

## WORKSHEET for PROPOSED Evidence-Based GUIDELINE RECOMMENDATIONS

<b>Worksheet Author:</b>	<b>Home Subcommittee:</b> UK resuscitation council
<b>Author's Home Resuscitation Council:</b> UK Resuscitation Council	<b>Date Submitted to Subcommittee:</b> 14 <sup>th</sup> October 2003; revised 15 Nov 2004

**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:**

Revision of current guideline

Excerpts from ILCOR 1999 statement - If assisted ventilation is given, higher inflation pressures and longer inflation times may be required for the first several breaths than for subsequent breaths. Some experts suggest very long inflation times (2 to 3 seconds) for initial inflations, but this has not been accepted for universal recommendation. The best method for initially assisting ventilation is with a bag-valve-mask apparatus. If the device contains a pressure release valve, it should release at approximately 30cm H<sub>2</sub>O pressure and should have an override feature to permit delivery of higher pressures if necessary to achieve good chest expansion.

**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).**

New question - Methods of achieving initial lung inflation during resuscitation of term infants are inappropriate for use in preterm infants

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

The textword terms "resuscitation," "infant newborn," and "positive pressure ventilation" were combined. This yielded 6598 articles.

The same search yielded 664 articles when "animal newborn" was substituted for infant newborn.

Substituting "inflation pressure" for "positive pressure ventilation" yielded 47 articles from human infants and 13 from animal studies.

Article titles and, where available on-line, abstracts were reviewed.

List electronic databases searched (at least MEDLINE (<http://igm.nlm.nih.gov/>) and hand searches of journals, review articles, and books.

Medline (Pub Med), EMBASE, Cochrane, hand searches, review articles, books, papers already known to me.

- 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 abstract only studies were included. Only peer reviewed studies were included. All articles, human and animal, relevant to the methods and pros and cons of the methods for applying positive pressure ventilation during resuscitation of preterm infants were selected from these lists. The reference lists of suitable studies were hand searched. Related articles of suitable studies were also searched on PubMed

Other papers already known to me were included and their reference lists were searched,

- 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; End Note 4+ preferred as reference manager, though other reference databases acceptable.

Few articles citing new information that justifies modification of the 1999 guideline were identified. Fifteen were selected as relevant to the hypothesis. Reference file supplied.

## 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.

<b>Level of Evidence</b>	<b>Definitions</b> (See manuscript for full details)
<b>Level 1</b>	Randomized clinical trials or meta-analyses of multiple clinical trials with substantial treatment effects
<b>Level 2</b>	Randomized clinical trials with smaller or less significant treatment effects
<b>Level 3</b>	<u>Prospective</u> , controlled, non-randomized, cohort studies
<b>Level 4</b>	<u>Historic</u> , non-randomized, cohort or case-control studies
<b>Level 5</b>	<u>Case series</u> : patients compiled in serial fashion, lacking a control group
<b>Level 6</b>	Animal studies or mechanical model studies
<b>Level 7</b>	Extrapolations from existing data collected for other purposes, theoretical analyses
<b>Level 8</b>	Rational conjecture (common sense); common practices accepted before evidence-based guidelines

**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.

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

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?**

<b>DIRECTION of study by results &amp; statistics:</b>	<b>SUPPORT the proposal</b>	<b>NEUTRAL</b>	<b>OPPOSE the proposal</b>
<b>Results</b>	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



<b>Quality of Evidence</b>	<b>Excellent</b>								
	<b>Good</b>								
	<b>Fair</b>								
		<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>
		<b>Level of Evidence</b>							

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

**META-ANALYSES: to provide a basis for Step 3**

<p><b>Are there two or more Level 1 studies in Step 2D that support the proposal and are statistically significant at <math>p &lt; 0.05</math>? No</b></p> <p><b>Do these supportive studies constitute at least one quarter of Level 1 clinical trials? No</b>          (If the answer to both questions is “yes”, the null hypothesis is very likely to be false.)</p> <p><b>Do you think there are sufficient data to perform a formal meta-analysis? No</b></p> <p><b>Summarize core numeric data.</b> <i>If you can provide a formal meta-analysis, attach the most critical tabulations, and cite the methodology used.</i></p>
---

