

WORKSHEET for PROPOSED Evidence-Based GUIDELINE RECOMMENDATIONS

Worksheet Author:	Taskforce/Subcommittee: __BLS __ACLS x PEDS __ID __PROAD __x_Other: NRP
Author's Home Resuscitation Council: _x_AHA __ANZCOR __CLAR __ERC __HSFC __HSFC __RCSA __IAHF __Other:	Date Submitted to Subcommittee: 6/1/04

STEP 1: STATE THE PROPOSAL. State if this is a proposed new guideline; revision to current guideline; or deletion of current guideline.

Existing guideline, practice or training activity, or new guideline: Revision to current guideline

The proposal is to create a new guideline describing the use of continuous positive airway pressure (CPAP) in neonates during resuscitation in the delivery room.

Step 1A: Refine the question; state the question as a positive (or negative) hypothesis. State proposed guideline recommendation as a specific, positive hypothesis. Use single sentence if possible. Include type of patients; setting (in-/out-of-hospital); specific interventions (dose, route); specific outcomes (ROSC vs. hospital discharge).

CPAP is a safe and effective intervention, compared with endotracheal intubation, in the resuscitation of newborns in the delivery room

Step 1B: Gather the Evidence; define your search strategy. Describe search results; describe best sources for evidence.

continuous positive airway pressure, CPAP, continuous distending pressure, CDP (AND neonate, newborn, birth, resuscitation (searched as text words)

List electronic databases searched (at least AHA EndNote 7 Master library [<http://ecc.heart.org/>], Cochrane database for systematic reviews and Central Register of Controlled Trials [<http://www.cochrane.org/>], MEDLINE

[<http://www.ncbi.nlm.nih.gov/PubMed/>], and Embase), and hand searches of journals, review articles, and books. Pubmed, Embase, Cochrane database ECC library, Review articles

PUBMED (MEDLINE), Embase, Cochrane database, EndNote master library, hand searches of journals

- State major criteria you used to limit your search; state inclusion or exclusion criteria (e.g., only human studies with control group? no animal studies? N subjects > minimal number? type of methodology? peer-reviewed manuscripts only? no abstract-only studies?)

No abstracts

- Number of articles/sources meeting criteria for further review: Create a citation marker for each study (use the author initials and date or Arabic numeral, e.g., "Cummins-1"). If possible, please supply file of best references; EndNote 6+ required as reference manager using the ECC reference library.

20

STEP 2: ASSESS THE QUALITY OF EACH STUDY

Step 2A: Determine the Level of Evidence. For each article/source from step 1, assign a level of evidence—based on study design and methodology.

Level of Evidence	Definitions (See manuscript for full details)
Level 1	
Level 2	
Level 3	
Level 4	Lundstrom KE
Level 5	Polin RA
Level 6	
Level 7	Elgellab A, Han VKM, Hegyi T, Allen LP, Belenky DA, Kroustop RW, Milner AD, Van Marter LJ, Guerrini P, Lindner W, Gitterman MK, Poets CF, Kamper J (1993), Latini G, Claris O, Kamper J (1990), Schmid ER, Gregory GA

Level 8	
----------------	--

Step 2B: Critically assess each article/source in terms of research design and methods.

Was the study well executed? Suggested criteria appear in the table below. Assess design and methods and provide an overall rating. Ratings apply within each Level; a Level 1 study can be excellent or poor as a clinical trial, just as a Level 6 study could be excellent or poor as an animal study. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study. For more detailed explanations please see attached assessment form.

Component of Study and Rating	Excellent	Good	Fair	Poor	Unsatisfactory
Design & Methods	Highly appropriate sample or model, randomized, proper controls AND Outstanding accuracy, precision, and data collection in its class	Highly appropriate sample or model, randomized, proper controls OR Outstanding accuracy, precision, and data collection in its class	Adequate, design, but possibly biased OR Adequate under the circumstances	<i>Small or clearly biased population or model</i> OR <i>Weakly defensible in its class, limited data or measures</i>	<i>Anecdotal, no controls, off target end-points</i> OR <i>Not defensible in its class, insufficient data or measures</i>

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint

B = Survival of event D = Intact neurological survival

Step 2C: Determine the direction of the results and the statistics: supportive? neutral? opposed?

DIRECTION of study by results & statistics:	SUPPORT the proposal	NEUTRAL	OPPOSE the proposal
Results	Outcome of proposed guideline superior, to a clinically important degree, to current approaches	Outcome of proposed guideline no different from current approach	Outcome of proposed guideline inferior to current approach

Step 2D: Cross-tabulate assessed studies by a) level, b) quality and c) direction (ie, supporting or neutral/ opposing); **combine and summarize.** Exclude the *Poor* and *Unsatisfactory* studies. Sort the *Excellent*, *Good*, and *Fair* quality studies by both *Level and Quality of evidence*, and *Direction of support* in the summary grids below. Use citation marker (e.g. author/ date/source). In the *Neutral* or *Opposing* grid use bold font for *Opposing* studies to distinguish them from merely neutral studies. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study.

Supporting Evidence

CPAP is a safe and effective intervention, compared with endotracheal intubation, in the resuscitation of newborns in the delivery room.

Quality of Evidence	Excellent								
	Good						Elgellab A ^E Milner AD ^E		
	Fair				Lindner W ^E	Polin RA ^E	Hegy T ^E Allen LP ^E Kroustop RW ^E Van Marter LJ ^E Latini G ^E Claris O ^E Lundstrom KE ^E Kamper J ^E Schmid ER ^E Gregory GA ^E Poets CF ^E		
		1	2	3	4	5	6	7	8
Level of Evidence									

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Neutral or Opposing Evidence

CPAP is a safe and effective intervention, compared with endotracheal intubation, in the resuscitation of newborns in the delivery room.

Quality of Evidence	Excellent								
	Good								
	Fair							Han VKM ^E Belenky DA ^E	
		1	2	3	4	5	6	7	8
		Level of Evidence							

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
 B = Survival of event D = Intact neurological survival

STEP 3. DETERMINE THE CLASS OF RECOMMENDATION. Select from these summary definitions.

