Chaten FC, Lucking SE, Young ES, Mickell JJ: Stridor: intracranial pathology causing postextubation vocal cord paralysis. Pediatrics 1987; 87:39-43.

During an 18-month period in a pediatric intensive care unit, nine patients with vocal cord paralysis were identified using flexible bronchoscopy. When tracheally extubated, each child was found to have stridor. The children ranged in age from 17 days to 5½ years. Two patients had unilateral paralysis, but neither required tracheostomy. Seven patients displayed bilateral abductor vocal cord paralysis. Of these, six patients required tracheostomy. Surgical injury to the recurrent laryngeal nerve was the probable cause in two patients. The other seven patients had neurologic disorders with documented or suspected increases of intracranial pressure. Four of the seven patients with bilateral abductor vocal cord paralysis regained cord mobility within 4 months. Both children with unilateral cord paralysis have no stridor and vocalize well 1 year later. Cord paralysis in the setting of intracranial hypertension probably results from compression or ischemia of the vagus nerve before it exits the skull. Early visualization of the larynx should be done in patients who become stridulous when extubated, especially those with prior thoracic procedures or with neurologic disorders associated with intracranial hypertension.

Hughes DM, McLeod M, Garner B, Goldbloom RB: Controlled trial of a home and ambulatory program for asthmatic children. Pediatrics 1991; 87:54-61.

Care of asthmatic children is often episodic and more therapeutic than preventive. A 2-year randomized, controlled trial involving 95 children measured the impact of a comprehensive home and ambulatory program for pediatric asthma management using objective outcome measures. Interventions for the study group during the first year included 3-month clinic visits, education, and home visits by a specially trained research nurse. Control subjects continued to receive regular care from a family physician or pediatrician. Eighty-nine subjects (93%) completed the study. Study subjects had less school absenteeism than control subjects (10.7 vs. 16.0 days, P = .04) and showed significantly better small airway function after 1 year. Asthma severity improved in 13 study subjects and worsened in 5. The reverse was true for control subjects. Study subjects exhibited better metered aerosol technique than control subjects (P = .0005). Fewer days were spent in hospital by the study subjects admitted compared with control subjects (3.67 vs 11.2 days, P = .02). After 1 year, more study than control families (72.1% vs 33.1%, P = .006) reported that their asthmatic child took responsibility for the asthma management. The intervention failed to reduce exposure to secondhand smoke or to household pets. There were no significant differences in medical visits, theophylline levels, or records of asthma symptoms. One year after discontinuing the intervention, a marked "washout" effect was observed. Comprehensive ambulatory programs of childhood asthma management can improve objective measures of illness severity but must be sustained.

Auten RL, Notter RH, Kendig JW, Davis JM, Shapiro DL: Surfactant treatment of full-term newborns with respiratory failure. Pediatrics 1991; 87:101-107.

Surfactant inactivation has been shown to be a significant factor in animal models of lung injury and may also be important in some forms of respiratory failure in full-term newborns. Fourteen full-term newborns with respiratory failure associated with pneumonia (7 patients) and meconium aspiration syndrome (7 patients) were treated with 90 mg/kg of a calf lung surfactant extract, given intratracheally up to every 6 hours for a maximum of four doses. The group mean fraction of inspired oxygen (Fio2) before treatment was 0.99 ± 0.01 SEM, and the mean airway pressure (MAP) was 14.6 ± 1.0 cm H2O. Patients showed significant improvement in oxygenation after initial surfactant treatment, with the arterial-alveolar oxygenation ratio (a/A ratio) rising from 0.09 ± 0.01 before surfactant treatment to 0.22 ± 0.05 by 15 minutes (P = .03) and remaining improved for 6 hours. The oxygenation index, incorporating MAP as well as oxygen variables, also improved significantly from 26.2 ± 3.1 to 11.2 ± 1.7 at 15 minutes (P < .001), with improvement sustained for more than 6 hours. Chest radiographs were blindly scored from 0 (normal) to 5 (severe opacification), and these improved with marginal significance after initial surfactant treatment (from 2.9 ± 0.2 to 2.5 ± 0.2, P = .05). Eight patients subsequently met retreatment criteria (Fio2 > 0.5 and MAP > 7 cm H2O) and received a second surfactant dose, with a/A ratio rising from 0.124 ± 0.02 before treatment to 0.26 ± 0.07 after 45 minutes (P = .03) and remaining improved for more than 4 hours; the oxygenation index was also significantly improved over similar times by the second surfactant dose. Six patients received a third surfactant dose, with no increase in a/A ratio and a less prominent improvement in oxygenation index. There were no significant improvements in oxygenation in the three patients who received a fourth surfactant dose. Of the 14 patients treated, none died, required extracorporeal membrane oxygenation, had tension pneumothorax after study entry, required oxygen supplementation for more than 14 days, or required oxygen supplementation at discharge. These findings suggest that surfactant supplementation may provide therapeutic benefits for newborns with respiratory failure due to pneumonia or meconium aspiration and that expanded controlled trials of this therapy are indicated.

