

# Current Trends in Neonatal and Pediatric Respiratory Care: Conference Summary

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## Introduction

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### Summary

**A summary of the 2-day Journal Conference on Current Trends in Neonatal and Pediatric Respiratory Care is provided. Topics included: diagnosis and management of common respiratory disorders of infants and children such as asthma, respiratory syncytial virus bronchiolitis, and cystic fibrosis; and common pediatric respiratory emergencies such as croup, epiglottitis, and inhalation injuries. Also discussed were developments in diagnostic and therapeutic modalities, including pulmonary function testing and pulse oximetry. Evidence-based strategies for the resuscitation of critically ill newborns and subsequent ventilator management strategies were presented. Several faculty members discussed controversies regarding mechanical ventilation and extracorporeal membrane oxygenation for treatment of acute respiratory distress syndrome and other causes of respiratory failure in children and infants. Key words: pediatric, neonatal, respiratory, pulmonary, asthma, bronchiolitis, mechanical ventilation, pulse oximetry, croup, epiglottitis, pulmonary function testing, PFT, cystic fibrosis, acute respiratory distress syndrome, ARDS. [Respir Care 2003;48(4):459–464. © 2003 Daedalus Enterprises]**

## Introduction

The Journal Conference on Current Trends in Neonatal and Pediatric Respiratory Care, although diverse in topics, contained one unifying theme: more data are clearly needed.

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Carolyn M Kercksmar MD presented a version of this report at the 31st RESPIRATORY CARE Journal Conference, Current Trends in Neonatal and Pediatric Respiratory Care, August 16–18, 2002, in Keystone, Colorado.

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Although this could be the battle cry for many topics in modern medicine, the key issue highlighted again and again was the paucity of studies on pediatric patients. Extending observations made on adults is not always advisable, but is frequently done, and is often the only way to practice evidence-based medicine in pediatrics. Any medical professional who deals primarily with pediatric patients knows that children are not small adults, yet too often we are forced to extrapolate care practices developed for adults to treat children and even neonates. In fact, only 2 other RESPIRATORY CARE Journal Conferences over the past 20 years have dealt specifically with infants and children. Conference faculty did an outstanding job of reviewing the available pediatric data on a wide variety of topics, conducting lively and scholarly discussions, and offering best practice guidelines. It is my privilege to summarize these excellent presentations.

### Common Pediatric Respiratory Disorders

Asthma remains the single most common chronic disorder of childhood, affecting over 10% of children. Despite great advances in understanding the pathophysiology of asthma and the development of effective medications for controlling and treating symptoms, substantial controversy remains as to the optimal management of acute and chronic asthma. The management of acute asthma is in general a far easier task than controlling chronic asthma. Patients who present to the emergency department or hospital are a captive population, and there are relatively few medications for treatment of status asthmaticus. The use of well-designed care paths can remove care practices that add cost but do not add benefit. Tracking the application of the care path and the outcomes from its use can provide powerful data for designing best practice care. Although there are relatively few studies on pediatric patients, assessment-driven care paths with well defined treatment options and discharge criteria appear to be highly effective in improving quality of care, decreasing length of stay, and decreasing cost of care.

The management of chronic asthma is often stymied by a number of factors, including inter-individual variability of response to medications, environmental exposures, and difficulty with adherence. Fortunately, most asthmatics can remain nearly symptom-free with the use of low-dose inhaled corticosteroids (ICS); however, a number of patients will require another controller medication in order to avoid frequent symptoms and maintain normal pulmonary function. Although numerous studies performed with adult asthmatics support the addition of a long-acting  $\beta$  agonist to the low-dose ICS regimen, there are very limited data from children. In adults the combination of low-dose ICS and a long-acting  $\beta$  agonist controls asthma as well as or better than a higher dose of steroids. However, the very limited data from pediatric patients suggest that that additive effect might not occur in children. Other treatment options exist and can be used to keep the ICS dose low, an important factor in the management of pediatric asthma. This is clearly a subject about which more data from pediatric patients are critical.