CLASS	CLINICAL DEFINITION	REQUIRED LEVEL OF EVIDENCE
Class I <i>Definitely recommended.</i> Definitive, excellent evidence provides support.	<ul style="list-style-type: none"> • Always acceptable, safe • Definitely useful • Proven in both efficacy & effectiveness • Must be used in the intended manner for proper clinical indications. 	<ul style="list-style-type: none"> • One or more Level 1 studies are present (with rare exceptions) • Study results consistently positive and compelling
Class II: <i>Acceptable and useful</i>	<ul style="list-style-type: none"> • Safe, acceptable • Clinically useful • Not yet confirmed definitively 	<ul style="list-style-type: none"> • Most evidence is positive • Level 1 studies are absent, or inconsistent, or lack power • No evidence of harm
<ul style="list-style-type: none"> • Class IIa: <i>Acceptable and useful</i> Good evidence provides support	<ul style="list-style-type: none"> • Safe, acceptable • Clinically useful • Considered treatments of choice 	<ul style="list-style-type: none"> • Generally higher levels of evidence • Results are consistently positive

<p>• <i>Class IIb:</i> <i>Acceptable and useful</i> Fair evidence provides support</p>	<ul style="list-style-type: none">• Safe, acceptable• Clinically useful• Considered optional or alternative treatments	<ul style="list-style-type: none">• Generally lower or intermediate levels of evidence• Generally, but not consistently, positive results
--	--	--

Class III: <i>Not acceptable, not useful, may be harmful</i>	<ul style="list-style-type: none"> • Unacceptable • Not useful clinically • May be harmful. 	<ul style="list-style-type: none"> • No positive high level data • Some studies suggest or confirm harm.
Indeterminate	<ul style="list-style-type: none"> • Research just getting started. • Continuing area of research • No recommendations until further research 	<ul style="list-style-type: none"> • Minimal evidence is available • Higher studies in progress • Results inconsistent, contradictory • Results not compelling

STEP 3: DETERMINE THE CLASS OF RECOMMENDATION. State a **Class of Recommendation** for the Guideline Proposal. State either **a) the intervention**, and then the conditions under which the intervention is either Class I, Class IIA, IIB, etc.; or **b) the condition**, and then whether the intervention is Class I, Class IIA, IIB, etc.

Indicate if this is a **Condition** or **Intervention**

Final Class of recommendation: **Class I-Definitely Recommended** **Class IIa-Acceptable & Useful; good evidence** **Class IIb-Acceptable & Useful; fair evidence** **Class III – Not Useful; may be harmful** **Indeterminate-minimal evidence or inconsistent**

Final class of recommendation: Class: Indeterminate

REVIEWER’S PERSPECTIVE AND POTENTIAL CONFLICTS OF INTEREST: Briefly summarize your professional background, clinical specialty, research training, AHA experience, or other relevant personal background that define your perspective on the guideline proposal. List any potential conflicts of interest involving consulting, compensation, or equity positions related to drugs, devices, or entities impacted by the guideline proposal. Disclose any research funding from involved companies or interest groups. State any relevant philosophical, religious, or cultural beliefs or longstanding disagreements with an individual.

I trained in general pediatrics and neonatal-perinatal medicine, and currently practicing in a level 3 NICU at Lucile Packard Children’s Hospital at Stanford in Palo Alto, California. I am also an Associate Professor in the Division of Neonatal and Developmental Medicine in the Department of Pediatrics at Stanford University. This review was undertaken as a component of my duties as a member of the Steering Committee of the Neonatal Resuscitation Program of the American Academy of Pediatrics. I have no conflict of interest, commercial or intellectual, in this matter and have no relationship with any commercial entity whose products could be impacted by the guideline proposal.

REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK: Summarize your final evidence integration and the rationale for the class of recommendation. Describe any mismatches between the evidence and your final Class of Recommendation. “Mismatches” refer to selection of a class of recommendation that is heavily influenced by other factors than just the evidence. For example, the evidence is strong, but implementation is difficult or expensive; evidence weak, but future definitive evidence is unlikely to be obtained. Comment on contribution of animal or mechanical model studies to your final recommendation. Are results within animal studies homogeneous? Are animal results consistent with results from human studies? What is the frequency of adverse events? What is the possibility of harm? Describe any value or utility judgments you may have made, separate from the evidence. For example, you believe evidence-supported interventions should be limited to in-hospital use because you think proper use is too difficult for pre-hospital providers. Please include relevant key figures or tables to support your assessment.

This review seeks to examine the data relevant to the use of continuous positive airway pressure (CPAP) during resuscitation of the human neonate (term or preterm) in the delivery room. The relevant clinical questions are:

- 1) When a full term neonate manifests respiratory distress in the delivery room, is CPAP a safe and effective therapy in comparison to endotracheal intubation and positive pressure
- 2) When a preterm neonate manifests respiratory distress in the delivery room, is CPAP a safe and effective therapy in comparison to endotracheal intubation and positive pressure ventilation?

If the answer to either of these questions is yes, additional questions include:

- 1) Which mode(s) of CPAP is (are) most effective during neonatal resuscitation and do the most

effective modes vary by gestational age? (Described methods of CPAP delivery include facemask, nasal mask, nasal prong(s), nasopharyngeal tube, and endotracheal tube.)

2) Should the pressure delivered during CPAP be generated by manual or mechanical means and does this vary by gestational age?

3) What is the optimal range of pressures to be delivered during use of CPAP and does this vary by gestational age?

4) What is the optimal method for monitoring the airway pressure and does this vary by gestational age?

This review is not meant to address the use of positive end-expiratory pressure (PEEP) during intubation and mechanical positive pressure ventilation.

There is a dearth of literature addressing the six questions listed above. Grunting as a mechanism to maintain lung volume and improve oxygenation in respiratory distress syndrome was described in 1968 (Harrison VC, Heese V, Klein M. The significance of grunting in hyaline membrane disease. *Pediatrics* 1968;41:549-59.). Even though CPAP has been used for decades in neonatal, pediatric and adult populations there are no prospective, randomized, clinical trials comparing CPAP and endotracheal intubation/positive pressure ventilation during neonatal resuscitation. Most of the literature describing CPAP in human term and preterm neonatal subjects describes its use in the neonatal intensive care unit (after resuscitation in the delivery room).