Martinez FD: Sudden infant death syndrome and small airway occlusion: facts and a hypothesis. Pediatrics 1991; 87:190-198.

Respiratory failure is almost certainly the cause of death in the majority of cases of sudden infant death syndrome (SIDS), but the mechanisms leading to it have not been elucidated. SIDS shares many environmental and socioeconomic risk factors with severe forms of bronchiolitis, and the age distribution of incident cases is similar. Present knowledge of lung and airway development during infancy, determinants of peripheral airway patency, changes in lung surface activity in infants with SIDS, and fluid film dynamics in small airways are reviewed. It is hypothesized that many cases of SIDS may be due to a final episode of progressive peripheral bronchial occlusion in infants with preceding critically diminished conductance of the smaller airways.

Bandini LG, Schoeller DA, Fukagawa NK, Wykes LJ, Dietz WH: Body composition and energy expenditure in adolescents with cerebral palsy or myelodysplasia. Pediatr Res 1991; 29:70-77.

We measured body composition, resting metabolic rate (RMR), and total energy expenditure (TEE) in a group of adolescents with cerebral palsy (CP) and myelodysplasia (M) aged 13- to 20-yr-old using indirect calorimetry and the doubly labeled water method. Fat-free mass (FFM), RMR, and TEE were significantly lower in both the CP and M groups than in controls. Although energy requirements were decreased in both groups, the relationships between FFM and body weight differed. FFM and body weight were significantly correlated with RMR only in the M group. These data suggest that the type of paralysis in a handicapped population may affect resting energy expenditure.
Sullivan KJ, Durand M, Chang HK: A forced perturbation method of assessing pulmonary mechanical function in intubated infants. *Pediatr Res* 1991; 29:82-88.

Short pulses in airway pressure were used to assess the pulmonary mechanical function of nine infants suffering acute respiratory distress syndrome or bronchopulmonary dysplasia. All patients were intubated, spontaneously breathing, and mechanically ventilated at the time they were examined. The endotracheal tube was disconnected from the ventilator and connected to a mechanical oscillator that produced brief pulses in airway pressure at a rate of two pulses/s. These pulses were applied to the infants' airway for 20–30 s, at which time the infant was replaced on the ventilator. The mean airway pressure during the procedure was maintained at the level of the positive end expiratory pressure that was set on the ventilator. Two classes of patients were identified from the pulse response primarily by the presence or absence of a local resonance in the impedance spectra. Similar results were obtained in five other patients who were examined with zero mean airway pressure, suggesting that the pulse response is little influenced by changes in mean lung volume or total lung compliance. Patient classification appeared related to the duration of ventilation therapy and the transition from one class to another was consistent with the development of high peripheral airway resistance and significant volume shunting in the central airways. These results suggest that brief pulses in airway pressure can be used to detect changes in the pulmonary mechanical function of preterm infants that result from long-term ventilation therapy.

Babb TG, Viggiano R, Hurley B, Staats B, Rodarte JR: Effect of mild-to-moderate airflow limitation on exercise capacity. *J Appl Physiol* 1991; 70:223–230.