If asthma is the most common chronic disease of childhood, then bronchiolitis and respiratory syncytial virus are the most common serious acute illnesses in infants and young children. Infection is ubiquitous, and all children have serologic evidence of infection by 3–5 years of age; those under age 2 years are at the greatest risk of developing serious lower respiratory tract infection. In infants, children, and adults, symptoms include rhinitis, cough, and fever, but infants and children typically develop wheezing. Viral infection of the airways causes a profound inflammatory response, with vascular engorgement in the airway wall, cellular infiltration, and mucus hypersecre-

tion. Ventilation-perfusion mismatch ensues and hypoxemia develops. Between 1 and 3% of infants infected with respiratory syncytial virus require hospitalization, and of these up to 3% die. Craig Black<sup>1</sup> noted that despite aggressive research there is still no effective cure, preventive vaccine, or effective treatment. Care remains largely supportive, and consists of adequate hydration, supplemental oxygen, nasal suctioning, and, in some cases, administration of an aerosolized bronchodilator. In general, epinephrine has been more effective than selective  $\beta$  agonists. There are ongoing efforts at developing an effective vaccine, but much more study is needed. The state of the art for respiratory syncytial virus bronchiolitis can be summarized with the word “no”: we currently have no cure, no effective preventative measure, no vaccine, no effective treatments, and not even consensus on how to apply supportive care. I am always humbled by how easily we are defeated by invisible agents of infectious disease.

Jeff Wagener<sup>2</sup> reminded us that, unlike asthma and bronchiolitis, cystic fibrosis (CF) is essentially an “orphan disease,” affecting about 30,000 individuals in the United States. However, the consequences of the illness are enormous, and essentially all affected individuals have a shortened life span. Major advances have been made in understanding the genetics and cell biology of CF, but a cure or definitive therapy is not at hand. Since nearly all CF patients die from respiratory causes, major emphasis is on treating the respiratory signs and symptoms that lead to progressive, severe chronic obstructive pulmonary disease. In order to control the airway disease, multiple modalities are used to remove excess mucus, decrease inflammation, and control chronic infection. A variety of inhalable medications can help accomplish these goals. Long-acting  $\beta$  agonists are probably superior to short-acting  $\beta$  agonists in improving pulmonary function. The mucolytic agent dornase alfa can thin airway mucus by cleaving the deoxyribonucleic acid released from the enormous number of neutrophils contained in the airways, and by thinning the mucus, can improve mucus clearance and preserve pulmonary function. A variety of airway clearance techniques can help remove airway secretions. Although the identities of the CF genes are known, a cure is not yet in hand. The research needs in this area are enormous. The role of the respiratory therapist is substantial in the treatment of CF, as the majority of treatment is directed at preventing loss of pulmonary function, maintaining respiratory health, and treating pulmonary exacerbations. New therapies being developed are targeting more effective and potent anti-inflammatory drugs, agents that restore normal electrolyte transport across the airway epithelium, and, ultimately, gene therapy to correct the genetic defect early in life in order to obliterate CF pulmonary disease entirely. Oh, to be put out of a job!

Alex Rotta<sup>3</sup> presented an excellent summary of the most common causes of respiratory emergencies in children. These pulmonary emergencies always engender fear and anxiety in both parents and health care providers. Although illness that compromises the airway is often an emergency in a patient of any age, children have unique characteristics (a relatively large head, small subglottic space encircled by the cricoid cartilage, and loosely attached connective tissue where edema easily accumulates) that put them at special risk in such situations. In dealing with airway obstruction in children, the risks of rapid worsening and progression to respiratory arrest must be understood and recognized by all medical personnel. The signs of respiratory distress and impending respiratory failure may be subtle and should be familiar to health care providers.

Croup, like bronchiolitis, remains an extremely common infectious process of the upper airway. The vast majority of children with infectious croup are treated successfully as out-patients; hospitalization rates range from 1 to 30%, with approximately 2% of those patients requiring intubation. The use of systemic or even high-dose ICS for treatment of croup has certainly reduced the severity of most episodes and shortened the length of hospital stay.

Although epiglottitis has almost been relegated to the medical history books in populations immunized for *Haemophilus influenzae*, sporadic cases do occur, and not all children are immunized. The classic presentation of the disease (acute onset, little prodrome, high fever, toxic appearance, drooling, and tripod posture) rarely occurs. The child with atypical croup (high fever, muffled voice, minimal cough) should be evaluated for epiglottitis, retropharyngeal abscess, or parapharyngeal abscess, the latter two of which are more common entities that may be the "new epiglottitis" in the United States. Bacterial tracheitis is another illness that can mimic epiglottitis, but it, too, is often over-diagnosed.

Acute injury to the airway usually results from aspiration of a foreign body or inhalation of toxic fumes. Toddlers are the primary risk group for foreign-body aspiration (mobile, fearless explorers who are fond of using their mouths to temporarily store food and non-food items while on the move). The esophagus as well as the airway can sequester a foreign body capable of compromising the airway in a more subtle but serious fashion. Suspicion is key as history may be vague or absent (1% of children without history), symptoms can be subtle and mimic other conditions (cough and wheeze suggestive of infection or asthma), radiographs negative (partial obstruction with negative radiograph or non-radiopaque foreign body). As with many aspects of pediatric care, prevention is key. Avoiding accidents by child-proofing the household, careful observation, supervised meal times, and universal use of smoke alarms can prevent most airway injury.