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

<b>CLASS</b>	<b>CLINICAL DEFINITION</b>	<b>REQUIRED LEVEL OF EVIDENCE</b>
<p><b>Class I</b>  <i>Definitely recommended.</i>            Definitive,  <b>excellent</b> evidence provides support.</p>	<ul style="list-style-type: none"> <li>• Always acceptable, safe</li> <li>• Definitely useful</li> <li>• Proven in both efficacy &amp; effectiveness</li> <li>• Must be used in the intended manner for proper clinical indications.</li> </ul>	<ul style="list-style-type: none"> <li>• One or more Level 1 studies are present (with rare exceptions)</li> <li>• Study results consistently positive and compelling</li> </ul>

<b>Class II:</b> <i>Acceptable and useful</i>	<ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Not yet confirmed definitively</li> </ul>	<ul style="list-style-type: none"> <li>• Most evidence is positive</li> <li>• Level 1 studies are absent, or inconsistent, or lack power</li> <li>• No evidence of harm</li> </ul>
<ul style="list-style-type: none"> <li>• <i>Class IIa: Acceptable and useful</i></li> </ul> <b>Good</b> evidence provides support	<ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Considered treatments of choice</li> </ul>	<ul style="list-style-type: none"> <li>• Generally higher levels of evidence</li> <li>• Results are consistently positive</li> </ul>
<ul style="list-style-type: none"> <li>• <i>Class IIb: Acceptable and useful</i></li> </ul> <b>Fair</b> evidence provides support	<ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Considered optional or alternative treatments</li> </ul>	<ul style="list-style-type: none"> <li>• Generally lower or intermediate levels of evidence</li> <li>• Generally, but not consistently, positive results</li> </ul>
<b>Class III:</b> <i>Not acceptable, not useful, may be harmful</i>	<ul style="list-style-type: none"> <li>• Unacceptable</li> <li>• Not useful clinically</li> <li>• May be harmful.</li> </ul>	<ul style="list-style-type: none"> <li>• No positive high level data</li> <li>• Some studies suggest or confirm harm.</li> </ul>

<b>Indeterminate</b>	<ul style="list-style-type: none"><li>• Research just getting started.</li><li>• Continuing area of research</li><li>• No recommendations until further research</li></ul>	<ul style="list-style-type: none"><li>• Minimal evidence is available</li><li>• Higher studies in progress</li><li>• Results inconsistent, contradictory</li><li>• Results not compelling</li></ul>
----------------------	--	---

**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.

**Intervention:**

Recommendation. Preterm infants may be susceptible to lung injury during resuscitation. Large volume sustained inflations may be harmful. Equipment used for resuscitating preterm infants should incorporate a pressure-monitoring device. Initial inflation pressure of 20-25 cmH<sub>2</sub>O is adequate for most preterm infants.

**Final Class of recommendation: Class III,**

**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 am a consultant neonatologist in Edinburgh, Scotland with a research interest in respiratory physiology. I am an Associate Neonatal Editor for Archives of Disease in Childhood. I have no conflict of interest relevant to this 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.

In newborn preterm animals it has been known for many years that histological lung injury is demonstrable within a few minutes of the onset of ventilation (Nilsson R et al 1980). More recent data now suggests that the lungs are especially prone to injury during their initial recruitment with the first few inflations after birth (Bjorklund LJ et al 1997, Bjorklund LJ et al 2001, Ingimarsson J et al 2004). There is some correlation between the tidal volumes of the initial inflations and the extent of the injury (Bjorklund LJ et al 2001), but the issue is not purely one of volutrauma because similar inflation volumes applied to the lungs after 10 minutes or 60 minutes of pressure controlled ventilation with PEEP are not injurious (Ingimarsson J et al 2004). Prior administration of surfactant does not appear to protect the lungs from this injury during initial inflation (Ingimarsson J et al 2004). This injury is associated with impaired response to surfactant over subsequent hours, worsening of gas exchange and is demonstrable histologically. Most of this work has been done by a single research group but there is some supporting evidence from another group (Wada K et al 1997).