Early research revealed that spontaneously breathing newborns establish FRC more quickly and with lower transpulmonary pressures than sick neonates; in fact, some healthy newborns exhibit measurable lung volume prior to taking their first breath. It is well accepted that CPAP helps establish FRC, increases lung volume, decreases atelectasis, improves lung compliance, improves oxygenation and ventilation, enhances the release of surfactant, reduces the incidence of apnea, decreases pulmonary vascular resistance, and reduces right-to-left shunting. In addition CPAP splints the upper airway (reducing upper airway resistance) and diaphragm, stabilizes the chest wall (which is highly compliant in the neonate), and reduces thoracoabdominal asynchrony. Potential benefits include improved oxygen content, reduced incidence and duration of intubation and mechanical ventilation, and decreased exposure to high airway pressure and high oxygen concentrations. In comparison with intubation, CPAP may result in improved mucociliary flow and decreased risk of infection. Problems described with the use of CPAP include an inability to accurately regulate the pressure delivered; excessive pressures can result in decreased tidal volume, increased dead space, increased work of breathing, decreased pulmonary compliance, reduced pulmonary perfusion, decreased cardiac output, increased ventilation-perfusion mismatching, and increased barotrauma resulting in pneumothorax, pneumomediastinum, and pneumopericardium. Excessive CPAP may also cause inappropriate secretion of antidiuretic hormone and excessive aldosterone secretion resulting in diminished urine output.

Physicians and nurses currently use CPAP in term and preterm neonates in the delivery room based upon their experience with the technique in the nursery and it seems intuitive that the level of respiratory support should be titrated to the degree of respiratory distress.(Graham AN, Finer NN. The use of continuous positive airway pressure and positive end expiratory pressure in the delivery room. *Pediatr Res* 2001;49:400A.) While a number of studies examine the efficacy of “early” CPAP (defined as applied sometime after resuscitation in the delivery room), no sufficiently powered, randomized, prospective, controlled clinical trial addressing the use of CPAP in any form from the first moments after birth could be found by this reviewer. Although written in 2001, the statement by Hammer that “the conclusive randomized controlled trial to verify the benefit of early CPAP application in preterm infants is still missing” is still true and applies to term neonates as well.(Hammer J. Nasal CPAP in preterm infants – does it work and how? *Intensive Care Med* 2001;27:1689-91.) A number of investigators have called for a clinical trial that also examines variables such as the method of delivery (face mask, nasal mask, nasal prongs, nasopharyngeal tube, endotracheal tube), source of positive pressure (manual vs mechanical), range of pressures delivered, and methods of monitoring airway pressure. Such a trial will need to examine clinically significant outcomes in addition to physiologic outcomes as well as compare the relative costs of each therapy.

Preliminary draft/outline/bullet points of Guidelines revision: Include points you think are important for inclusion by the person assigned to write this section. Use extra pages if necessary.

Attachments:

Bibliography in electronic form using the Endnote Master Library. It is recommended that the bibliography be provided in annotated format. This will include the article abstract (if available) and any notes you would like to make providing specific comments on the quality, methodology and/or conclusions of the study.

Citation List

Citation Marker	Full Citation*
----------------------------	-----------------------

<p>{ Allen, 1977 #24 }</p>	<p>Allen LP, Reynolds EOR, Rivers RPA, Le Souef PN, Wimberly PD. Controlled trial of continuous positive airway pressure given by face mask for hyaline membrane disease. Arch Dis Child 1977;52:373-8.</p> <p>ABSTRACT: A controlled trial of elective intervention with continuous positive airway pressure (CPAP) was performed on 24 infants with hyaline membrane disease whose arterial oxygen tension (PaO₂) fell below 8Kpa (60 mmHg) while they were breathing a fractional inspired oxygen concentration (F₁O₂) greater than 0.60. A face mask was used to apply the CPAP. The progress of the 12 infants who were treated on entry to the trial was compared with that of 12 infants who were treated later. All 12 infants in the early-intervention group and 8 infants in the late-intervention group survived. When CPAP was started, Pao₂ increased and the early-treated breathed high concentrations of oxygen for a shorter period than the late-treated infants. The 4 infants in the early-intervention group who required mechanical ventilation needed lower mean airway pressures to conclude that a Pao₂ <8Kpa while breathing a F₁O₂ >0.60 is an adequate indication for giving CPAP in a hyaline membrane disease, and that early intervention with CPAP allows infants who go on to require mechanical ventilation to be ventilated at lower pressures.</p> <p><i>COMMENT: Twenty-four preterm neonates with clinical features of respiratory distress syndrome were randomized to two groups of 12 receiving either early or late mask CPAP when their PaO₂ fell to < 60 mm Hg when breathing FIO₂ > 0.60. Duration of oxygen therapy and need for higher concentrations of oxygen were significantly greater in the late treatment group. This is a prospective, randomized, controlled but under-powered trial. The authors state that "infants assigned to the late-intervention group were managed exactly as the early-intervention group except that CPAP was not started when the criteria for entry into the trial were met." It is unclear exactly when "late" CPAP was started. This study does not address the issue of CPAP during neonatal resuscitation as all of the subjects received CPAP at several hours of age.</i></p> <p>LOE: 7 QA: FAIR</p>
<p>{ Belenky, 1976 #25 }</p>	<p>Belenky DA, Orr RJ, Woodrum DE, Hodson WA. Is continuous transpulmonary pressure better than conventional respiratory management of hyaline membrane disease? A controlled study. Pediatrics 1976;58:800-8.</p> <p>ABSTRACT: The influence of continuous positive airway pressure (CPAP) and positive end-expiratory (PEEP) on mortality and complication rates in severe hyaline membrane disease (HMD) was evaluated in a randomized, prospective study. Patients were admitted to the study if the Po₂ was less than 50 mmHg with FiO₂ greater than 0.6. Twenty-four patients in each of three weight groups were equally divided between treatment and control groups. The treatment regimen included CPAP (6 to 14 cm H₂O) for spontaneously breathing patients and PEEP for patients requiring mechanical ventilation for apnea or hypercapnia (Pco₂ greater than 65 mm Hg). Control patients received oxygen and were mechanically ventilated if they had apnea, hypercapnia, or Po₂ less than 50 mm Hg with FiO₂ greater than 0.8. Oxygenation improved after the start of CPAP or PEEP: however, Pco₂ rose after CPAP was initiated. There was no significant difference between treatment and control groups in mortality, requirement for mechanical ventilation, or incidence of pulmonary sequelae. The incidence of pulmonary air-leak was increased with PEEP. The findings suggest that CPAP and PEEP have not significantly altered the outcome of HMD.</p> <p><i>COMMENT: Seventy-two patients at the University of Washington Hospital, Seattle, Washington, U.S.A., were equally divided among three weight categories (1001-1500, 1501-2000, and > 2001 grams). The 24 patients in each weight category were then equally and randomly divided between treatment and control groups (12 in each group). The treatment group consisted of patients receiving CPAP (6-14 cm H₂O) if spontaneously breathing and PEEP if requiring intubation and mechanical ventilation. Control patients received only oxygen unless they manifested clinical or blood gas signs of respiratory failure. There were no significant differences between treatment and control groups in mortality, requirement for mechanical ventilation, or incidence of pulmonary sequelae. The authors conclude "while useful, continuous transpulmonary pressure should not be considered a breakthrough." This is a prospective, randomized, controlled but under-powered trial. Its relevance to current clinical care, given the tremendous strides in neonatal intensive care technology in the years since its publication, is limited. It does not address the issue of CPAP during neonatal resuscitation.</i></p>

