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An Official American Thoracic Society/European Respiratory Society Workshop Report: Evaluation of Respiratory Mechanics and Function in the Pediatric and Neonatal Intensive Care Units

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Abstract

Ready access to physiologic measures, including respiratory mechanics, lung volumes, and ventilation/perfusion inhomogeneity, could optimize the clinical management of the critically ill pediatric or neonatal patient and minimize lung injury. There are many techniques for measuring respiratory function in infants and children but very limited information on the technical ease and applicability of these tests in the pediatric and neonatal intensive care unit (PICU, NICU) environments. This report summarizes the proceedings of a 2011 American Thoracic Society Workshop critically reviewing techniques available for ventilated and spontaneously breathing infants and children in the ICU. It outlines for each test how readily it is performed at the bedside and how it may impact patient management as well as indicating future areas of potential research collaboration. From expert panel discussions and literature reviews, we conclude that many of the techniques can aid in optimizing respiratory support in the PICU and NICU, quantifying the effect of therapeutic interventions, and guiding ventilator weaning and extubation. Most techniques now have commercially available equipment for the PICU and NICU, and many can generate continuous data points to help with ventilator weaning and other interventions. Technical and validation studies in the PICU and NICU are published for the majority of techniques; some have been used as outcome measures in clinical trials, but few have been assessed specifically for their ability to improve clinical outcomes. Although they show considerable promise, these techniques still require further study in the PICU and NICU together with increased availability of commercial equipment before wider incorporation into daily clinical practice.

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Overview

The American Thoracic Society (ATS) workshop on Evaluation of Respiratory Mechanics and Function in the Pediatric and Neonatal Intensive Care Units was funded by the ATS and was held at the 2011 ATS International Conference meeting in Denver, Colorado, with a follow-on meeting at the 2012 ATS Conference. The workshop was initiated by the joint ATS/European Respiratory Society Working Group on Infant and Young Children Pulmonary Function Testing to address the lack of information on respiratory function techniques available to assist in the management of patients in pediatric and neonatal intensive care units (PICU, NICU).

The principal conclusions are as follows:

- The main clinical issues for which respiratory function measurements can provide useful information to guide management are:
  - assessing the physiologic nature and progression of respiratory disease
  - optimizing respiratory support and minimizing ventilator-associated lung injury
  - assessing the effect of therapeutic interventions (e.g., drugs, physiotherapy)
  - assessing readiness to wean from respiratory support
- The techniques considered currently useful or promising in providing this information are:
  - measurement of respiratory mechanics (compliance and resistance of lung or respiratory system) using both dynamic and passive techniques
  - measurement of forced expiratory flows and volumes using the negative pressure forced deflation technique
  - measurement of respiratory resistance and reactance using the forced oscillation technique (FOT)
  - use of ventilator graphics to provide qualitative visual information (both time-based and XY plots)
  - measurement of carbon dioxide elimination as a function of exhaled volume of gas (volumetric capnography)
  - measurement of lung volumes and ventilation distribution using inert gas washout techniques
  - dynamic assessment of regional ventilation using electrical impedance tomography
  - measurement of tidal volumes, flow parameters, and thoracoabdominal asynchrony at the chest wall (±simultaneous esophageal manometry)
  - assessment of respiratory drive and respiratory muscle strength using occlusion pressures
- All of these techniques are feasible and have been performed in PICU/NICU settings.
  - Suitable commercial equipment is currently available for all techniques except FOT, forced deflation, and occlusion pressures.
  - Adequate training and quality control are essential before any of the techniques are introduced into a PICU or NICU setting.
  - Once equipment is *in situ*, each technique can be performed within approximately 15 minutes on each patient, and some can give continuous real-time data during supported ventilation.
  - Additional time needs to be allowed for equipment setup, to await patient stability, and for calculation/interpretation of results; this will depend on the technique, the child's clinical condition, and the experience of the operator.
  - Risks are minimal, but the following precautions are important:
    - infection control issues must be addressed
    - awareness of increased dead space during some types of measurement
    - disconnection times must be minimized to avoid derecruitment in positive end-expiratory pressure (PEEP)–dependent patients
- There is a wealth of published data on the validity and technical aspects of the various techniques. Most techniques have been used as outcome measures in studies on therapeutic interventions. Empirical data on the ability of these measurements to assist in clinical management of individual patients are scarce: available data are restricted primarily to respiratory mechanics measurements, ventilator graphics, and volumetric capnography.

Introduction

Respiratory disease dominates admissions to both pediatric and neonatal intensive care units (PICU, NICU) to a greater extent than equivalent adult units (1). Nonetheless, the use of respiratory measurement techniques to guide management in children has lagged behind adult intensive care practices. Rapid advances in the development of respiratory function tests applicable to infants and young children have been achieved in recent years.

Since its establishment in 1990, the joint American Thoracic Society/European Respiratory Society (ATS/ERS) Working Group on Infant and Young Children Pulmonary Function Testing has published several statements and guidelines on the use of pediatric respiratory function tests for researchers and clinicians (2–14), but to date these publications have focused on the stable child in the outpatient or ambulatory setting. Discussions within and beyond the Working Group in 2010 to 2011 indicated (*1*) the availability of respiratory measurement techniques potentially applicable in pediatric intensive care unit/neonatal intensive care unit (PICU/NICU), and (*2*) a desire by clinicians to know more about these techniques. These discussions led directly to an ATS-funded project: "Evaluation of respiratory mechanics and function in the pediatric and neonatal intensive care units."

The aim of this Workshop Report document is to identify and concisely review respiratory function tests that show the most promise for the clinical monitoring of vulnerable and critically ill young patients, requiring care in a PICU, NICU, or similar facility. The objectives were to (*1*) review the safety, feasibility, and published data to date on the relevant techniques; (*2*) list possible applications to guide clinical management in the PICU and NICU; and (*3*) identify future directions and research needs. Use of such techniques in the PICU and NICU may benefit patients through enhancing optimization of ventilator management and monitoring the response to therapeutic interventions. In addition, measurements can form a baseline to aid with monitoring evolution of respiratory disease both acutely in the PICU/NICU and at follow up.

Finally, it should be stressed that despite the potential clinical benefit many of these tests may provide, more research is warranted for each technique before any clinical recommendations on specific ages, disease entities, or outcome measures associated with testing. We aim to provide the pediatric and neonatal intensivist with a guide for choosing potential respiratory function tests and information regarding future research areas of interest, specifically bedside evaluations of lung volumes, ventilation inhomogeneity, and respiratory mechanics in ventilated patients.

Methods

This project originated in a Clinical Workshop run at the American Thoracic Society Annual Conference in New Orleans in 2010 (May 18, 2010) entitled "Making the Physiology Work for You: Lung Function Tests in the Pediatric and Neonatal Intensive Care Units." This educational workshop was proposed by the ATS/ERS

Working Group on Infant and Young Children Pulmonary Function Testing and was organized and chaired by S.P.-C. and P.C.S. Formal feedback was sought from the 45 attendees: the responses indicated the need for increased knowledge of the various techniques available and how these might influence clinical practice. Participants expressed a desire to have information regarding the application and interpretation of data from these various techniques. Furthermore, they noted that there was limited published information on the clinical applicability of lung function techniques in the PICU/NICU settings.

