease**

Authors: Orenstein SR et al.


URL: http://www.jpeds.com/article/PIIS0022347608008640/fulltext

Comment: In this multicentre, double-blind, parallel-group study, 162 infants with persistent symptoms attributed to gastroesophageal reflux disease (GERD) were randomized to treatment with lansoprazole or placebo for four weeks. This study showed no difference in efficacy between lansoprazole and placebo for symptoms attributed to GERD in infants aged 1 to 12 months. The importance and relevance of this study for pulmonologists is the finding that serious adverse events, particularly lower respiratory tract infections, occurred more frequently with lansoprazole than with placebo. Lansoprazole also had no significant effect on the infants (n = 119) who had a cough. While studies on proton pump inhibitors in adults have shown that their use is associated with an increased risk of clinically important events (e.g. pneumonia), this is the first high quality study in a paediatric population.
An objective study of acid reflux and cough in children using an ambulatory pHmetry-cough logger

Authors: Chang AB et al.

Reference: Arch Dis Child 2010, June 1; Epub ahead of print, doi:10.1136/adc.2009.177733

URL: http://adc.bmj.com/content/early/2010/05/31/adc.2009.177733.long

Comment: This is the first study that has evaluated in an objective manner the temporal relationship between acid reflux and cough in ambulatory children. Commercial pHmetry loggers have slow capture rates (0.25 Hz) that limit objective quantification. The authors used a specifically designed cough-pH logger with a capture rate of 10 Hz. This was a small study of 20 children, but a large number of coughs (n = 5628) were analysed in the children suspected of having gastroesophageal reflux disease (GERD). The number of participants was similar to that in other objective studies in adults. The study showed that most coughs (83.9%) were independent of a reflux event within 120 seconds. Taken in conjunction with the study of Orenstein et al. (previous page), the findings suggest that cough in young children should not be attributed to gastroesophageal reflux without additional evidence.

Parent initiated prednisolone for acute asthma in children of school age: randomised controlled crossover trial

Authors: Vuillermin PJ et al.


URL: http://www.bmj.com/content/340/bmj.c843.long

Comment: In this crossover RCT, 230 children were enrolled. However only 131 (57%) participants had exacerbations, for which the parent initiated treatment with prednisolone (1 mg/kg/day) or placebo. During the exacerbations that were treated with prednisolone, asthma symptoms, use of health resources, and absenteeism from school were reduced. Parent initiated early use of oral corticosteroids is mostly standard in asthma action plans for children who have frequent exacerbations. This study provides evidence supporting this step, but it has to be interpreted in the context of the study design and the limitations of crossover trials (see Cochrane handbook).