{Claris, 1996 #7}

LOE: 7
QA: FAIR

Claris O, Salle BL, Lapillone A, Ronin E, Picaud JC, Besnier S. Nouvelle technique de pression positive continue par voie nasale en neonatologie. Arch Pediatr 1996;3:452-6.

ABSTRACT: Nasal Continuous positive airway pressure in the treatment of neonatal respiratory distress syndrome. Background- Early treatment with nasal continuous positive airway pressure (CPAP) in newborns with respiratory distress syndrome is useful, by recruiting alveoli and restoring the functional residual capacity. Population and methods-Nasal CPAP was supplied by the Infant Flow Driver (Electro Medical Equipment). From 15 June 1994 to 15 December 1994, 42 neonates received nasal CPAP. Their mean birth weight and gestational age were 1511 ± 411 g and 30.9 ± 2.5 weeks, respectively. Fifteen infants had been ventilated for hyaline membrane disease and nasal CPAP was applied immediately after extubation. In the other 27 infants, nasal CPAP was given soon after birth (respiratory distress syndrome): 20 neonates; apneic spells: seven neonates). Results- Three infants needed subsequent mechanical ventilation because of the severity of the disease (one had spontaneous pneumothorax); four infants received exogenous surfactant (Cerosurf), one single dose) within a brief period of mechanical ventilation (30-45 minutes). There were no failure of extubation, and no intracranial lesions. Excess of pharyngeal secretion abdominal distension were common. Conclusion-Early treatment with nasal CPAP reduces the need for mechanical ventilation. Furthermore, surfactant therapy required by a moderate to severe disease is possible with a rather short period of artificial ventilation.

COMMENT: This is a retrospective, non-randomized, non—controlled study with multiple confounding variables.

{Elgellab, 2001 #17}

LOE: 7
QA: POOR

Elgellab A, Riou Y, Abbazine A, Truffert P, Matran R, Lequien P, Storme L. Effects of nasal continuous positive airway pressure (NCPAP) on breathing pattern in spontaneously breathing premature newborn infants. Intensive Care Med 2001 27:1689-91.

ABSTRACT:

OBJECTIVE: The aim of the study was to assess the influence of nasal continuous positive airway pressure (NCPAP) on breathing pattern in preterm newborns.

DESIGN: Prospective study. **SETTING:** Neonatal intensive care unit. **PATIENTS:** Ten premature newborn infants on NCPAP (gestational age range from 27 to 32 weeks, mean birth weight 1300 ± 460 g) admitted in our neonatal intensive care unit (NICU) for respiratory distress syndrome. **METHODS:** Breathing patterns and plethysmography (RIP), at random CPAP levels (0, 2, 4, 6, and 8 cm H₂O). Raw data were analyzed for end-expiratory lung volume level (EELV-level), tidal volume (V_t), respiratory rate, phase angle and labour breathing index (LBI). **RESULTS:** CPAP increased EELV level by $2.1 \pm 0.3 \times V_t$ from 0 to 8 cmH₂O ($p < 0.01$). V_t increased by 43% from CPAP of 0 cmH₂O ($p < 0.01$). We also found that CPAP lowered the phase angle (from 76 ± 21 degrees at CPAP of 0 cmH₂O to 30 ± 15 degrees of CPAP of 8 cmH₂O) and LBI (from 1.7 ± 0.8 at CPAP of 0 cmH₂O to 1.2 ± 0.8 at CPAP of 8 cmH₂O; $p < 0.05$).

CONCLUSION: NCPAP improves the breathing strategy of premature infants with respiratory failure, as reflected by improved thoraco-abdominal synchrony, increases V_t and reduction of the LBI. This effect is associated with an increase in EELV-level with CPAP level. However, further investigations are necessary to establish the best CPAP level that ensures both safety and efficiency.

COMMENT: The authors prospectively examined breathing patterns and lung volumes using respiratory inductive plethysmography at CPAP levels of 0, 2, 4, 6, and 8 cm H₂O in ten preterm neonates ranging from 27 to 32 weeks estimated gestational age at Centre Hospitalier et Universitaire, Lille cedex, France. They found a steady increase in end expiratory volume and tidal volume as the level of CPAP was increased from 0 to 8 cm H₂O and a corresponding decrease in labour breathing index. This is a prospective, non-randomized, controlled study that examines the efficacy of CPAP using physiologic endpoints. Subjects ranged from 1 to 21 days of age upon