Consequently, we submitted an application to the ATS on behalf of the Working Group for a project entitled "Evaluation of respiratory mechanics and function in the pediatric and neonatal intensive care units." P.C.S. and S.P.-C. contacted members of the ATS/ERS Working Group on Infant and Young Children Pulmonary Function Testing to collect opinion on (*1*) techniques to assess respiratory function that have been used in PICU/NICU, and (*2*) relevant experts who could contribute for each technique.

A provisional list of techniques was drawn up, and the identified experts for each technique were invited to a workshop at the ATS Annual Conference in Denver in 2011. The workshop was attended by advisors from the Working Group to give an overview, together with a technical advisor and a librarian from the ATS. Data for the various techniques were presented, and the scope and overall plan of the document was discussed. At the end of the workshop, attendees agreed on the finalized list of techniques to be covered within the document. For each technique, a subgroup of individuals was then tasked with searching the literature for evidence on each of the techniques to address the following issues:

1. Background physiology of the technique
2. Logistics and procedural requirements:
   a. What equipment is needed?/technical specifications
   b. What technical data are gathered/presented/available?
   c. Variability, including interrater/intrarater, repeatability within/between occasions
3. Feasibility
   a. Availability of commercial equipment/approximate costs
   b. How long do measurements take to obtain?
   c. Any risks to patient?/Which patients are suitable/unsuitable?
   d. Ease of interpretation/training required
4. Existing published data
   a. Reference data
   b. Data in disease conditions outside NICU/PICU
   c. Research studies to date in NICU/PICU
5. Clinical Indications based on published data

The ATS/ERS Evaluation of Respiratory Mechanics and Function in the Pediatric and Neonatal Intensive Care Units writing group was created, consisting of working groups for each of the physiologic parameters to be evaluated. Each working group was charged with performing a comprehensive literature search of standardized content for its specific lung function test, including background physiology, procedural requirements, procedural feasibility in a clinical setting, and existing published data with possible clinical indications.

Thorough literature searches were performed on multiple occasions up to finalization of the Workshop Report by the members of the subgroups using the following databases: MEDLINE, PubMed, and EMBASE. Initial searches and topic reviews by the individual subgroup/section authors were often done with the aid of medical librarians at each author's individual academic institution. Studies and reports relevant to the subgroup's assigned physiologic technique were selected, and reference lists of identified studies were further perused for additional relevant studies.

Subsequent follow-on meetings were held at ERS 2011 and ATS 2012, at which each subgroup presented its findings, which were then collated and discussed. Further work was done at these workshops to address overarching issues of topic relevance, study methodology, outcome measures, and clinical applicability. Table 1 is a checklist summarizing the methods used. Conflicts of interest were disclosed, vetted, and managed in accordance with ATS policy and procedures. The Workshop Report was written by the co-chairs (P.C.S., S.P.-C., and S.C.R.) then modified with detailed feedback from the workshop participants. The online supplement consists of the detailed sections on individual techniques, written by the participant subgroups and then collated and edited by the co-chairs.

Measurement Techniques

The measurement techniques are described briefly for the clinician. The online supplement includes detailed sections on each reviewed technique and references.

Dynamic/Passive Mechanics

These techniques use classical mechanics to derive measurements of the resistance and compliance of the lung or the entire respiratory system (i.e., including chest wall). Airflow is measured at the airway opening (usually endotracheal tube or facemask) using a pneumotachometer or ultrasonic flowmeter and integrated to give volume changes. The pressure driving airflow (the driving pressure) is estimated in a variety of ways. In dynamic mechanics, the driving pressure is measured continuously. For the spontaneously breathing child, driving pressure is generated by respiratory muscles creating a negative intrapleural pressure; this is measured via a catheter, balloon, or transducer in the midesophagus. For the ventilated and paralyzed child, the driving pressure is positive pressure at the airway opening, measured within the ventilator circuit as close as possible to the airway opening. Flow and volume are measured continuously and simultaneously to driving pressure.

For passive mechanics, driving pressure is measured during a brief airway occlusion, when respiratory muscles are relaxed (Hering-Breuer reflex) and pressures equilibrate across the airways during a period of no flow. Flow and volume are measured during the passive expiration (respiratory muscles still relaxed) that follows release of the occlusion.

In both dynamic and passive techniques, these values of flow, volume, and driving pressure are used to solve the equation of motion of the lung and yield values for compliance and resistance. For situations where airflow cannot be measured accurately, a variant of dynamic mechanics uses esophageal pressure measurements alone to derive measures of respiratory effort (e.g., amplitude or amplitude-time

Table 1. Methods used in producing this Workshop Report Document

Panel assembly	
Included experts from relevant clinical and nonclinical disciplines	Yes
Included an individual who represents views of patients and society at large	No
Included methodologist with appropriate expertise (documented expertise in development of conducting systematic reviews to identify the evidence base and development of evidence-based recommendations)	Applicable only to clinical practice guidelines
Literature review	
Performed in collaboration with librarian	No
Searched multiple electronic databases	Yes
Reviewed reference lists of retrieved articles	Yes
Evidence synthesis	
Applied prespecified inclusion and exclusion criteria	Yes
Evaluated included studies for sources of bias	No
Explicitly summarized benefits and harms	Yes
Used PRISMA1 to report systematic review	Applicable only to systematic reviews
Used GRADE to describe quality of evidence	Applicable only to clinical practice guidelines
Generation of recommendations	
Used GRADE to rate the strength of recommendations	Applicable only to clinical practice guidelines

Definition of abbreviations: GRADE = Grading of Recommendations Assessment, Development, and Evaluation; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

product of esophageal pressure swings). This is referred to below as esophageal manometry. This technique is sometimes used in combination with chest wall measurements (*see below*).

Forced Deflation

Forced deflation is essentially a form of spirometry for the intubated, ventilated child, aiming to produce a maximal expiratory flow-volume curve. For the test procedure, the lungs are first inflated by manual ventilation to +40 cm H_2O inflation pressure (defined as the total lung capacity). After the inflation pressure is held static for at least 3 seconds, the lung is deflated by applying a constant negative pressure of −40 cm H_2O to the endotracheal tube until expiratory flow ceases. The rapid deflation produces reproducible maximal expiratory flow-volume curves demonstrating flow limitation, from which measures including FVC and maximal expiratory flow at 25% and 10% of FVC are derived.

Forced Oscillation Technique

Forced oscillation technique (FOT) is an alternative technique for measuring respiratory system mechanics, in which a high-frequency driving pressure waveform is superimposed on the tidal (spontaneous or ventilator-driven) breathing pattern. The resulting high-frequency changes in flow and volume are separated out from the tidal flow/volume changes by signal processing. Pressure, flow, and volume changes are then used to calculate the resistance and reactance (and the combined measure, impedance) of the respiratory system at the imposed frequency. The technique is also performed at low frequencies during apneic pauses (essentially equivalent to dynamic mechanics as described above in the ventilated, paralyzed child). Alternatively, measurements can be made during high-frequency oscillatory ventilation, when the imposed high-frequency waveform temporarily replaces the ventilator waveform.

Ventilator Graphics

Ventilator graphics refers to the real-time display of continuous measurements of pressure, flow, and volume change on a screen at the bedside, either as time-based plots or as XY loops (e.g., flow–volume or pressure–volume). Rather than yielding numerical variables, pattern recognition is used to identify specific pathophysiological situations—for example, small airway obstruction (flow–volume loop) or excessive inflation pressure (pressure–volume loop). In conjunction with ventilator graphics, additional information can be obtained by plotting esophageal pressures (obtained by esophageal manometry), as mentioned in Tables 2 and 3.