The same question has not been evaluated directly in human infants but the results of a surfactant trial suggest that human infants respond in a similar way (Kendig JW et al 1998). The results of this trial were somewhat surprising in that chronic lung disease was significantly more common in a population of infants randomized to surfactant treatment immediately after birth than in those administered surfactant at 10 minutes of age. Aside from the difference in timing of surfactant in this trial protocol, the infants treated early were exposed to a different, more vigorous initial bagging procedure. A large body of data from the surfactant trial literature has failed to show any important influence of variations in surfactant

type, or timing on the incidence of chronic lung disease. This leaves the possibility that the increased risk of chronic lung disease was attributable to the difference in initial manual ventilation, as observed in the animal studies.

Comparative studies of different inflation pressures have not been done in preterm infants so recommendations can only be based on what has been described in term infants and animal models as well as on the general principle that excess pressures should be avoided to minimize barotrauma/volutrauma. Three descriptive studies in human newly born infants suggest that most can be effectively resuscitated with an inflation pressure of 20-25 cmH<sub>2</sub>O (Hird MF et al 1991, Hoskyns EW et al 1987, Lindner W et al 1999). Ventilation with self inflating bags generally generates pressures well in excess of this so these should be used with a pressure monitoring device (Howard Glen L et al 1990, Finer NN et al 2001). With the onset of effective ventilation, heart rate increases almost immediately, typically before the resolution of cyanosis (Palme-Kilander C et al 1993). Assessments of chest wall movements are subjective (Spears RS et al 1991, Stenson BJ et al 1995) and inflation of the oesophagus and stomach can be mistaken for adequate ventilation so they are not reliable indicators of adequate ventilation.

The guideline should place greater emphasis on an improving heart rate as the first indication of effective ventilation and less emphasis on good chest wall movement. Placing the greatest emphasis on obtaining good chest wall movement may encourage clinical staff to deliver large, potentially damaging inflations to preterm infants at a time when their lungs are most susceptible to injury. Although most of the data supporting this statement come from observations made on immature animals, good quality human data examining these issues will be very difficult to obtain. The recommendations in the 1999 statement were largely derived from limited data evaluating the first few breaths after birth in term infants. They are irrelevant to preterm infants and continuing to apply them without modification may subject preterm infants to avoidable lung injury during their initial stabilization.

**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:

- Printed (paper) bibliography; and on diskette using a reference manager. It is recommended that the bibliography be printed in annotated format. This will include the article abstract and any notes you would like to make providing specific comments on the quality, methodology and/or conclusions of the study.
- Key figures or tables from evidence-based analysis
- Full hard copies of most critical cited papers

### *Citation List*

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

Bjorklund  
L.J.-1

L. J. Bjorklund, J. Ingimarsson, T. Curstedt, J. John, B. Robertson, O. Werner, and C. T. Vilstrup. Manual ventilation with a few large breaths at birth compromises the therapeutic effect of subsequent surfactant replacement in immature lambs. *Pediatr Res* 42 (3):348-355, 1997.