<p>{Gittermann, 1997 #11}</p>	<p><i>initiation of CPAP; therefore this study does not specifically address the use of CPAP during neonatal resuscitation in the delivery room.</i></p> <p>LOE: 7 QA: GOOD</p> <p>Gitterman MK, Fusch C, Gitterman AR, Regazzoni BM, Moessinger AC. Early nasal continuous positive airway pressure treatment reduces the need for intubation in low birth weight infants. Eur J Pediatr 1998;157:384-8.</p> <p>ABSTRACT: Nasal continuous positive airway pressure (CPAP) applied shortly after birth is said to be an effective treatment of respiratory distress in very low birth weight infants (VLBW). We tested the hypothesis that the use of early nasal CPAP (applies as soon as signs of respiratory distress occurred, usually within 15 min. after birth) reduces the need for intubation, the duration of intermittent mandatory ventilation and the incidence of bronchopulmonary dysplasia. All live-born VLBW infants (birth weight of < 1500 g) admitted to our tertiary neonatal intensive care unit in 1990 (historical controls) and in 1993 (early nasal CPAP group) entered the study. The intubation rate was significantly lower after the introduction of nasal CPAP (30% vs 53%, P= 1.016). Median duration of intubation was 4.5 days (interquartile range 3-7 days) before versus 6.0 (2.8-9 days) after nasal CPAP was introduced (P= .073). The incidence of bronchopulmonary dysplasia was not reduced significantly (32% vs 30 %, P=.94). CONCLUSION: Early nasal CPAP is an effective treatment of respiratory distress in VLBW infants, significantly reducing the need for intubation and intermittent mandatory ventilation, without worsening the other standard measures of neonatal outcome. We found no significant decrease in the incidence of bronchopulmonary dysplasia.</p> <p><i>COMMENT: Until 1991 CPAP was not available at the University Women's Hospital, Berne, Switzerland, and therefore all neonates were immediately intubated at the first sign of respiratory distress any time after birth. The authors report their experience during 1990 (prior to use of CPAP) with and 1993 (when they introduced a policy of using CPAP prior to intubation for spontaneously breathing neonates manifesting signs of respiratory distress). Seventy-one and 97 preterm neonates with birth weights < 1500 grams were reviewed in each time period, respectively. The rate of intubation dropped from 53% to 30% but the rate of bronchopulmonary dysplasia did not change significantly (32% vs 30%). None of the potential sequelae of CPAP were noted in the study population. The authors conclude that early nasal CPAP is an adequate initial treatment for mild to moderate respiratory distress in this preterm patient population. This is a retrospective, non-randomized, controlled study that examines differences in patient treatment and outcome in two separate time periods. It defines "early" CPAP as being instituted as soon as signs of respiratory distress occurred, "usually" within 15 minutes of birth; because of this variability it does not directly address the issue of CPAP use during resuscitation. It is also confounded by the fact that the use of prenatal steroids was significantly different during the two study periods (49% in 1990 and 70% in 1993, p = 0.017).</i></p>
<p>{Gregory, 1971 #27}</p>	<p>LOE: 7 QA: POOR</p> <p>Gregory, G. A.Kitterman, J. A.Phibbs, R. H. et al. Treatment of the idiopathic respiratory-distress syndrome with continuous positive airway pressure. N Engl J Med 1971;284:1333-40</p> <p>ABSTRACT: We applied a continuous positive airway pressure to 20 infants (birth weight 930 to 3800 g) severely ill with the idiopathic respiratory-distress syndrome. They breathed spontaneously. Pressure up to 12 mm of mercury, was delivered through an endotracheal tube to 18 infants and via a pressure chamber around the infant's head to two. Arterial oxygen tension rose in all, permitting us to lower the inspired oxygen at an average of 37.5% within 12 hours. Minute ventilation decreased with increased continuous positive airway pressure, but this had little effect on arterial carbon dioxide tension, pH, arterial blood pressure and lung compliance. Sixteen infants survived, including seven of 10 weighing less than 1500 g at birth.</p>
<p>{Guerrini, 2000 #13}</p>	<p><i>COMMENT: This is a prospective, non-randomized, non-controlled study that examines the effects of CPAP used at anywhere from 0.05 to 41 hours of age in patients weighing 930 to 3800 grams.</i></p>

LOE: 7
QA: POOR

Guerrini P, Brusamento S, Rigon F. Assistenza respiratoria con CPAP nasale nei neonati con peso alla nascita inferiore a 1500 g. Acta Biomed Ateneo Parmense 2000;71:S447-52.

ABSTRACT: Objective: To evaluate the efficacy and safety of early nasal continuous airway pressure (CPAP) in the pulmonary management of very low birth weight (VLBW) infants. Method: Since 1993 in our neonatal intensive care unit we decided to reduce the rate of tracheal intubation and mechanical ventilation (IPPV) using more extensively nasal CPAP. By Student's t test and χ^2 analysis, VLBW infants with gestational age <32 weeks born in 1988-92 were compared with those born in 1993-97. Results: The 144 enrolled infants were comparable for birth weight and gestational age. There was a difference in the rate of antenatal steroid administration and cesarean section delivery, significantly more used in the second period. In both groups, 93% of the infants required respiratory support. The use of IPPV decreased from 68% in the first period to 30% in the second, conversely the use of CPAP increased from 25 to 63%. With regard to the primary outcome, in the second period the mortality rate and the incidence of pneumothorax were significantly lower. Conclusions: As the long-term survival of VLBW neonates continues to improve, pulmonary management is increasingly directed at minimizing the invasivity. This study demonstrated that early nasal CPAP may be successfully used in most VLBW infants. Also in the smallest neonates the procedure is safe and effective and may be important in lowering pulmonary morbidity and subsequent mortality.

COMMENT: The authors examined the results of their active decision to reduce the rate of intubation and increase the use of CPAP in very low birth weight neonates in their NICU. They showed a decrease in the rate of intubation (68% to 30%) and increase in the use of CPAP (25% to 63%) from the period 1988-1992 compared to 1993-1997. Mortality rate and the incidence of pneumothorax were significantly lower in the second study period. This is a retrospective, non-randomized, controlled (historical) study with all of the limitations inherent in that design. Significantly more antenatal steroids were used in the second period of study, possibly confounding the results. This study does not address the issue of CPAP during neonatal resuscitation.

LOE: 7
QA: POOR

Han VKM, Beverley DW, Clarson C, Sumabat WO, Shaheed WA, Brabyn DG, Chance GW. Randomized controlled trial of very early continuous distending pressure in the management of preterm infants. Early Hum Dev 1987;15:21-32.

ABSTRACT: Application of continuous distending pressure at birth (very early CDP) should stabilize the immature airways and reduce the severity of respiratory distress syndrome (RDS) in preterm infants. Eighty-two preterm infants of less than 32 weeks gestation were randomly assigned at birth to early treatment group (TG), in which CDP of 6 cm water pressure was applied at birth by the nasopharyngeal route (NP-CDP), or to control group (CG), in which CDP was applied when indicated for established criteria ($pO_2 < 50$ mmHg in $FiO_2 > 0.5$). Characteristics of the infants in the two groups were comparable.