Volumetric Capnography

Capnography describes the continuous display of carbon dioxide (CO_2) partial pressure in expired breath—widely used clinically in, for example, end-tidal CO_2 monitoring. Volumetric capnography combines end-tidal CO_2 monitoring with continuous flow (and hence volume) measurement, to provide a continuous measure and visual display of quantity of CO_2 eliminated and how it relates to expired breath volume. The measurements are used to estimate anatomical and physiological dead space and ventilation effectiveness, whereas pattern recognition of displayed waveforms is used to identify pathophysiological problems (e.g., airway distension due to excessive positive end-expiratory pressure, esophageal intubation).

Inert Gas Washout

This technique measures how an inert gas marker (artificially introduced [SF_6, He] or naturally present [N_2]) is eliminated or "washed out" from the lungs. The measurement applicable to PICU and NICU is performed during a period of tidal breathing (ventilator or spontaneous) and is hence called multiple breath washout (MBW). For SF_6 or He, the gas is first washed into the lungs by adding it to the inspired air. For N_2, the gas already present in the lungs is washed out by breathing 100% O_2. Inert gas concentration in expired breath is measured continuously using a mass spectrometer or ultrasonic flowmeter, and expiratory airflow and/or volume are measured using a pneumotachometer or ultrasonic flowmeter. The total inert gas volume washed out allows the measurement of lung volume (FRC), and the rate at which it is washed out yields measures of gas mixing efficiency (e.g., lung clearance index), a marker of ventilation inhomogeneity that is sensitive to small airway disease.

Electrical Impedance Tomography

Electrical impedance tomography (EIT) is a radiation-free dynamic imaging technique that transmits very small alternating

Table 2. Clinical issues that could be addressed by respiratory function measurements in the pediatric and neonatal intensive care units

Clinical Issue	Specific Clinical Question	Physiological Parameters	Measurement Techniques
Nature of disease?	Obstructive, restrictive, or mixed lung disease?	Lung/respiratory system compliance, resistance, and impedance Lung volume	Dynamic/passive mechanics FOT Inert gas washout
	Lung disease diffuse or patchy, large or small airways?	Ventilation inhomogeneity Regional distribution of ventilation, perfusion	Capnography Inert gas washout EIT
	Regional mismatching of ventilation and perfusion?	Regional distribution of ventilation, perfusion	EIT
	Chest wall or respiratory muscle problems?	Chest wall compliance $P_{I_{max}}$	Dynamic mechanics Occlusion pressures
Optimizing respiratory support, minimizing ventilator-associated lung injury?	On optimal portion of the pressure-volume curve?	Pressure-volume curve	Dynamic mechanics Vent graphics EIT
	At optimal lung volume for pulmonary blood flow and $\dot{V}/\dot{Q}$ matching?	Regional distribution of ventilation, perfusion Gas exchange efficiency	EIT Capnography
	Minimizing patient–ventilator dyssynchrony?	Timing of respiratory effort vs. ventilator breaths	Vent graphics Esophageal manometry
	Inspiratory time/flow sufficient to deliver adequate tidal volume?	Time-based flow and volume waveforms	Vent graphics
	Expiratory time sufficient to prevent breath-stacking/auto-PEEP?	Measurement of respiratory time constant Time-based flow and volume waveforms ± expiratory hold	Passive mechanics Vent graphics
	Identify problems before serious complication (e.g., tube blockage/malposition, pneumothorax)?	Continuous measurement of R and C Time-based and XY plots of pressure, flow, volume Gas exchange efficiency Ventilation distribution	Dynamic mechanics Vent graphics Capnography EIT
Effect of therapeutic interventions?	Suctioning, positioning, chest physiotherapy?	Lung/respiratory system compliance, resistance and impedance Lung volume Gas exchange efficiency	Dynamic/passive mechanics Vent graphics FOT EIT Inert gas washout Capnography
	Medications (e.g., mucolytics, bronchodilators, surfactant, steroids)?	Lung/respiratory system compliance, resistance, and impedance Lung volume Gas exchange efficiency	Dynamic/passive mechanics Vent graphics FOT EIT Inert gas washout Capnography
	Changes in ventilator settings?	Lung/respiratory system compliance, resistance, and impedance changes Lung volume Gas exchange efficiency	Dynamic/passive mechanics Vent graphics FOT EIT Esophageal manometry Inert gas washout Capnography
Ready to wean?	Work of breathing too high?	Resistance, compliance, impedance, work of breathing Esophageal pressure-rate product Thoracoabdominal asynchrony	Dynamic/passive mechanics Esophageal manometry Chest wall measurements
	Respiratory muscle strength too poor?	$P_{I_{max}}$	Occlusion pressures
	Respiratory drive too poor, inconsistent, or uncoordinated?	$P_{0.1}$	Occlusion pressures
	Respiratory dead space a problem?	Physiological dead space	Capnography (volumetric) Inert gas washout

Definition of abbreviations: EIT = electrical impedance tomography; FOT = forced oscillation technique; $P_{0.1}$ = negative pressure developed after 100 ms of occlusion; PEEP = positive end-expiratory pressure; $P_{I_{max}}$ = maximum inspiratory pressure.

electrical currents through the lungs from a belt-like array of electrical transmitter/receivers around the outside of the chest wall. The resulting voltages are used to construct a two-dimensional "slice" showing the distribution of electrical impedance throughout the chest at that level. Because the major factor in determining impedance in any area of lung tissue is the air content, the image maps out the relative distribution of air in the lungs at that time point. By taking repeated scans (up to 50 per second) during tidal breathing, a measure of total and regional ventilation of the lungs is obtained. Although absolute lung volume is not measured, relative changes in end-expiratory volume are estimated from the cross-section sampled.

Chest Wall Measurements

Chest wall measurement techniques involve assessment of tidal breathing by estimating change in volume of the chest at the chest wall, rather than by airflow at the airway opening. Chest wall measurements are useful in the sick but nonintubated child, in whom measuring flow at the airway opening is impracticable. The best known technique is respiratory inductance plethysmography, which measures changes in the cross-sectional area of the chest by changes in inductance in coils bearing weak current around the chest and abdomen. As well as giving a measure of changes in overall tidal volume, the time lag between abdominal and chest excursions (thoracoabdominal asynchrony [TAA]) is used as an indirect measure of work of breathing. A number of newer chest wall techniques, using for example electromagnetic inductance or light reflection, are now available.

Occlusion Pressures

Occlusion pressure techniques focus on the respiratory muscles and central respiratory drive rather than respiratory mechanics, lung volumes, and gas exchange. Pressure at the airway opening during a complete airway occlusion will tend to equilibrate with alveolar pressure. The negative pressure developed after 100 ms of occlusion ($P_{0.1}$) is a measure of respiratory drive, because it reflects the alveolar pressure that would have been developed by the respiratory muscles in an unobstructed breath (100 ms is too short a time to allow a response to occlusion). By contrast, maximum inspiratory pressure (PI_{max}) is the maximum negative pressure measured at the airway opening during an occlusion sustained for a number of breaths (usually five to seven) and is used to estimate respiratory muscle strength. In the cooperative child, maximal effort is requested; in the infant it is inferred. Table 2 summarizes the potential of each technique for assessing important clinical issues in the PICU or NICU.

