

## Clippings

❑ Inhaled hypertonic saline improves mucociliary clearance and, in short-term trials, improves lung function in people with cystic fibrosis but its long-term efficacy is not known. This was assessed in a double-blind, parallel-group trial with 164 patients with stable cystic fibrosis who were at least six years old were randomly assigned to inhale 4 ml of either 7 percent hypertonic saline or 0.9 percent (control) saline twice daily for 48 weeks, with quinine sulfate (0.25 mg per milliliter) added to each solution to mask the taste. A bronchodilator was given before each dose, and other standard therapies were continued during the trial. The study found that the primary outcome measure, the rate of change (slope) in lung function (reflected by the FVC, FEV1 and FEF25-75) during the 48 weeks of treatment, did not differ significantly between groups ( $P = 0.79$ ). However, the absolute difference in lung function between groups was significant ( $P = 0.03$ ) when averaged across all post-randomization visits in the 48-week treatment period. The hypertonic-saline group had significantly higher FVC (by 82 mL; 95% CI, 12-153) and FEV1 (by 68 mL; 95% CI, 3-132) values than controls, but similar FEF25-75 values. The hypertonic-saline group also had significantly fewer pulmonary exacerbations (relative reduction, 56%;  $P = 0.02$ ) and a significantly higher percentage of patients without exacerbations (76%, as compared with 62% in the control group;  $P = 0.03$ ). Hypertonic saline was not associated with worsening bacterial infection or inflammation and the authors concluded that hypertonic saline preceded by a bronchodilator is an inexpensive, safe, and effective additional therapy for patients with cystic fibrosis in the long term. *NEJM* 2006; 354(3): 229-240.

❑ While on the subject of Cystic Fibrosis, another disorder that is similar to CF in many ways but is caused by congenital defects in mucociliary clearance is Primary Ciliary Dyskinesia (PCD). A study compared the biophysical and transport properties of CF and PCD sputa, in subjects matched for age and degree of lung function impairment, by measuring the dynamic viscoelasticity, wettability, cohesivity, interfacial (surface) tension, solids composition, DNA and Interleukin (IL)-8 concentration, *in vitro* mucociliary transportability, and cough transportability of sputum samples. The authors found that inflammation, as measured by IL-8 concentration, was 3 times greater in the PCD sputa ( $p < 0.0001$ ). There were no significant differences in the sputum biophysical or transport properties comparing CF with PCD sputum. For both disorders, the biophysical and transport properties reflect disease severity, regardless of whether bronchiectasis is due to CF or PCD. *Chest* 2006; 129: 118-123.

❑ Is microvascular development of the lung disrupted in infants with bronchopulmonary dysplasia (BPD)? A study of postmortem lung samples collected from ventilated preterm infants who died between 23 and 29 week ("short-term ventilated") or between 36 and 39 week ("long-term ventilated") corrected postmenstrual age, in which microvascular growth was studied by anti-platelet endothelial cell adhesion molecule (PECAM)-1 immunohistochemistry and analysis of endothelial cell proliferation, and these results were compared with age-matched infants or stillborn infants ("early" and "late" control subjects). The lungs of long-term ventilated infants showed a significant (>

twofold) increase in volume of air-exchanging parenchyma and a 60% increase in total pulmonary microvascular endothelial volume compared with late control subjects, associated with 60% higher pulmonary PECAM-1 protein levels. The marked expansion of the pulmonary microvasculature in ventilated lungs was, at least partly, attributable to brisk endothelial cell proliferation but it appeared immature, retaining a saccular architectural pattern. These findings challenge the paradigm of microvascular growth arrest as a major pathogenic factor in BPD. *Am J Resp Crit Care Med* 2006; 173: 204-211.

□ Is there a way to characterize the inflammatory subtypes in asthma that could help in its management based on the predominant inflammatory cell type in the airways? This was the hypothesis of a study where adult non-smokers with asthma and healthy controls underwent sputum induction and hypertonic saline challenge and the authors set out to identify non-eosinophilic asthma which was defined as symptomatic asthma with normal sputum eosinophil counts, with the normal range of sputum eosinophil count being determined from the healthy control group. The authors found that airway inflammation in asthma could be categorized into four inflammatory subtypes based on sputum eosinophil and neutrophil proportions. These subtypes were neutrophilic asthma, eosinophilic asthma, mixed granulocytic asthma and paucigranulocytic asthma. Subjects with increased neutrophils (neutrophilic asthma and mixed granulocytic asthma) were found to be older and had an increased total cell count and cell viability compared with other subtypes. *Respirology* 2006; 11: 54.