No statistically significant difference between the two groups was found in the incidence of RDS. The course of RDS, and oxygen and ventilatory requirements also did not appear to be changed. In blood gas parameters of most the time frames, no significant difference was found between the two groups when results were analyzed according to the assigned group. When the results were analyzed separately for the infants who developed RDS, infants in the TG appear to have fared worse from the therapy in terms of oxygenation, as indicated by significantly higher FiO_2 ($P < 0.01$) and lower a/A ($P < 0.01$) values on the third day of the course of RDS, as compared to infants in the CG. The incidence of complications was comparable in the two groups. Four infants from TG (9.3%) and one from CG (2.6%) died ($P = NS$). We conclude that VECDP by nasopharyngeal route does not reduce the incidence of RDS and does not appear to improve the outcome may worsen the severity of RDS when compared to application of CDP for established criteria.

COMMENT: Eighty-seven neonates at 32 weeks estimated gestational age or less delivered at St. Joseph's Hospital, London, Ontario, Canada, during an 18 month period were enrolled in this trial. All infants were initially resuscitated by manual bag-mask ventilation at 20-25 cm H₂O; those failing to respond to this intervention were intubated and then extubated if found to be breathing

{Han, 1987
#21}

{Hegy, 1981}

<p>#22}</p>	<p><i>spontaneously. Only those who could maintain adequate ventilation after extubation were included in this trial. Thirty-nine subjects were randomized to receive early nasopharyngeal CPAP (6 cm H2O) and 43 to receive oxygen in a hood; five were excluded because of congenital anomalies or protocol deviations. The study was terminated early due to poor outcomes (worse oxygenation, higher mortality) in the early CPAP group. This is a prospective, randomized, controlled trial. However it does not address the issue of CPAP during neonatal resuscitation.</i></p> <p><i>LOE: 7</i> <i>QA: FAIR</i></p> <p>Hegy T, Hiatt IM. The effect of continuous positive airway pressure on the course of respiratory distress syndrome: The benefits of early initiation. Crit Care Med 1981;9:38-41.</p> <p>ABSTRACT: The course of idiopathic respiratory distress syndrome (IRDS) treated with continuous positive airway pressure (CPAP) was studied in 38 infants with a respiratory index (RI) based on AaDO₂ and PO₂ measurements. Thirteen infants were treated with early CPAP (FiO₂ = 0.3, PO₂ > 50 torr (6.7k Pa)) at a mean age of 15.1 h. Significant differences were demonstrated between the two groups in duration of CPAP (42 vs 72 hours) peak RI (3.7 vs 6.7), time to peak RI from start of therapy (10.0 vs 19.4h), number of infants ventilated (0 vs 5) and number of air leaks (0 vs 3). The rate of disease worsening as measured by changes in RI/h before CPAP and after CPAP initiation was comparable in the respective treatment groups.</p>
<p>{ Kamper, 1993 #5 }</p>	<p><i>COMMENT: Thirty-eight preterm neonates with respiratory distress syndrome at Monmouth Medical Center, Long Branch, New Jersey, U.S.A., were enrolled in this study. Thirteen were randomized to the early and 25 to the late nasal CPAP group. Subjects in the early CPAP group spent significantly less time on CPAP, required intubation less frequently, and experienced less exposure to oxygen and less air leak. This is a prospective, randomized, controlled but under-powered trial. CPAP was initiated in the early CPAP group at an average of seven hours of age; thus this study does not address the issue of CPAP during neonatal resuscitation in the delivery room.</i></p> <p><i>LOE: 7</i> <i>QA: FAIR</i></p>
<p>{ Kamper, 1990 }</p>	<p>Kamper J, Wulff K, Larsen C, Lindequist S. Early treatment with nasal continuous positive airway pressure in very low-birth-weight infants. Acta Paediatr 1993;82:193-7.</p> <p>ABSTRACT: During 1988 and 1989, a regional cohort of 81 infants with birth weights less than 1501 g were treated with oxygen only (n = 11), early continuous positive airway pressure (CPAP) (n = 68) or mechanical ventilation from birth (n = 2). We used an easily applicable lightweight CPAP system with nasal prongs and a gas jet supplemented with ventilator treatment if necessary, but with conservative criteria for ventilator treatment with tolerance of high PCO₂. A total of 65 infants (80%) survived to discharge, 61 of whom were supported solely with CPAP or oxygen. Nineteen infants (26%) developed periventricular-intraventricular haemorrhage, but only 4 survivors (6%) developed prognostically significant bleedings grade 2-4. No survivors had bronchopulmonary dysplasia. Follow-up at 12-39 months of age revealed definite disabilities in 6 (10%) and suspected disabilities in 2 of 62 long-term survivors. The results suggest that treatment by early CPAP with nasal prongs with tolerance of high PCO₂ may be effective and lenient in most infants more than 25 weeks gestation.</p> <p><i>COMMENT: During 1988-1989 81 preterm neonates with birth weight < 1501 grams at Odense University Hospital, Odense, Denmark, were treated with a minimal handling protocol as soon as they arrived at that institution; two were delivered at home and eight were delivered at outside hospitals and transferred. Sixty-eight received CPAP, 11 received oxygen only, and 2 were intubated and received positive pressure ventilation. The failure rate (need for subsequent intubation) was 26% in the CPAP group. The authors conclude that early CPAP and toleration of higher than normal PaCO₂'s is an effective therapy in very low birth weight neonates. This is a prospective, non-randomized, non-controlled study that simply states that the early use of CPAP may have benefits in the very low birth weight population. The timing (in the first minutes? hours? days? of life) of the initiation of CPAP is not clearly stated and thus no comment can be</i></p>