Discussion and Future Directions

The respiratory function techniques reviewed in this document could aid in the clinical management of individual patients in the PICU and NICU setting. Specifically, they could potentially help pediatric and neonatal intensive care clinicians to identify the nature of respiratory disease, optimize respiratory support to minimize ventilator-associated lung injury, assess the effect of therapeutic interventions, and assess readiness to wean from ventilatory support. Commercial equipment is now available for most of the aforementioned techniques; measurements are obtained quickly to avoid undue interference with clinical care, and patient risks are minimal.

The future impact in the PICU and NICU of the various techniques presented depends on a few key questions: How invasive is the technique, and does it interfere with normal care? Is there commercially available equipment, at a price affordable to most units? Can the procedure be easily taught to staff? Can it be used easily in the intubated pediatric patient to provide continuous data? Does it improve clinical outcomes? Based on these criteria, the most likely bedside clinical tools in the near future are: dynamic and passive respiratory mechanics, volumetric capnography, EIT, MBW, and chest wall measurements. To date, the volumetric capnogram has been used successfully in the measurement of anatomical dead space, pulmonary capillary perfusion, and effective ventilation (15). Randomized controlled trials evaluating routine use of capnography are needed to evaluate associated potential improvements in patient care.

Further technological development of EIT hardware and software and availability of commercial EIT devices at a reasonable cost will likely enhance the future clinical use of EIT. The practicability of EIT examinations will improve with development of electrode belts for the smallest neonatal patients and by increased robustness of the devices against electrical interference. It is crucial that EIT-derived indices relevant for clinical decision making are available online to clinicians. Following these necessary steps, EIT has the potential to be of great value in the NICU and PICU as a bedside, noninvasive tool to monitor changes in the distribution of lung volume and ventilation, especially in those infants and children receiving respiratory support.

Potential future clinical indications of MBW in the PICU and NICU are dependent on widespread availability of suitable portable low dead space equipment and the evolving availability of MBW as an integrated option within ventilators and circuits. An additional consideration is the potential impact of leak around uncuffed endotracheal tubes on some of these measurements. This remains a significant issue for many of these measures in the NICU, especially for measures of lung volume. This issue can be minimized with the use of cuffed endotracheal tubes for the purpose of the measurements of pulmonary mechanics but may impact standard clinical practice.

In addition, true "normal" reference values for FRC in ventilated patients in the PICU and NICU do not exist and will require a large series of measurements across a range of gestations and postnatal ages using standardized conditions. Equipment needs to be able to cope with the warm, humidified environment of a ventilator circuit and ideally with rapid respiratory rates. Measurements during high-frequency oscillatory ventilation represent a particular technical challenge but have been achieved for FOT, EIT (16), and chest wall measurements (17). Adaptation of techniques for bedside assessment of the alveolar capillary membrane surface such as the diffusing capacity and the diffusing coefficient may facilitate noninvasive measures of the pulmonary circulation

Table 3. Technical issues for pulmonary function testing techniques in the neonatal and pediatric intensive care units

Question	Dynamic/Passive Mechanics	Forced Deflation	FOT	Graphics	Capnography	Inert Gas Washout	EIT	Chest Wall Measurements	Occlusion Pressures
Logistics									
What equipment is needed?	Low dead space flowmeter, airway; with or without esophageal pressure transducer	Flowmeter, timed positive and negative pressure sources, 3-way valve	Low dead space oscillatory signal generator; pressure transducer and flowmeter	Mechanical ventilator or stand-alone respiratory monitor with graphics software	Low dead space sidestream or mainstream capnograph	Low dead space flowmeter and rapid response gas analyzer	Electrode array, EIT hardware and analysis software	Inductance bands or alternative (e.g., magnetic inductance, light reflection)	Airway pressure transducer, balloon or slide valves
What is measured?	Dynamic/passive resistance and compliance, of lungs or respiratory system Work of breathing	FVC, maximal flows at specific volumes	Resistance and reactance of respiratory system	Airway pressure-time, flow-time, and volume-time plots; airway pressure-volume and flow-volume loops (esophageal pressure)	End-tidal partial pressure of CO_2; partial pressure of CO_2 exhaled over time; quantity of CO_2 as a function of exhaled gas volume	FRC, lung clearance index, other indices of ventilation distribution	Dynamic cross-sectional scans of regional ventilation	Quantitative or semiquantitative tidal volumes and flows; thoracoabdominal asynchrony	$P_{0.1}$ PI_{max}
Feasibility									
Availability of commercial equipment	Available	Available (outside United States)	Not available	Available	Available	Available	Available	Available	Components available at low cost—no specific system for PICU/NICU use
How long do measurements take to obtain?	15 min	15 min	10 min	Continuous data	Continuous data	10 min (3 × 3-min tests)	Continuous data	Continuous data	10 min
Risks to patient?	Minimal	Low	Minimal	Minimal	Minimal	Minimal	Minimal	Minimal	Minimal
Which patients are unsuitable?	Leak > 10% at airway opening (20); strong respiratory drive (passive mechanics)	Leak > 10%, unintubated patients; most patients with uncuffed ETT's	Leak > 10%	Leak > 10%	Leak > 10%	Leak > 10%	Birth weight < 600 g Fragile or broken skin on chest; chest tube	None	Leak > 10%, muscle relaxants.
Studies in NICU/PICU									
Technical/validation studies	Yes (21–30)	Yes (31–35)	Yes (36–44)	Yes (20, 45–51)	Yes (52–55)	Yes (47, 56–60)	Yes (61–64)	Yes (65)	Yes (66, 67)
Using technique as outcome measure in trial	Yes (68–94)	Yes (95–99)	Yes (100)	Yes (101, 102)	Yes (103, 104)	Yes (105–111)	No	No	Yes (112)
Using technique to guide clinical management	Yes (113–115)	No	Yes (116–118)	Yes (119–121)	Yes (15, 122, 123)	No	No	Yes (18)	No

Definition of abbreviations: EIT = electrical impedance tomography; ETT = endotracheal tube; FOT = forced oscillation technique; NICU = neonatal intensive care unit; $P_{0.1}$ = negative pressure developed after 100 ms of occlusion; PICU = pediatric intensive care unit; PI_{max} = maximum inspiratory pressure.

and help achieve optimal balance between ventilation and perfusion. In the future, this would be an amazing technical advance for the population of patients in the NICU and PICU.

For chest wall measures such as TAA, normal values for phase angles in full-term infants and children have been reported independent of sleep state (18, 19), but further studies will be needed to explore whether the integration of new and automated analysis procedures will increase the clinical potential of TAA monitoring in the intensive care unit. Although there are some data on TAA in preterm infants, there are still inadequate normative data for respiratory inductance plethysmography measures in this population. Thus, we first require preterm normative data before studying preterm infants in the acute phases of lung injury.

Finally, it should be stressed that more research is warranted for each technique before issuing detailed recommendations on specific ages, disease entities, or outcome measures associated with testing. There is a requirement to develop standardized procedures/protocols, minimum standards for equipment, and ideally normative data to differentiate normal from disease states before incorporation of a technique into our daily clinical practice. Nonetheless, there is already a body of experience with these techniques as research tools, most are noninvasive, and they can provide additional data not easily obtained otherwise.