## Monitoring and Diagnostics

Making informed decisions about patient management hinges on the availability of solid data, and the paucity of data from studies of infants and children often hinders the development of best practices for pediatric patients. Some of the difficulty in conducting studies of children is due to the lack of means to obtain objective data and measure outcomes. In recent years new means of measuring pulmonary function in infants and young children have become available, and refinements in existing technology, such as pulse oximetry and capnography, have also occurred.

Stephanie Davis<sup>4</sup> reviewed the advances made in infant pulmonary function testing and the recently reported successes in routine spirometry with toddlers. Capitalizing on the Hering-Breuer reflex, sedated (conscious, using chloral hydrate) infants can "perform" adult-type pulmonary function tests using the raised-volume, rapid-thoracic-compression technique and an infant body box. The infant wears a face mask that covers the nose and mouth and is lightly sealed in place with non-toxic putty. Measures are made during tidal breathing (tidal volume, lung volumes, pulmonary compliance), using standard plethysmographic techniques. For spirometry, at end-expiration the infant receives one or more inflated breaths (to 30 cm H<sub>2</sub>O) until a brief respiratory pause is noted. At end-inspiration an inflatable bladder (secured around the infant's chest with a jacket) inflates to a preset pressure and causes a forced expiratory maneuver. Reproducible, adult-type measures of forced expiratory volumes (forced expiratory volume in the first 0.5 s [FEV<sub>0.5</sub>] or the first 0.75 s [FEV<sub>0.75</sub>], and forced expiratory flow during the middle half of the forced vital capacity [FEF<sub>25-75</sub>]) and lung volumes can be obtained and response to bronchodilator measured. Prediction equations for normative standard values have been reported, thus making feasible comparative measures among subjects for both clinical use and research.

Another age group that poses particular challenges to obtaining objective measures of pulmonary function are those in the 2–5-year-old range, who are too large for infant pulmonary function testing but too young to perform routine spirometry. More experience in this age group has been obtained using forced oscillation technique to obtain measures of airway resistance or reactance. Though these measures have considerable inter-individual variability, they are useful for following intra-individual trends, response to treatment, or inhalation challenge testing. Pre-school-age children appear to be able to perform routine spirometry with fairly minimal, albeit expert and patient coaching. The group led by Howard Eigen in Indianapolis recently published 2 reports containing pulmonary function testing data on several hundred normal children<sup>5</sup> and CF patients.<sup>6</sup> In their hands the technique appears valid

and reproducible; hopefully their expertise will be replicable by other groups. Lastly, other non-spirometry, non-invasive, objective measures of pulmonary function useful in infants and young children are being developed. Measurement of the nitric oxide, carbon monoxide, and inflammatory mediators (leukotrienes, pH) contained in exhaled breath may provide insight into the inflammatory milieu of the airways.

Devices to noninvasively measure oxyhemoglobin saturation and exhaled carbon dioxide have been available for some time. Advances in technology have substantially increased the reliability and quantity of data obtained in a variety of patient scenarios. In contrast to the theme of needing more data, the questions posed by John Salyer,<sup>7</sup> concerned what to do with these large data sets and how to interpret the results. Are patient outcomes different because we can continuously monitor oxygenation and exhaled carbon dioxide? And what is the most useful format in which to provide data to managing health care personnel? Several examples were provided. Perhaps one of the best roles for capnography is determination of endotracheal tube placement during intubation for operative anesthesia and anesthesia monitoring. Pulse oximetry has been improved by Masimo signal extraction technology (SET) which compensates for motion artifact and produces a more accurate and reliable reading. The ready availability of fairly inexpensive oximeters has resulted in the pulse oximetry measure becoming the "fifth vital sign" as well as being continuously monitored in a variety of clinical situations. Unfortunately, the availability of these data does not always result in improved clinical outcomes, either because the data are not used appropriately or because they do not provide any more useful information than standard clinical assessment. A systematic approach is warranted for evaluating the usefulness of pulse oximetry measurements in a variety of clinical settings, such as pre-operative and postoperative monitoring.