<p>{Lindner, 1999 #12}</p>	<p>age developed bronchopulmonary dysplasia at 36 weeks (BPD 36-wk). The BPD-36wk incidence observed in our population is significantly lower than expected (30%) from the literature ($p = 0.000002$). <i>Conclusion:</i> Our experience supports the effectiveness of the minitouch regime as a way to ventilate premature babies, reducing BPD risk.</p> <p><i>COMMENT: This is a retrospective, non-randomized, non-controlled study where the timing of the initiation of CPAP was unclear. The major outcome was the incidence of BPD. A confounder during the study was a “minimal handling” protocol.</i></p> <p><i>LOE: 7</i> <i>QA: POOR</i></p> <p>Lindner W, Voßbeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weight infants: Spontaneous breathing or intubation? <i>Pediatrics</i> 1999;103:961-7.</p> <p>ABSTRACT: To study the effect of two different delivery room (DR) policies on the rate of endotracheal intubation and mechanical ventilation (EI/MV) and short term morbidity in extremely low-birth-weight infants (ELBWI;<1000 g, >=24 weeks). METHODS: Retrospective cohort study of 123 inborn ELBWI's were intubated immediately after delivery when presenting the slightest signs of respiratory distress or asphyxia after initial resuscitation using a face mask and handbag. During 1995, the guidelines for respiratory support were changed. In 1996, continuous (15 to 20 seconds), pressure controlled (20 to 25 cm H2O) inflation of the lungs using a nasal pharyngeal tube, followed by continuous positive airway pressure (CPAP; 4 to 6 cm H2O) was applied to all ELBWIs immediately after delivery to established functional residual capacity and perhaps to avoid EI/MV. In addition to the changes in respiratory support, the prevention of conductive and evaporative heat loss was improved in 1996. For analysis of morbidity and mortality, infants were matched for gestational age and birth weight. RESULTS: The rate of EI/MV in the DR decreased from 84% in 1994 to 40% in 1996. In 1996, 25% of the ELBWIs were never intubated (7% in 1994), but 35% of the ELBWIs needed secondary EI/MV attributable to RDS in the intensive care unit. ELBWIs with no EI/MV that was caused by RDS had a lower morbidity (i.e., bronchopulmonary dysplasia, intraventricular hemorrhage>grade 2 and/or periventricular leukomalacia), mortality, and fewer hospital days (mean 79 vs 105 days). The incidence of gastrointestinal adverse effects feeding intolerance or necrotizing enterocolitis was not increased in 1996. PaCO2 was significantly higher at admission to the neonatal unit in ELBWIs with CPAP in 1996 (54 ± 15 mmHg, 7.2 ± 2.0 kPa) compared with infants with EI/MV in 1994 (38 ± 11 mmHg, 5.1 ± 1 kPa). A total of 26% of spontaneously breathing infants had hypercapnia ($\text{PaCO}_2 > +60$ mmHg [8.0 kPa]), compared with 7% of infants with EI/MV in 1994. Within the first few hours of life, PaCO2 decreased to 46 (32 to 57) mmHg (6.1 [4.3 to 7.6] kPa) in never intubated ELBWIs ($n = 17$), but increased to 70 (57 to 81) mmHg (9.3 [7.6 to 10.8] kPa) in ELBWIs ($n = 14$) with RDS and secondary EI/MV attributable to RDS. We speculate that an individualized intubation strategy of the ELBWI is superior to immediate intubation of all ELBWIs with slight signs of respiratory distress after birth.</p> <p><i>COMMENT: Until 1994 the delivery room management of all extremely low birth weight neonates at the University of Ulm, Germany, included immediate intubation at the first sign of respiratory distress any time after birth. Subsequently this policy was revised to require intubation only when clear signs of respiratory failure were present; patients first received continuous (15–20 seconds) pressure-controlled (20-25 cm H2O) ventilation via a nasopharyngeal tube followed by CPAP at 4-6 cm H2O. The rate of intubation dropped from 84% to 40% as did the rate of bronchopulmonary dysplasia from 32% to 12%. None of the potential sequelae of CPAP were noted in the study population. The authors speculate that an individualized intubation strategy of extremely low birth weight neonates is superior to a non-selective policy of intubating all such patients who manifest respiratory distress in the delivery room. This is a retrospective, non-randomized, controlled (historical) study that examines the difference in patient treatment and outcome in two separate time periods. It may represent “study effect” in that it may have positively influenced outcome by merely establishing a protocol for the uniform approach to treatment of these patients. It is one of the few studies that examines some aspect of the use of CPAP during resuscitation in the delivery room.</i></p> <p><i>LOE: 4</i> <i>QA: FAIR</i></p>
<p>{Lundstrom, 1996 #9}</p>	

<p>{Milner, 1977}</p>	<p>Lundstrom, KE. Initial treatment of preterm infants—continuous positive airway pressure or ventilation? <i>Eur J Pediatr</i> 1996 Aug;155 Suppl 2:S25-9</p> <p>ABSTRACT: The question of which strategy is the best in the initial treatment of preterm infants has been on debate for years. Especially in Scandinavia, but also in other parts of the world, there is a strong tradition of early treatment with nasal continuous positive intubation and mechanical ventilation. This article gives a brief overview of the history of CPAP, and current treatment strategies as well as the outcomes from a tertiary care Danish neonatal centre are presented. These data suggests that early nasal CPAP may be as good as initial mechanical ventilation with regard to mortality rates and adverse cerebral outcome and perhaps better in preventing chronic lung disease. The results must, however, be interpreted with caution, as the populations in different centres may be incomparable, even when adjustment for severity of illness is performed. A clinical randomized trial comparing initial intubation and mechanical ventilation with initial nasal CPAP using current techniques is therefore not only warranted but is indeed an absolute necessity to answer the question of which treatment is the best</p> <p><i>COMMENT: This is a retrospective, non-randomized, non-controlled study with multiple confounding variables.</i></p> <p><i>LOE: 7</i> <i>QA: POOR</i></p>
<p>{Poets, 1996 #10}</p>	<p>Milner AD, Saunders RA, Hopkin IE. Effects of continuous distending pressure on lung volumes and lung mechanics in the immediate neonatal period. <i>Biol Neonate</i> 1977;31:111-5.</p> <p>ABSTRACT: Twelve healthy term neonates received mask CPAP while in a total body plethysmograph. Intrathoracic pressure was measured using an esophageal balloon system. During CPAP respiratory rate, tidal volume, minute ventilation, total pulmonary resistance and mean dynamic compliance fell whereas thoracic gas volume rose.</p> <p><i>COMMENT: Extrapolation of the data obtained from the use of CPAP in healthy term neonates to the sick term or preterm neonate must be made with caution. This study does not address the issue of CPAP during neonatal resuscitation in the delivery room.</i></p> <p><i>LOE: 7</i> <i>QA: GOOD</i></p> <p>Poets CF, Sens B. Changes in intubation rates and outcome of very low birth weight infants: A population-based study. <i>Pediatrics</i> 1996;98:24-7.</p> <p>ABSTRACT: There have been indications of a recent decrease in intubation rates of veery low birth weight (VLBW) infants sin Germany. We wanted to quantify this decrease and analyze its effect on clinical outcome. <i>Methods:</i> Population-based data on the treatment and outcome at hospital discharge from a statewide quality assurance program were analyzed for 2001 VLBW infants (500 to 1499 g) born from 1992 to 1994 in Lower Saxony, North Germany. <i>Results:</i> The proportion of patients not intubated and mechanically ventilated increased from 28% to 44% in those greater than or equal to 1000 g (P<0.02 and < 0.1, respectively). This increase was not associated with any significant increase in adverse outcome such as death, intraventricular hemorrhage, periventricular leucomalacia, or bronchopulmonary dysplasia (BPD). Instead, there was an increase in the proportion of infants less that 1000 g who survived without BPD (from 38% in 1992 to 48% in 1994; P<0.05) and a decrease in the proportion of infants greater than or equal to 1000 g in whom BPD developed (from 14% to 9%; P<0.05). <i>Conclusions:</i> The data from a statewide quality assurance program show a significant reduction in the aggressiveness of the treatment of VLBW infants, which was not associated with an increased mortality or morbidity. This observational study, however, cannot define whether a more selective approach to the intubation of VLBW infants will ultimately result in a better outcome. A randomized, controlled trial would be required to answer this clinically important question.</p>