Proposed Areas of Future Research Collaboration

- For all techniques, establish "normal" reference values using current commercial equipment in ventilated patients (e.g., studies of surgical patients without respiratory disease/chest or abdominal surgery).
- Conduct pre- and postintervention studies (surfactant, altered ventilation strategy, mucolytics, etc.) studying effect on dead space using capnography and MBW (FRC).
- Conduct randomized trials to assess if knowledge of/discussion of routine measures of respiratory mechanics affects patient outcomes in the PICU and NICU, such as length of mechanical ventilation and/or length of stay.
- Conduct randomized controlled trial of patients in the PICU to evaluate the impact of volumetric capnography on length of ventilation, length of stay, and cost effectiveness.
- Work with ventilator manufacturers to incorporate appropriate measurement and display of resistance, compliance, and volumetric capnography in commercial ventilators for the PICU and NICU.
- Measure oscillation mechanics during mechanical ventilation in a large group of patients in the PICU.
- Establish clinical protocols for the reviewed techniques and rigorous models for data analysis.
- Study whether the use of EIT can shorten time to weaning from ventilation and minimize lung injury. ■

This official statement was prepared by the ATS/ERS Evaluation of Respiratory Mechanics and Function in the Pediatric and Neonatal Intensive Care Units writing group

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References

1 Groeger JS, Guntupalli KK, Strosberg M, Halpern N, Raphaely RC, Cerra F, Kaye W. Descriptive analysis of critical care units in the United States: patient characteristics and intensive care unit utilization. *Crit Care Med* 1993;21:279–291.
2 American Thoracic Society/European Respiratory Society. Respiratory mechanics in infants: physiologic evaluation in health and disease. *Am Rev Respir Dis* 1993;147: 474–496.
3 American Thoracic Society/European Respiratory Society. Respiratory function measurements in infants: symbols, abbreviations, and units. *Am J Respir Crit Care Med* 1995;151: 2041–2057.
4 American Thoracic Society/European Respiratory Society. Respiratory function measurements in infants: measurement conditions. *Am J Respir Crit Care Med* 1995;151:2058–2064.
5 The Joint American Thoracic Society/European Respiratory Society Working Group on Infant Lung Function. The raised volume rapid thoracoabdominal compression technique. *Am J Respir Crit Care Med* 2000;161:1760–1762.
6 Frey U, Stocks J, Coates A, Sly P, Bates J; European Respiratory Society/American Thoracic Society. Specifications for equipment used for infant pulmonary function testing: ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. *Eur Respir J* 2000;16:731–740.
7 Sly PD, Tepper R, Henschen M, Gappa M, Stocks J; European Respiratory Society/American Thoracic Society. Tidal forced expirations: ERS/ATS task force on standards for infant respiratory function testing. European Respiratory Society/American Thoracic Society. *Eur Respir J* 2000;16:741–748.
8 Frey U, Stocks J, Sly P, Bates J; European Respiratory Society/American Thoracic Society. Specification for signal processing and data handling used for infant pulmonary function testing: ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. *Eur Respir J* 2000;16:1016–1022.
9 Bates JHT, Schmalisch G, Filbrun D, Stocks J; European Respiratory Society/American Thoracic Society. Tidal breath analysis for infant pulmonary function testing: ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. *Eur Respir J* 2000;16: 1180–1192.
10 Gappa M, Colin AA, Goetz I, Stocks J; ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. European Respiratory Society/American Thoracic Society. Passive respiratory mechanics: the occlusion techniques. *Eur Respir J* 2001;17: 141–148.