### **Critical Respiratory Distress in Neonates and Children**

Neonatology espouses several preventive strategies, including preventing prematurity and preventing adverse consequences associated with the birthing process. Unfortunately, prematurity is still a major problem, but more informed guidelines for directing neonatal resuscitation have been established. Tom Wiswell<sup>8</sup> reviewed the recently released, evidence-based guidelines for many aspects of neonatal resuscitation, but cautioned that substantial evidence is lacking for most of the recommendations. New practices include not suctioning the airway in the case of meconium aspiration, unless the infant is not vigorous, use of 100% oxygen and not room air or other oxygen concentrations for resuscitation, and volume ex-

pansion with normal saline or Ringers lactate but not albumin. Ethical issues should also be considered; for instance, for whom should resuscitation not be instituted (certain fatal genetic conditions, extreme prematurity) and when should efforts be discontinued? The paucity of data on the short-term and long-term morbidity and mortality of neonatal resuscitation efforts was noted.

Ric Rodriguez discussed the current state of the art of neonatal respiratory distress syndrome (RDS). He reminded us that extremely small, immature babies are now surviving and that the incidence of RDS is inversely related to gestational age and birth weight. The pathophysiology of RDS is related to surfactant deficiency and structural immaturity of the airways and lungs and is complicated by respiratory and metabolic acidosis, epithelial and endothelial injury, and the release of inflammatory mediators and cytokines. Administration of exogenous surfactant has improved survival and reduced some complications (eg, pneumothorax) but unfortunately has not reduced the rate of bronchopulmonary dysplasia (BPD) development. In fact we are experiencing a BPD epidemic. Ventilator strategies may in part be responsible for the prevalence of BPD, but data supporting this notion are incomplete. Optimal ventilator strategies for managing RDS are not well characterized. The permissive hypercapnia ventilation strategy popular for ventilating older children is not well studied with neonates. There is probably little difference in the major outcomes of developing BPD or dying, but risk of intestinal perforation may be higher. There appears to be a resurgence in the popularity of continuous positive airway pressure (CPAP) and some data that CPAP is associated with less need for mechanical ventilation, shorter duration of mechanical ventilation for those babies requiring intubation, and a lower incidence of BPD in infants with RDS. There is also interest in using inhaled nitric oxide to treat RDS, but this is still quite experimental. Data thus far suggest that inhaled nitric oxide, an expensive therapy, does not reduce mortality, but it may decrease the need for extracorporeal membrane oxygenation and decrease the incidence of BPD.

Steven Donn<sup>9</sup> discussed in great depth the use of non-invasive and invasive mechanical ventilation of neonates, the goals of which are to produce acceptable gas exchange, decrease work of breathing, assure patient comfort, and minimize the risk of lung injury. Echoing Ric Rodriguez's comments,<sup>10</sup> Steven indicated that the "new BPD" occurs in extremely small premature infants who have very different ventilator needs than seen in the previous decade. These extremely premature babies have substantially less alveolarization and fibrosis, but continue to have inflammatory changes; BPD results from a combination of barotrauma, volutrauma, and biotrauma. Protective strategies for ventilator management should be paramount, but again the data set is incomplete regarding selection of the best

options. Outcome measures need to focus on both short-term and long-term morbidity. In spite of the aforementioned revival in the use of CPAP, there have been no randomized, controlled trials to examine its efficacy or even safety in the era of surfactant replacement therapy. Though the uncontrolled experience at some centers suggests that early use of CPAP decreases the need for mechanical ventilation and perhaps decreases BPD, the impact on neurologic outcomes is uncertain. In contrast to the old modality of CPAP there are numerous new mechanical ventilation strategies that, in theory, could more effectively improve gas exchange, but data on comparative efficacy with respect to important clinical outcomes await further study.

The use of specialty gases, including nitric oxide, was discussed by Tim Myers.<sup>11</sup> In addition to its use in treating RDS, inhaled nitric oxide could have salutary effects on other airway and pulmonary vascular diseases by virtue of its actions as a vascular smooth muscle relaxant and anti-inflammatory. Unfortunately, the results with some conditions, such as persistent pulmonary hypertension, have been mixed. The best results (reduced need for ECMO) are obtained when inhaled nitric oxide is combined with high-frequency oscillatory ventilation (HFOV). Nitric oxide does not appear to be useful for congenital diaphragmatic hernia management.

Helium-oxygen mixture (heliox) is another specialty gas that can provide a bridge therapy by decreasing the work of breathing in the presence of air flow obstruction. Best results occur in children with croup and post-extubation stridor, as might be expected given the highly turbulent flow seen in those conditions. Results of heliox use in asthma and bronchiolitis have been less impressive and consistent. Also, the "specialty mixing" of some not-so-special gases (oxygen and carbon dioxide) might prove useful in the post-operative management of infants following repair of complex cyanotic congenital heart disease. Use of subambient oxygen concentrations can help maintain patency of the ductus arteriosus. Tim described a novel method for safely and effectively delivering such hypoxic gases. The efficacy of such maneuvers remains controversial and needs more study.