□ Is there clinical benefit in extensively investigating young children <5 yrs of age with severe recurrent wheeze? A total of 47 young children (25 males, with a median age of 26

(range 5-58) months) who were refractory to conventional asthma therapy were evaluated by a protocol of investigations including a chest computed tomography scan, blood tests, nasal ciliary brushings, fiberoptic broncho-scopy, bronchoalveolar lavage (BAL), endo-bronchial biopsy and esophageal pH probe study. The authors found that 39% were atopic, two-thirds had evidence of gastro-esophageal reflux and 37 out of 47 had abnormal broncho-scopy findings. These findings included structural abnormalities (13 out of 37), excessive mucus (20 out of 37) and macroscopic inflammation (10 out of 37). BAL revealed bacterial growth in 12 out of 44 (27%) patients and endobronchial biopsies obtained from 36 out of 46 (78%) patients showed that 44% had tissue eosinophilia and 28% had a thickened reticular basement membrane. This suggested protocol could help develop future interventional studies in this age group. *Eur Respir J* 2006; 27:29-35.

□ What is the incidence and patient pro-file primary airway malacia (tracheomalacia and bronchomalacia) in children? A retrospective analysis of data from 512 bronchoscopies found 160 children (94 males) with airway malacia, diagnosed at a median age of 4.0 years (range, 0 to 17 years). Airway malacia was classified as primary in 136 children and secondary in 24 children and the incidence of former was estimated to be at least 1 in 2,100. When pediatric pulmonologists expected to find airway malacia (based on symptoms, history, and lung function) prior to bronchoscopy, this was correct in 74% of the cases but in 52% of the cases, the diagnosis was not suspected prior to bronchoscopy. Presenting clinical features of children with airway malacia were variable and atypical, showing considerable overlap with features of allergic asthma but they had greater reduction in peak expiratory flow than FEV1. Hence the

authors suggest that bronchoscopy should be considered in patients with impaired exercise tolerance, recurrent lower airways infection, and therapy-resistant, irreversible, and/or atypical asthma to rule out airway malacia. *Chest* 2005; 128: 3391-3397.

□ Continuing on the subject of bronchoscopy, what are the sedative drug requirements during flexible bronchoscopy procedures in immunosuppressed patients? A review of the 239 bronchoscopies performed under local anesthesia, using sedation with intermittent boluses of intravenous midazolam and intravenous hydrocodone 5 mg, was compared with 91 non-immunosuppressed patients acting as controls. Procedures in immunosuppressed patients who received midazolam consisted of stem cell transplant (34), solid organ transplant (25), chemo-therapy (33), HIV with drug abuse (10), HIV (5), prednisone (17) and immuno-suppression for other diseases (12). Intravenous propofol was administered during 12 procedures due to inability to achieve optimal sedation with midazolam in a previous bronchoscopy and during the same bronchoscopy due to inadequate sedation with a high dose of midazolam, with mean dose of propofol being  $2.8 \pm 1.3$  mg/kg. The study concluded that midazolam requirement was significantly higher in patients with stem cell transplantation and in HIV patients with drug abuse. *Respiration* 2005; 72: 617-621.

□ Increased levels of fractional exhaled nitric oxide (FeNO) reflect airway inflammation, but can this modality be used for screening for patients with asthma? In a study from Oxford, FeNO was measured using an on-line single exhalation analyzer in 368 children aged 8-10 years in six Oxfordshire primary schools, by two investigators blinded to the disease status of the children. The children were then categorised into 'normal', 'atopic asthma', 'non-atopic asthma' and 'atopy only' groups, according to their responses to the ISAAC questionnaire and children's medical records. Increased levels of FeNO were found in 'atopic asthmatic', 'non-atopic asthmatics' and 'atopy only' groups (median values of 24.4, 7.8 and 15.3 ppb, respectively, compared to normal controls' of 6.9 ppb). Levels were increased in atopic children regardless of whether they had asthma and were significantly higher than non-atopic asthmatics. The study concluded that FeNO measurement is not a useful tool for identifying children with asthma in the community, as increased levels did not discriminate between those with asthmatic and atopic symptoms. *Respir Med* 2006; 100: 167-173.

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## NOTES AND NEWS

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