11 Stocks J, Godfrey S, Beardsmore C, Bar-Yishay E, Castile R; ERS/ATS Task Force on Standards for Infant Respiratory Function Testing; European Respiratory Society/ American Thoracic Society. Plethysmographic measurements of lung volume and airway resistance: ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. *Eur Respir J* 2001;17:302–312.
12 Morris MG, Gustafsson P, Tepper R, Gappa M, Stocks J; ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. The bias flow nitrogen washout technique for measuring the functional residual capacity in infants: ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. *Eur Respir J* 2001;17:529–536.
13 American Thoracic Society; European Respiratory Society. ATS/ERS statement. Raised volume forced expirations in infants: guidelines for current practice. *Am J Respir Crit Care Med* 2005;172:1463–1471.
14 Beydon N, Davis SD, Lombardi E, Allen JL, Arets HG, Aurora P, Bisgaard H, Davis GM, Ducharme FM, Eigen H, *et al*.; American Thoracic Society/European Respiratory Society Working Group on Infant and Young Children Pulmonary Function Testing. An official American Thoracic Society/European Respiratory Society statement: pulmonary function testing in preschool children. *Am J Respir Crit Care Med* 2007;175:1304–1345.
15 Hamel DS, Cheifetz IM. Do all mechanically ventilated pediatric patients require continuous capnography? *Respir Care Clin N Am* 2006;12:501–513.
16 Miedema M, de Jongh FH, Frerichs I, van Veenendaal MB, van Kaam AH. Changes in lung volume and ventilation during lung recruitment in high-frequency ventilated preterm infants with respiratory distress syndrome. *J Pediatr* 2011;159:199–205.e2.
17 Tingay DG, Mills JF, Morley CJ, Pellicano A, Dargaville PA. The deflation limb of the pressure-volume relationship in infants during high-frequency ventilation. *Am J Respir Crit Care Med* 2006;173:414–420.
18 Sivan Y, Deakers TW, Newth CJ. Thoracoabdominal asynchrony in acute upper airway obstruction in small children. *Am Rev Respir Dis* 1990;142:540–544.
19 Sivan Y, Ward SD, Deakers T, Keens TG, Newth CJ. Rib cage to abdominal asynchrony in children undergoing polygraphic sleep studies. *Pediatr Pulmonol* 1991;11:141–146.
20 Main E, Castle R, Stocks J, James I, Hatch D. The influence of endotracheal tube leak on the assessment of respiratory function in ventilated children. *Intensive Care Med* 2001;27:1788–1797.
21 Davis GM, Stocks J, Gerhardt T, Abbasi S, Gappa M. Measurement of dynamic lung mechanics in infants. In: Stocks J, Sly PD, Tepper RS, Morgan WJ, editors. Infant respiratory function testing. New York: Wiley-Liss; 1996. pp. 259–281.
22 Fletcher ME, Baraldi E, Steinbrugger B. Passive respiratory mechanics. In: Stocks J, Sly PD, Tepper RS, Morgan WJ, editors. Infant respiratory function testing. New York: Wiley-Liss; 1996. pp. 283–327.
23 Gerhardt T, Hehre D, Feller R, Reifenberg L, Bancalari E. Pulmonary mechanics in normal infants and young children during first 5 years of life. *Pediatr Pulmonol* 1987;3:309–316.
24 Masters IB, Seidenberg J, Hudson I, Phelan PD, Olinsky A. Longitudinal study of lung mechanics in normal infants. *Pediatr Pulmonol* 1987;3:3–7.
25 Coates AL, Vallinis P, Mullahoo K, Seddon P, Davis GM. Pulmonary impedance as an index of severity and mechanisms of neonatal lung disease. *Pediatr Pulmonol* 1994;17:41–49.
26 Greenspan JS, Abbasi S, Bhutani VK. Sequential changes in pulmonary mechanics in the very low birth weight (less than or equal to 1000 grams) infant. *J Pediatr* 1988;113:732–737.
27 Kugelman A, Keens TG, deLemos R, Durand M. Comparison of dynamic and passive measurements of respiratory mechanics in ventilated newborn infants. *Pediatr Pulmonol* 1995;20:258–264.
28 Lanteri CJ, Sly PD. Changes in respiratory mechanics with age. *J Appl Physiol (1985)* 1993;74:369–378.
29 Pandit PB, Pyon KH, Courtney SE, England SE, Habib RH. Lung resistance and elastance in spontaneously breathing preterm infants: effects of breathing pattern and demographics. *J Appl Physiol (1985)* 2000;88:997–1005.
30 Seddon PC, Davis GM. Validity of esophageal pressure measurements with positive end-expiratory pressure in preterm infants. *Pediatr Pulmonol* 2003;36:216–222.
31 Newth CJ, Amsler B, Anderson GP, Morley J. The effects of varying inflation and deflation pressures on the maximal expiratory deflation flow-volume relationship in anesthetized rhesus monkeys. *Am Rev Respir Dis* 1991;144:807–813.
32 Hammer J, Newth CJ. Effort and volume dependence of forced-deflation flow-volume relationships in intubated infants. *J Appl Physiol (1985)* 1996;80:345–350.
33 Hammer J, Newth CJ. Influence of endotracheal tube diameter on forced deflation flow-volume curves in rhesus monkeys. *Eur Respir J* 1997;10:1870–1873.
34 Hammer J, Patel N, Newth CJ. Effect of forced deflation maneuvers upon measurements of respiratory mechanics in ventilated infants. *Intensive Care Med* 2003;29:2004–2008.
35 von Ungern-Sternberg BS, Trachsel D, Erb TO, Hammer J. Forced expiratory flows and volumes in intubated and paralyzed infants and children: normative data up to 5 years of age. *J Appl Physiol (1985)* 2009;107:105–111.
36 Babik B, Peták F, Asztalos T, Deák ZI, Bogáts G, Hantos Z. Components of respiratory resistance monitored in mechanically ventilated patients. *Eur Respir J* 2002;20:1538–1544.
37 Beydon L, Malassiné P, Lorino AM, Mariette C, Bonnet F, Harf A, Lorino H. Respiratory resistance by end-inspiratory occlusion and forced oscillations in intubated patients. *J Appl Physiol (1985)* 1996;80:1105–1111.
38 Farré R, Ferrer M, Rotger M, Navajas D. Servocontrolled generator to measure respiratory impedance from 0.25 to 26 Hz in ventilated patients at different PEEP levels. *Eur Respir J* 1995;8:1222–1227.
39 Navajas D, Farré R. Forced oscillation assessment of respiratory mechanics in ventilated patients. *Crit Care* 2001;5:3–9.
40 Lorx A, Szabó B, Hercsuth M, Pénzes I, Hantos Z. Low-frequency assessment of airway and tissue mechanics in ventilated COPD patients. *J Appl Physiol (1985)* 2009;107:1884–1892.
41 Lutchen KR, Kaczka DW, Suki B, Barnas G, Cevenini G, Barbini P. Low-frequency respiratory mechanics using ventilator-driven forced oscillations. *J Appl Physiol (1985)* 1993;75:2549–2560.
42 Lorx A, Suki B, Hercsuth M, Szabó B, Pénzes I, Boda K, Hantos Z. Airway and tissue mechanics in ventilated patients with pneumonia. *Respir Physiol Neurobiol* 2010;171:101–109.
43 Peták F, Babik B, Asztalos T, Hall GL, Deák ZI, Sly PD, Hantos Z. Airway and tissue mechanics in anesthetized paralyzed children. *Pediatr Pulmonol* 2003;35:169–176.
44 Scholz AW, Weiler N, David M, Markstaller K. Respiratory mechanics measured by forced oscillations during mechanical ventilation through a tracheal tube. *Physiol Meas* 2011;32:571–583.
45 Marchese AD, Sulemanji D, Chipman D, Villar J, Kacmarek RM. Performance of current intensive care unit ventilators during pressure and volume ventilation. *Respir Care* 2011;56:928–940.
46 Ghuman AK, Newth CJ, Khemani RG. The association between the end tidal alveolar dead space fraction and mortality in pediatric acute hypoxemic respiratory failure. *Pediatr Crit Care Med* 2012;13:11–15.
47 Schibler A, Hammer J, Isler R, Buess C, Newth CJ. Measurement of lung volume in mechanically ventilated monkeys with an ultrasonic flow meter and the nitrogen washout method. *Intensive Care Med* 2004;30:127–132.
48 Newth CJ, Rachman B, Patel N, Hammer J. The use of cuffed versus uncuffed endotracheal tubes in pediatric intensive care. *J Pediatr* 2004;144:333–337.
49 Tuxen DV, Lane S. The effects of ventilatory pattern on hyperinflation, airway pressures, and circulation in mechanical ventilation of patients with severe air-flow obstruction. *Am Rev Respir Dis* 1987;136:872–879.
50 Castle RA, Dunne CJ, Mok Q, Wade AM, Stocks J. Accuracy of displayed values of tidal volume in the pediatric intensive care unit. *Crit Care Med* 2002;30:2566–2574.
51 Cannon ML, Cornell J, Tripp-Hamel DS, Gentile MA, Hubble CL, Meliones JN, Cheifetz IM. Tidal volumes for ventilated infants should be determined with a pneumotachometer placed at the endotracheal tube. *Am J Respir Crit Care Med* 2000;162:2109–2112.