To determine the effect of mild-to-moderate airflow limitation on exercise tolerance and end-expiratory lung volume (EELV), we studied 9 control subjects with normal pulmonary function [forced expired volume in 1 s (FEV₁) 105% pred; % of forced vital capacity expired in 1 s (FEV₁/FVC%) 81] and 12 patients with mild-to-moderate airflow limitation (FEV₁ 72% pred; FEV₁/FVC% 58) during progressive cycle ergometry. Maximal exercise capacity was reduced in patients [69% of pred maximal O₂ uptake (Vo₂max) compared with controls (104% pred Vo₂max, P < 0.01); however, maximal expired minute ventilation-to-maximum voluntary ventilation ratio and maximal heart rate were not significantly different between controls and patients. Overall, there was a close relationship between Vo₂max and FEV₁ (r² = 0.62). Resting EELV was similar between controls and patients [53% of total lung capacity (TLC)], but at maximal exercise the controls decreased EELV to 45% of TLC (P < 0.01), whereas the patients increased EELV to 58% of TLC (P < 0.05). Overall, EELV was significantly correlated to both Vo₂max (r = −0.71, P < 0.001) and FEV₁ (r = −0.68, P < 0.001). This relationship suggests a ventilatory influence on exercise capacity; however, the increased EELV and associated pleural pressures could influence cardiovascular function during exercise. We suggest that the increase in EELV should be considered a response reflective of the effect of airflow limitation on the ventilatory response to exercise.

Sorkness R, Lemanske RF Jr, Castleman WL: Persistent airway hyperresponsiveness after neonatal viral bronchiolitis in rats. *J Appl Physiol* 1991; 70:375–383.

Viral bronchiolitis in human infants has been associated with permanent changes in small airways and gas exchange and an increased incidence of hyperresponsive airways later in life. Respiratory infection by Sendai virus in neonatal rats also has been reported to cause permanent changes in lung morphology and increased numbers of bronchiolar mast cells and eosinophils. We evaluated pulmonary mechanics, gas exchange, and airway responsiveness in rats at 7 and 13–16 wk after neonatal Sendai virus infection. Rats from the virus group had lower arterial P0₂ and increased total lung resistance compared with controls. There were no significant differences between groups for arterial P0₂, dynamic lung compliance, quasi-static respiratory system compliance, or vital capacity. Rats from the infected group were significantly more sensitive to aerosolized methacholine than were controls, although both virus and control groups became less sensitive with age. We conclude that neonatal Sendai virus infection in rats results in persistent alterations in lung function and airway responsiveness. This phenomenon may be valuable for the study of the relationships among airway inflammation, lung morphology, and airway hyperresponsiveness, and it may be relevant to human airway disease.

Rigatto H, Kwiatkowski KA, Hasan SV, Cates DB: The ventilatory response to endogenous CO₂ in preterm infants. *Am Rev Respir Dis* 1991; 143:101–104.

The measurement of the ventilatory response to inhaled CO₂ is unphysiologic because the CO₂ that normally stimulates breathing is endogenous (tissue or venous CO₂). We took advantage of the spontaneous changes in alveolar P0₂ and ventilation occurring in preterm infants during periodic breathing to calculate the ventilatory response to endogenous CO₂. This response was obtained in 20 infants and compared with those obtained using the more conventional methods of steady-state inhalation of CO₂ (12 infants) and rebreathing of CO₂ (11 infants); it was also compared with a transient change in alveolar CO₂ obtained by inhalation of 7% CO₂ in air for 10 s (CO₂ "bolus"; 11 infants). All groups of infants had similar birth weight and gestational ages. To calculate the response to endogenous CO₂, ΔPACO₂ was measured as the difference between lowest and highest PACO₂ and ΔVe was the difference between the corresponding instantaneous ventilation. To adjust for circulation time, values for PACO₂ were made lowest for the last breath before apnea and highest for the first breath after apnea. The coefficient of variation of the method was 8%. The slope of the ventilatory response to endogenous CO₂ was 0.067 ± 0.009 (mean ± SE) L·min⁻¹·kg⁻¹·mm Hg PACO₂⁻¹, a value greater than that using steady-state and rebreathing methods (0.038 ± 0.004 and 0.040 ± 0.006 L·min⁻¹·kg⁻¹·mm Hg PACO₂⁻¹), respectively. But similar to that of infants inhaling a CO₂ "bolus" (0.051 ± 0.009 L·min⁻¹·kg⁻¹·mm Hg PACO₂⁻¹). We suggest that the ventilatory response to endogenous CO₂ is a more physiologic approach to test the responsiveness of the respiratory system than the more conventional methods using inhaled CO₂. It is much easier to perform.