Doug Hansell<sup>12</sup> delivered a compelling and impassioned discussion on the uses and efficacy of ECMO. He carefully pointed out that the definition of ECMO is prolonged extracorporeal support for patients with reversible cardiac and/or respiratory disease unresponsive to maximal medical therapy. In addition the selection of patients for whom ECMO is an appropriate therapy is critical: best results are obtained when criteria for use are restricted to patients for whom the managing physician believes the chances of dying are > 80% without a trial of ECMO. Although ECMO is not used in premature infants, based on a report from the United Kingdom,<sup>13</sup> it might be considered the

new gold standard for term neonates suffering acute respiratory failure and who meet the inclusion criteria previously mentioned. Survival rates of 80–94% have been reported for ECMO candidates with conditions such as RDS, persistent pulmonary hypertension of the newborn, and meconium aspiration syndrome. Questions that remain to be answered include refining the inclusion criteria for use of ECMO, particularly in pediatric patients, and determining the costs and benefits of ECMO compared to other therapies.

Drs Anderson<sup>14</sup> and Cheifetz<sup>15</sup> discussed the related topics of acute respiratory distress syndrome (ARDS) and mechanical ventilation in pediatric patients. Once again the themes of effectively managing the patient with severe lung and even multisystem injury and dysfunction were controversial. Mike Anderson reviewed the experience with using several modalities to treat ARDS: lung-protective ventilator strategies, inhaled nitric oxide, surfactant, prone positioning, and ECMO. The simple maneuver of prone positioning may improve oxygenation in these critically ill children. Inhaled nitric oxide has a similar effect at a much greater cost; the improved oxygenation may be short-lived and might not ultimately affect morbidity or mortality. Surfactant may also improve oxygenation and decrease the duration of ventilation and intensive care. Effect on short- and long-term morbidity and survival needs more analysis. The role of protective ventilator strategies was also discussed, with specific reference to the use of HFOV. The study by Arnold et al<sup>16</sup> was cited as supportive of the early institution of HFOV for treatment of ARDS. Patients who received early HFOV had better outcomes than patients who received conventional ventilation or crossed over to HFOV after a trial of conventional ventilation.

Ira Cheifetz also discussed the use of HFOV in pediatric ARDS and made several critical analyses. His interpretation of the Arnold et al data was that the study, as well as his clinical experience, provided substantial evidence that HFOV was superior to conventional ventilation and argued that it should be instituted as regular therapy, not rescue therapy. The point was made that there is currently little about HFOV that is "nonconventional" and that it should be considered essentially standard of care for ARDS.

Ira also clearly reviewed the utility of noninvasive mechanical ventilation in selected groups of pediatric patients, such as those with neuromuscular disorders and chronic respiratory failure. There are few data to help predict which patients might benefit from noninvasive ventilation, and large randomized trials are sorely needed. The process of extubation and weaning strategies was also discussed. There are no widely accepted criteria for weaning and extubation of pediatric patients. In contrast to studies of adults, in which weaning protocols reduced ventilator time, data currently available suggest that there may be no benefit to using a standardized weaning protocol with chil-

dren. Likewise, objective measures to predict successful extubation are lacking. Measuring the physiologic dead space ratio (ratio of dead space to tidal volume) may prove useful and is easily determined with modern computer and capnography technology. However, the literature contains conflicting reports as to the utility of protocols (versus clinical judgment) for assessing readiness for and predicting the success of extubation. The conclusion of Ira's excellent discussion was that high quality, multicenter, randomized, prospective trials on all aspects of pediatric mechanical ventilation are needed in order to provide recommendations for optimal treatment.

### Summary

Although the state of the art of management of neonatal and pediatric respiratory diseases has advanced dramatically over the past decade, much work remains to be done. There have been substantially more studies performed with adults suffering respiratory failure and needing mechanical ventilation than with infants and children. As with many aspects of therapeutics in pediatrics, the clinician is often left with extrapolating adult data to the management of the pediatric patient. Using clinical judgment alone and either ignoring existing data or minimizing the importance of collecting new data is hubristic and dangerous. Children are not small adults, and it is our job as pediatricians to provide our patients with optimal care, designed for them, that will permit them to grow into healthy adults.

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