52 McSwain SD, Hamel DS, Smith PB, Gentile MA, Srinivasan S, Meliones JN, Cheifetz IM. End-tidal and arterial carbon dioxide measurements correlate across all levels of physiologic dead space. *Respir Care* 2010;55:288–293.
53 McDonald MJ, Montgomery VL, Cerrito PB, Parrish CJ, Boland KA, Sullivan JE. Comparison of end-tidal CO2 and Paco2 in children receiving mechanical ventilation. *Pediatr Crit Care Med* 2002;3:244–249.
54 Tobias JD, Meyer DJ. Noninvasive monitoring of carbon dioxide during respiratory failure in toddlers and infants: end-tidal versus transcutaneous carbon dioxide. *Anesth Analg* 1997;85:55–58.
55 Berkenbosch JW, Lam J, Burd RS, Tobias JD. Noninvasive monitoring of carbon dioxide during mechanical ventilation in older children: end-tidal versus transcutaneous techniques. *Anesth Analg* 2001;92: 1427–1431.
56 Sivan Y, Deakers TW, Newth CJ. An automated bedside method for measuring functional residual capacity by N2 washout in mechanically ventilated children. *Pediatr Res* 1990;28:446–450.
57 Sivan Y, Deakers TW, Newth CJ. Functional residual capacity in ventilated infants and children. *Pediatr Res* 1990;28:451–454.
58 Sivan Y, Hammer J, Newth CJ. Measurement of high lung volumes by nitrogen washout method. *J Appl Physiol (1985)* 1994;77: 1562–1564.
59 Hammer J, Numa A, Newth CJ. Total lung capacity by N2 washout from high and low lung volumes in ventilated infants and children. *Am J Respir Crit Care Med* 1998;158:526–531.
60 Proquitté H, Kusztrich A, Auwärter V, Pragst F, Wauer RR, Schmalisch G. Functional residual capacity measurement by heptafluoropropane in ventilated newborn lungs: in vitro and in vivo validation. *Crit Care Med* 2006;34:1789–1795.
61 Frerichs I, Hinz J, Herrmann P, Weisser G, Hahn G, Dudykevych T, Quintel M, Hellige G. Detection of local lung air content by electrical impedance tomography compared with electron beam CT. *J Appl Physiol (1985)* 2002;93:660–666.
62 Hinz J, Neumann P, Dudykevych T, Andersson LG, Wrigge H, Burchardi H, Hedenstierna G. Regional ventilation by electrical impedance tomography: a comparison with ventilation scintigraphy in pigs. *Chest* 2003;124:314–322.
63 Richard JC, Pouzot C, Gros A, Tourevieille C, Lebars D, Lavenne F, Frerichs I, Guérin C. Electrical impedance tomography compared to positron emission tomography for the measurement of regional lung ventilation: an experimental study. *Crit Care* 2009;13:R82.
64 Victorino JA, Borges JB, Okamoto VN, Matos GF, Tucci MR, Caramez MP, Tanaka H, Sipmann FS, Santos DC, Barbas CS, *et al*. Imbalances in regional lung ventilation: a validation study on electrical impedance tomography. *Am J Respir Crit Care Med* 2004; 169:791–800.
65 Hammer J, Newth CJ, Deakers TW. Validation of the phase angle technique as an objective measure of upper airway obstruction. *Pediatr Pulmonol* 1995;19:167–173.
66 Harikumar G, Moxham J, Greenough A, Rafferty GF. Measurement of maximal inspiratory pressure in ventilated children. *Pediatr Pulmonol* 2008;43:1085–1091.
67 Greenspan JS, Wolfson MR, Locke RG, Allen JL, Shaffer TH. Increased respiratory drive and limited adaptation to loaded breathing in bronchopulmonary dysplasia. *Pediatr Res* 1992;32:356–359.
68 Bhat R, Dziedzic K, Bhutani VK, Vidyasagar D. Effect of single dose surfactant on pulmonary function. *Crit Care Med* 1990;18: 590–595.
69 Bhutani VK, Abbasi S, Long WA, Gerdes JS. Pulmonary mechanics and energetics in preterm infants who had respiratory distress syndrome treated with synthetic surfactant. *J Pediatr* 1992;120:S18–S24.
70 Blondheim O, Abbasi S, Fox WW, Bhutani VK. Effect of enteral gavage feeding rate on pulmonary functions of very low birth weight infants. *J Pediatr* 1993;122:751–755.
71 Cabal LA, Larrazabal C, Ramanathan R, Durand M, Lewis D, Siassi B, Hodgman J. Effects of metaproterenol on pulmonary mechanics, oxygenation, and ventilation in infants with chronic lung disease. *J Pediatr* 1987;110:116–119.
72 Courtney SE, Weber KR, Siervogel RM, Spohn WA, Guo S, Malin SW, Bender CV. Effects of dexamethasone on pulmonary function following extubation. *J Perinatol* 1992;12:246–251.
73 Durand M, Mendoza ME, Tantivit P, Kugelman A, McEvoy C. A randomized trial of moderately early low-dose dexamethasone therapy in very low birth weight infants: dynamic pulmonary mechanics, oxygenation, and ventilation. *Pediatrics* 2002;109: 262–268.
74 Kugelman A, Durand M, Garg M. Pulmonary effect of inhaled furosemide in ventilated infants with severe bronchopulmonary dysplasia. *Pediatrics* 1997;99:71–75.
75 Gappa M, Gärtner M, Poets CF, von der Hardt H. Effects of salbutamol delivery from a metered dose inhaler versus jet nebulizer on dynamic lung mechanics in very preterm infants with chronic lung disease. *Pediatr Pulmonol* 1997;23:442–448.
76 Gomez-Del Rio M, Gerhardt T, Hehre D, Feller R, Bancalari E. Effect of a beta-agonist nebulization on lung function in neonates with increased pulmonary resistance. *Pediatr Pulmonol* 1986;2:287–291.
77 Heldt GP, Pesonen E, Merritt TA, Elias W, Sahn DJ. Closure of the ductus arteriosus and mechanics of breathing in preterm infants after surfactant replacement therapy. *Pediatr Res* 1989;25:305–310.
78 Janai HK, Stutman HR, Zaleska M, Rub B, Eyzaguirre M, Marks MI, Nussbaum E. Ribavirin effect on pulmonary function in young infants with respiratory syncytial virus bronchiolitis. *Pediatr Infect Dis J* 1993;12:214–218.
79 Kao LC, Warburton D, Cheng MH, Cedeño C, Platzker AC, Keens TG. Effect of oral diuretics on pulmonary mechanics in infants with chronic bronchopulmonary dysplasia: results of a double-blind crossover sequential trial. *Pediatrics* 1984;74:37–44.
80 Kao LC, Keens TG. Decreased specific airway conductance in infant apnea. *Pediatrics* 1985;76:232–235.
81 Khalaf MN, Brodsky N, Hurley J, Bhandari V. A prospective randomized, controlled trial comparing synchronized nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure as modes of extubation. *Pediatrics* 2001;108:13–17.
82 LaForce WR, Brudno DS. Controlled trial of beclomethasone dipropionate by nebulization in oxygen- and ventilator-dependent infants. *J Pediatr* 1993;122:285–288.
83 Morrow B, Futter M, Argent A. Effect of endotracheal suction on lung dynamics in mechanically-ventilated paediatric patients. *Aust J Physiother* 2006;52:121–126.
84 Morrow B, Futter M, Argent A. A recruitment manoeuvre performed after endotracheal suction does not increase dynamic compliance in ventilated paediatric patients: a randomised controlled trial. *Aust J Physiother* 2007;53:163–169.
85 Panitch HB, Allen JL, Alpert BE, Schidlow DV. Effects of CPAP on lung mechanics in infants with acquired tracheobronchomalacia. *Am J Respir Crit Care Med* 1994;150:1341–1346.
86 Rush MG, Engelhardt B, Parker RA, Hazinski TA. Double-blind, placebo-controlled trial of alternate-day furosemide therapy in infants with chronic bronchopulmonary dysplasia. *J Pediatr* 1990;117:112–118.
87 Sasidharan P, Heimler R. Alterations in pulmonary mechanics after transfusion in anemic preterm infants. *Crit Care Med* 1990;18: 1360–1362.
88 Schmalisch G, Wauer RR, Böhme B. Changes in pulmonary function in preterm infants recovering from RDS following early treatment with ambroxol: results of a randomized trial. *Pediatr Pulmonol* 1999; 27:104–112.
89 Szymankiewicz M, Gadzinowski J, Kowalska K. Pulmonary function after surfactant lung lavage followed by surfactant administration in infants with severe meconium aspiration syndrome. *J Matern Fetal Neonatal Med* 2004;16:125–130.
90 Zinman R. Tracheal stenting improves airway mechanics in infants with tracheobronchomalacia. *Pediatr Pulmonol* 1995;19:275–281.
91 Stenson BJ, Glover RM, Parry GJ, Wilkie RA, Laing IA, Tarnow-Mordi WO. Static respiratory compliance in the newborn. III: Early changes after exogenous surfactant treatment. *Arch Dis Child Fetal Neonatal Ed* 1994;70:F19–F24.
92 McEvoy C, Bowling S, Williamson K, Collins J, Tolaymat L, Maher J. Timing of antenatal corticosteroids and neonatal pulmonary mechanics. *Am J Obstet Gynecol* 2000;183:895–899.
93 Durand M, Sardesai S, McEvoy C. Effects of early dexamethasone therapy on pulmonary mechanics and chronic lung disease in very low birth weight infants: a randomized, controlled trial. *Pediatrics* 1995;95:584–590.