Bel EH, Timmers MC, Zwiersman AH, Dijkman JJ, Sterk PJ: The effect of inhaled corticosteroids on the maximal degree of airway narrowing to methacholine in asthmatic subjects. *Am Rev Respir Dis* 1991; 143:109–113.

Airway hyperresponsiveness in asthma is characterized by an increase in sensitivity and in maximal response to airway-narrowing stimuli. Long-term therapy with inhaled corticosteroids is known to reduce airway hypersensitivity in asthmatic patients. To investigate whether these drugs also reduce the maximal degree of airway narrowing we studied the effects of inhaled budesonide on the maximal response plateau of the dose-response curve to methacholine in mildly asthmatic patients in whom a raised plateau could be measured. Sixteen atopic patients with mild asthma were placed randomly into two parallel treatment groups to receive double-blindly either budesonide (400 µg twice daily) or placebo, inhaled via a Turbuhaler®, for 4 wk. Before treatment, after 2 and 4 wk of treatment, and after 2 and 4 wk of wash-out, complete dose-response curves to methacholine were obtained using a standardized 2-min tidal breathing method. The response was measured by FEV₁, expressed in % fall from baseline. A plateau on the log dose-response curve was considered if three or more data points fell within a 5% response range. The maximal response was obtained by averaging the values on the plateau (MFEV₁), and the sensitivity was calculated from the provocative concentration of methacholine, causing a 20% fall in FEV₁ (PC₂₀). After 4 wk of budesonide treatment, mean MFEV₁ decreased from 41.6 to 33.7% fall (p = 0.0004). The changes in MFEV₁ were significantly different between placebo and budesonide (p = 0.03). The geometric mean PC₂₀ increased from 3.4 to 6.3 mg/ml (p = 0.02), but the changes in PC₂₀ were not different between the two groups (p = 0.23). We conclude that budesonide limits the increased maximal airway narrowing in asthmatic patients. The dose-response curve to methacholine was obtained using a standardized 2-min tidal breathing method. The response was measured by FEV₁, expressed as % fall from baseline. A plateau on the log dose-response curve was considered if three or more data points fell within a 5% response range. The maximal response was obtained by averaging the values on the plateau (MFEV₁), and the sensitivity was calculated from the provocative concentration of methacholine, causing a 20% fall in FEV₁ (PC₂₀). After 4 wk of budesonide treatment, mean MFEV₁ decreased from 41.6 to 33.7% fall (p = 0.0004). The changes in MFEV₁ were significantly different between placebo and budesonide (p = 0.03). The geometric mean PC₂₀ increased from 3.4 to 6.3 mg/ml (p = 0.02), but the changes in PC₂₀ were not different between the two groups (p = 0.23). We conclude that budesonide limits the increased maximal airway narrowing in asthmatic patients.
Saetta M, Di Stefano A, Rosina C, Thiene G, Fabbri LM: Quantitative structural analysis of peripheral airways and arteries in sudden fatal asthma. *Am Rev Respir Dis* 1991; 143:138-143.

The peripheral airways and the adjacent muscular pulmonary arteries were studied by morphometric methods in the autopsy lungs of six asthmatic subjects who died suddenly during an asthma attack, and they were compared with those of six control subjects who died of other causes and had no history of respiratory diseases. Bronchioles of asthmatic subjects had an increased amount of luminal occlusion (p < 0.01), smooth muscle thickness (p < 0.001), and inflammatory infiltrate (p < 0.001), and both mononuclear cells and eosinophils contributed to this increased inflammation. The muscular pulmonary arteries adjacent to occluded and inflamed bronchioles did not have the morphologic features of chronic hypoxia, as shown by the normal medial and intimal thickness, but they had an important inflammatory process in their walls that was particularly marked at sites adjacent to airways. Although the functional significance of these findings is unknown, they may be responsible in part for the gas exchange abnormalities observed in acute severe asthma.