<p>{ Polin, 2002 #19 }</p>	<p><i>COMMENT: This manuscript describes changes in the treatment of preterm neonates weighing < 1000 grams during the years 1992-1994 in hospitals in northern Germany. The authors report a non-significant increase in the number who were treated with CPAP and not intubated (from 4% to 6%) and a significant increase in the number who were not intubated and ventilated (from 22% to 34%, p < 0.05) during the three-year period. They also cite an increase in the rate of neonates surviving without bronchopulmonary dysplasia (38% to 48%, p < 0.05). This is a retrospective, non-randomized, controlled (historical) study that while hinting at possible benefits of selective intubation does not specifically address the issue of the use of CPAP during resuscitation. In fact, the rate of use of CPAP did not change significantly during the study period</i></p> <p><i>LOE: 7</i> <i>QA: FAIR</i></p> <p>Polin RA, Sahni R. Newer experience with CPAP. Semin Neonatol 2002;7:379-89.</p>
<p>{ Schmid, 1976 #1 }</p>	<p>ABSTRACT: The authors describe their experience at Children's Hospital of New York/Columbia University, New York, New York, U.S.A., in placing all spontaneously breathing neonates < 1500 grams on nasal prong CPAP (combined with tolerating elevated PaCO₂ levels) as the first mode of respiratory support. They state that the initiation of CPAP occurred between five to ten minutes of life. The authors compare their results during a three-year period (1998-2000) with those of the Vermont Oxford Network during the same time period and show a decrease in the rate of bronchopulmonary dysplasia in their population.</p> <p><i>COMMENT: This is a retrospective, non-randomized review where the control population is from a network comprised of a large number of different institutions. It does not specifically address the use of CPAP during neonatal resuscitation in the delivery room.</i></p> <p><i>LOE: 5</i> <i>QA: FAIR</i></p> <p>Schmid E R, Dangel P H, Duc G V The use of nasal CPAP in newborns with respiratory distress syndrome. Eur J Intensive Care Med 1976 Nov;2:125-30</p>
<p>{ Van Marter, 2000 #15 }</p>	<p>ABSTRACT: The efficiency of applying continuous positive airway pressure (CPAP) by the nasal route was retrospectively analyzed in 32 newborns with RDS (23 uncomplicated HMD with additional cardiac or pulmonary complications and 7 RDS of non-hyaline membrane etiology) who underwent nasal CPAP treatment at the Kinderspital Zurich from 1972-1974. 16 of the 23 infants with uncomplicated HMD were successfully treated with CPAP. They showed a significant rise in PaO₂ as well as a significant drop in respiratory frequency during nasal CPAP application, the PaCO₂ did not change significantly. The remaining 7 infants in this group (7/23) had to be intubated and mechanically ventilated owing to a persistently high FiO₂ (4 infants), technical difficulties (1) or nasal hypersecretion (2). Two of these 23 infants died, one of meningitis, one of cerebral hemorrhage. The two infants with HMD and additional cardiac or pulmonary complications and 3 of 7 infants with RDS of non-hyaline membrane etiology had to be intubated and mechanically ventilated after failure of nasal CPAP. All 9 infants in these two groups survived. The nasal CPAP system as described is a simple, inexpensive, and effective method of applying CPTPP in newborns with uncomplicated HMD, except radiological stage IV. In HMD with additional cardiac or pulmonary complications and in RDS of non-hyaline membrane etiology the results of nasal CPAP treatment were not convincing.</p> <p><i>COMMENT: This is a retrospective, non-randomized, non-controlled study where CPAP was initiated between 3 and 63 hours of age.</i></p> <p><i>LOE: 7</i> <i>QA: POOR</i></p>

Van Marter LJ, Allred EN, Pagano M, Sanocka U, Parad R, Moore M, Susser M, Paneth N, Levitron A. Do clinical markers of barotrauma and oxygen toxicity explain interhospital variation in rates of chronic lung disease? *Pediatrics* 2000;105:1194-1201.

ABSTRACT: The authors compared the rates of bronchopulmonary dysplasia at one New York (Babies' and Children's) and two Boston (Beth Israel and Brigham and Women's) hospitals in 452 preterm neonates born between 500 and 1500 grams during a three-year period (1991-1993). The Boston hospitals displayed a combined rate of 22% whereas the rate at the New York site was only 4%. Performing multivariate logistic regression analyses and after adjusting for baseline risk they determined that most of the increased risk of bronchopulmonary dysplasia was secondary to intubation and the initiation of mechanical ventilation. Sixty-three percent of the subjects at Babies' and Children's Hospital were managed with CPAP while 75% of the subjects at the Boston hospitals were intubated.

COMMENT: This is a retrospective, non-randomized, controlled study whose subjects were enrolled in an epidemiologic study of intracranial white matter disease. As such it has all of the limitations of any study where the original endpoint was designed to be something other than what is described. While hinting at the potential benefits of CPAP it does not specifically address the use of CPAP during neonatal resuscitation in the delivery room.

LOE: 7

QA: FAIR

*Type the citation marker in the first field and then paste the full citation into the second field. You can copy the full citation from EndNote by selecting the citation, then copying the FORMATTED citation using the short cut, Ctrl-K. After you copy the citation, go back to this document and position the cursor in the field, then paste the citation into the document (use Ctrl-V). For each new citation press Tab to move down to start a new field.