94 McEvoy C, Schilling D, Peters D, Tillotson C, Spitale P, Wallen L, Segel S, Bowling S, Gravett M, Durand M. Respiratory compliance in preterm infants after a single rescue course of antenatal steroids: a randomized controlled trial. *Am J Obstet Gynecol* 2010;202:544.e1–544.e9.
95 Hammer J, Numa A, Newth CJ. Albuterol responsiveness in infants with respiratory failure caused by respiratory syncytial virus infection. *J Pediatr* 1995;127:485–490.
96 Newth CJ, Stretton M, Deakers TW, Hammer J. Assessment of pulmonary function in the early phase of ARDS in pediatric patients. *Pediatr Pulmonol* 1997;23:169–175.
97 Mallory GB Jr, Motoyama EK, Koumbourlis AC, Mutich RL, Nakayama DK. Bronchial reactivity in infants in acute respiratory failure with viral bronchiolitis. *Pediatr Pulmonol* 1989;6:253–259.
98 Motoyama EK, Fort MD, Klesh KW, Mutich RL, Guthrie RD. Early onset of airway reactivity in premature infants with bronchopulmonary dysplasia. *Am Rev Respir Dis* 1987;136:50–57.
99 Mallory GB Jr, Chaney H, Mutich RL, Motoyama EK. Longitudinal changes in lung function during the first three years of premature infants with moderate to severe bronchopulmonary dysplasia. *Pediatr Pulmonol* 1991;11:8–14.
100 Sellares J, Acerbi I, Loureiro H, Dellaca RL, Ferrer M, Torres A, Navajas D, Farre R. Respiratory impedance during weaning from mechanical ventilation in a mixed population of critically ill patients. *Br J Anaesth* 2009;103:828–832.
101 The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301–1308.
102 Khemani RG, Conti D, Alonzo TA, Bart RD III, Newth CJ. Effect of tidal volume in children with acute hypoxemic respiratory failure. *Intensive Care Med* 2009;35:1428–1437.
103 Hubble CL, Gentile MA, Tripp DS, Craig DM, Meliones JN, Cheifetz IM. Deadspace to tidal volume ratio predicts successful extubation in infants and children. *Crit Care Med* 2000;28:2034–2040.
104 Roberts WA, Maniscalco WM, Cohen AR, Litman RS, Chhibber A. The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit. *Pediatr Pulmonol* 1995;19:262–268.
105 Numa AH, Hammer J, Newth CJ. Effect of prone and supine positions on functional residual capacity, oxygenation, and respiratory mechanics in ventilated infants and children. *Am J Respir Crit Care Med* 1997;156:1185–1189.
106 von Ungern-Sternberg BS, Hammer J, Schibler A, Frei FJ, Erb TO. Decrease of functional residual capacity and ventilation homogeneity after neuromuscular blockade in anesthetized young infants and preschool children. *Anesthesiology* 2006;105:670–675.
107 von Ungern-Sternberg BS, Frei FJ, Hammer J, Schibler A, Doerig R, Erb TO. Impact of depth of propofol anaesthesia on functional residual capacity and ventilation distribution in healthy preschool children. *Br J Anaesth* 2007;98:503–508.
108 von Ungern-Sternberg BS, Regli A, Frei FJ, Hammer J, Jordi Ritz EM, Erb TO. Decrease in functional residual capacity and ventilation homogeneity after neuromuscular blockade in anesthetized preschool children in the lateral position. *Paediatr Anaesth* 2007;17:841–845.
109 von Ungern-Sternberg BS, Regli A, Schibler A, Hammer J, Frei FJ, Erb TO. The impact of positive end-expiratory pressure on functional residual capacity and ventilation homogeneity impairment in anesthetized children exposed to high levels of inspired oxygen. *Anesth Analg* 2007;104:1364–1368.
110 von Ungern-Sternberg BS, Regli A, Frei FJ, Ritz EM, Hammer J, Schibler A, Erb TO. A deeper level of ketamine anesthesia does not affect functional residual capacity and ventilation distribution in healthy preschool children. *Paediatr Anaesth* 2007;17:1150–1155.
111 von Ungern-Sternberg BS, Regli A, Frei FJ, Hammer J, Schibler A, Erb TO. The effect of caudal block on functional residual capacity and ventilation homogeneity in healthy children. *Anaesthesia* 2006;61:758–763.
112 Kassim Z, Greenough A, Rafferty GF. Effect of caffeine on respiratory muscle strength and lung function in prematurely born, ventilated infants. *Eur J Pediatr* 2009;168:1491–1495.
113 Garg M, Lew CD, Ramos AD, Platzker AC, Keens TG. Serial measurement of pulmonary mechanics assists in weaning from extracorporeal membrane oxygenation in neonates with respiratory failure. *Chest* 1991;100:770–774.
114 Veness-Meehan KA, Richter S, Davis JM. Pulmonary function testing prior to extubation in infants with respiratory distress syndrome. *Pediatr Pulmonol* 1990;9:2–6.
115 Stenson BJ, Glover RM, Wilkie RA, Laing IA, Tarnow-Mordi WO. Randomised controlled trial of respiratory system compliance measurements in mechanically ventilated neonates. *Arch Dis Child Fetal Neonatal Ed* 1998;78:F15–F19.
116 Dellacà RL, Zannin E, Kostic P, Olerud MA, Pompilio PP, Hedenstierna G, Pedotti A, Frykholm P. Optimisation of positive end-expiratory pressure by forced oscillation technique in a lavage model of acute lung injury. *Intensive Care Med* 2011;37:1021–1030.
117 Franke KJ, Nilius G, Morgenstern S, Ruhle KH. Removal of the tracheal tube after prolonged mechanical ventilation: assessment of risk by oscillatory impedance. *Respiration* 2011;81:118–123.
118 Vendettuoli V, Veneroni C, Zannin E, Mercadante D, Matassa P, Pedotti A, Colnaghi M, Dellacà RL, Mosca F. Positional effects on lung mechanics of ventilated preterm infants with acute and chronic lung disease. *Pediatr Pulmonol* 2015;50:798–804.
119 Graham AS, Chandrashekharaiah G, Citak A, Wetzel RC, Newth CJ. Positive end-expiratory pressure and pressure support in peripheral airways obstruction: work of breathing in intubated children. *Intensive Care Med* 2007;33:120–127.
120 Willis BC, Graham AS, Yoon E, Wetzel RC, Newth CJ. Pressure-rate products and phase angles in children on minimal support ventilation and after extubation. *Intensive Care Med* 2005;31:1700–1705.
121 Tuxen DV, Williams TJ, Scheinkestel CD, Czarny D, Bowes G. Use of a measurement of pulmonary hyperinflation to control the level of mechanical ventilation in patients with acute severe asthma. *Am Rev Respir Dis* 1992;146:1136–1142.
122 Sullivan KJ, Kissoon N, Goodwin SR. End-tidal carbon dioxide monitoring in pediatric emergencies. *Pediatr Emerg Care* 2005;21:327–332; quiz 333–325.
123 Short JA, Paris ST, Booker PD, Fletcher R. Arterial to end-tidal carbon dioxide tension difference in children with congenital heart disease. *Br J Anaesth* 2001;86:349–353.