Ruffin RE, Latimer KM, Schembri DA: Longitudinal study of near fatal asthma. *Chest* 1991; 99:77-83.

The effect of careful follow-up and treatment modification for 45 patients with an admission for NFA has been studied. In 24 of 45, inciting events were recognized. BDP was used by 14 patients pre-NFA. In the mean follow-up of 863 days, there have been no deaths and seven patients have been readmitted with asthma. Six of the 45 patients have attained normal FEV1 and PC25. Blunted perception of breathlessness, change in VAS ratio/change in FEV1, was found when first measured, but normalized to be no different than that of other asthmatic subjects as airway responsive-ness became milder. The CO2 ventilatory response did not differentiate individual NFA patients from non-NFA asthmatic or normal subjects. Comparison of the NFA cohort with the 1985 asthma admission cohort showed that an asthma admission within the last five years was a risk factor for a NFA episode.

Baydur A: Respiratory muscle strength and control of ventilation in patients with neuromuscular disease. *Chest* 1991; 99:330-338.

To assess the relationship between respiratory mechanics and muscle strength and control of ventilation in patients with neuromuscular disease (NMD), we compared Pmax and Pmum at RV, FRC and TLC, total respiratory elastance (Ers) with VT, Ti, TV, Ve, V/TV, TV/VT, P:0.1, and P:0.1(Vr/Ti) effective impedance in 21 patients with NMD and 21 healthy control (C) subjects, in seated position breathing room air. Ers in NMD patients was 39 percent higher than in the C subjects. While Ti, TV, and VT in NMD were approximately half the corresponding C values, P:0.1 was 66 percent greater than in the C subjects (both p < 0.001). NMD Pmax and Pmum ranged from 37 to 52 percent of corresponding C values, respecti-vely. Despite significant respiratory muscle weakness, only 7 of 16 patients demonstrated a PacO2 > 45 mm Hg. Ventilatory output in NMD was modulated by respiratory mechanics as indicated by the increased P:0.1. In spite of muscle weakness, central drive in patients with NMD is not decreased, and in fact, is often increased. Ve is not an accurate measure of central drive because of abnormal intrinsic respiratory mechanics and the effects of conscious responses or reflexes.

McColey SA, Rosenstein BJ, Cutting GR: Differences in expression of cystic fibrosis in blacks and whites. *Am J Dis Child* 1991; 145:94-97.

The recent identification of the cystic fibrosis (CF) gene confirms that genetic heterogeneity occurs in CF. A three-base-pair deletion in exon 10 resulting in a loss of the phenylalanine residue at amino acid position 508 of the gene product, termed the CF conductance regulator protein, accounts for 70% of cases of CF in white subjects. However, this gene defect occurs in only 37% of affected blacks. Analysis of CF genes from American blacks has revealed a number of mutations, most of which are unique to that population. We therefore searched for potential differences in expression of CF between 24 black and 48 white patients with CF matched for birth date and gender. Black patients more frequently presented with only respiratory symptoms (38% vs 10%). Black patients had fewer hospitalizations for pulmonary exacerbations (2 vs 6.9), a better mean forced vital capacity (77% vs 62% of predicted), and higher chest roentgenogram scores (18.2 vs 14.4) than white patients. Complication rates were similar except for a higher incidence of hypotensive dehydra-tion (21% vs 2%) and peptic ulcer disease (13% vs 0%) in blacks. Survival time appeared to be longer in blacks, but the difference was not statistically significant. We conclude that phenotypic differences exist between black and white patients with CF, which may be due to the genetic heterogeneity between these two populations.

Hennes HM, Lee MB, Rimm AA, Shapiro DL: Surfactant replacement therapy in respiratory distress syndrome. Meta-analysis of clinical trials of single-dose surfactant extracts. *Am J Dis Child* 1991; 145:102-104.

Replacement therapy with surfactant extracts in premature infants with respiratory distress syndrome has been evaluated in several clinical trials. The results of individual trials do not provide conclusive evidence that administration of a single dose of surfactant improves morbidity or mortality. Meta-analysis is a statistical method to combine the results of such clinical trials, and combined analysis provides a means to overcome the problem of not being able to detect significant small differences in individual trials due to these small sample sizes. Seven clinical trials (277 patients treated with nonhuman surfactant extract and 263 controls) met the criteria for analysis; five outcome measurements (mortality, patent ductus arteriosus, pneumothorax, intraventricular hemorrhage, and bronchopul-monary dysplasia) were selected to estimate the treatment effect. The meta-analysis showed that a single dose of surfactant administered before the first breath or within 15 hours of birth significantly decreased the mortality rate (95% confidence interval = -0.19 to -0.03) and the risk of developing pneumothorax (95% confidence interval = -0.28 to -0.14) in infants with respiratory distress syndrome. Further clinical trials are needed to evaluate other aspects of surfactant replacement therapy in premature infants because inconsistent results were observed among the seven analyzed studies.

Wilson DC, McClure G, Halliday HL, Reid MMCC, Dodge JA: Nutrition and bronchopulmonary dysplasia. *Arch Dis Child* 1991; 66:37-38.

Twenty two babies who developed bronchopulmonary dysplasia were compared with 22 babies matched for gestational age who did not. Those with bronchopulmonary dysplasia weighed less at birth and had lower energy intakes from day 7 to day 56. Undernutrition before and after birth is a major problem in babies who develop bronchopulmonary dysplasia.

Potter PC, Klein M, Weinberg EG: Hydration in severe acute asthma. *Arch Dis Child* 1991; 66:124-129.

Twenty children were studied during severe attacks of acute asthma to find out how dehydrated they were on admission to hospital. Mean body weight on admission was 97.8% of their reference stable weight seven to 10 days after the attack and in only three children was it less than 95% of the stable weight. Bedside assessment of dehydration was unreliable. The mean packed cell volume was significantly higher on admission than 7-10 days later (0.44 compared with 0.42, difference 0.02 SE 0.01). Serum sodium and potassium concentrations and osmolality on admission were within normal ranges. The degree of dehydration correlated best with a fall in blood pH. There was no association between the degree of dehydration and the recovery of the peak expiratory flow rate during the first 24 hours or thereafter. We conclude that mild dehydration is common in severe acute childhood asthma. Fluid given at a rate of 50 ml/kg/24 hours was safe and appropriate for these children.

Mertsola J, Ziegler T, Ruuskanen O, Vanto T, Kuivikko A, Halonen P: Recurrent wheezy bronchitis and viral respiratory infections. *Arch Dis Child* 1991; 66:216-219.

Fifty four patients aged from 1 to 6 years who had had recurrent attacks of wheezy bronchitis were prospectively followed up for three months to find
out if there was an association between different viral respiratory infections and episodes of wheezing. Of the 115 episodes of upper or lower respiratory tract symptoms, virus or Mycoplasma pneumoniae infections were diagnosed in 52 (45%). Thirty four of these (65%) were caused by coronaviruses or rhinoviruses. The patients had an average of 2.1 episodes of respiratory tract symptoms the total mean (SD) duration of which was 30 (2) days of the 92 days that followed. Wheezing occurred during 76 (66%) of the 115 episodes and during a third of these the patient was admitted to hospital because of severe dyspnoea. Wheezing started a mean (SD) of 43 (7) hours after the first symptoms of respiratory infection and persisted for 3.8 (4.2) days in patients in whom virus infection was diagnosed. The incidence of wheezing was not associated with IgE mediated atopy, with positive virological tests, or with fever during virus infection, but was associated with parental smoking and more than one sibling.

Selected Reviews and Statements

Bar-Maor JA, Lammd M: Experience and reason—briefly recorded. Pediatrics 1991; 87:113–114.

Rosenstein BJ, Eigen H: Special article: risks of alternate-day prednisone in patients with cystic fibrosis. Pediatrics 1991; 87:245–246.