**Abstract:** The reason why some infants with respiratory distress syndrome fail to respond to surfactant, or respond only transiently, is incompletely understood. We hypothesized that resuscitation with large breaths at birth might damage the lungs and blunt the effect of surfactant. **Methods** Five pairs of lamb siblings were delivered by cesarean section at 127-128 d of gestation. One lamb in each pair was randomly selected to receive six manual inflations of 35-40 mL/kg ("bagging") before the start of mechanical ventilation, a volume roughly corresponding to the inspiratory capacity of lamb lungs after prophylactic surfactant supplementation. Both siblings were given rescue porcine surfactant, 200 mg/kg, at 30 min of age. Blood gases and deflation pressure-volume (P-V) curves of the respiratory system were recorded until the lambs were killed at 4 h. **Results** The P-V curves became steeper after surfactant in the control group, but no such effect was seen in those subjected to bagging. At 4 h, inspiratory capacity and maximal deflation compliance were almost three times higher ( $p < 0.01$ ) in the controls than in the bagged lambs. The latter were also more difficult to ventilate and tended to have less well expanded alveoli and more widespread lung injury in histologic sections. **Conclusion** We conclude that a few inflations with volumes that are probably harmless in other circumstances might, when forced into the surfactant-deficient lung immediately at birth, compromise the effect of subsequent surfactant rescue treatment. Our findings challenge current neonatal resuscitation practice of rapidly establishing a normal lung volume by vigorous manual ventilation

**Critique:**

*Five very large volume sustained inflations immediately after birth, without intervening PEEP and before any preceding pressure controlled ventilation were associated with histological lung injury and sustained impairment of compliance and response to surfactant. These inflations were very large, but this gives rise to anxiety about the appropriateness of an approach to neonatal resuscitation that utilizes sustained inflations delivered by a self-inflating bag without an associated manometer.*

Bjorklund  
L.J.-2

L. J. Bjorklund, J. Ingimarsson, T. Curstedt, A. Larsson, B. Robertson, and O. Werner. Lung recruitment at birth does not improve lung function in immature lambs receiving surfactant. *Acta Anaesthesiol.Scand.* 45 (8):986-993, 2001.

Abstract: **BACKGROUND:** In mature animals with surfactant deficiency induced by lung lavage, the therapeutic effect of exogenous surfactant is enhanced by a lung recruitment maneuver. We then tested whether a lung recruitment maneuver at birth immediately before surfactant treatment would improve lung function also in preterm lambs with surfactant deficiency due to immaturity. **METHODS:** Ten newborn lambs with a gestational age of 127 days were randomized to receive surfactant either before the first breath or immediately after a lung recruitment maneuver consisting of five sustained inflations of 8, 16 or 32 ml/kg. Functional residual capacity was measured by sulfur hexafluoride washout, and inspiratory capacity as well as maximal compliance were obtained from a static expiratory pressure-volume curve after the lungs had been inflated to 35 cm H<sub>2</sub>O. In addition, blood gases were obtained. Measurements were made at 15, 45, 175, 135, 170 and 230 min after birth. Post mortem histological examinations of the lungs were performed in a blinded fashion. **RESULTS:** The lung recruitment maneuvers did not improve oxygenation. Inspiratory capacity, static compliance and functional residual capacity at 4 h, as well as post mortem intrapulmonary air volume, had an inverse relation to the size of inflations given at birth. There was also a negative correlation between size of inflations at birth and response to surfactant therapy, as assessed by lung microscopy. **CONCLUSION:** Lung recruitment at birth does not improve the response to surfactant in immature lambs, but may instead have an adverse effect on lung function and morphology

**Critique:**

*Newborn preterm lambs were given 5 sustained lung inflations without intervening PEEP immediately after birth and before surfactant. Inflation size was normal (8 mL/kg), large (16mL/kg) and very large (32 mL/kg). They then placed on pressure-controlled ventilation with PEEP. Compared to controls without sustained inflations, these animals showed dose-dependent histological lung injury, impaired surfactant response and stiffer lungs over the next 4 hours.*

Finer N.N.

N. N. Finer, W. Rich, A. Craft, and C. Henderson. Comparison of methods of bag and mask ventilation for neonatal resuscitation. *Resuscitation* 49 (3):299-305, 2001.

Abstract: **BACKGROUND:** There are a variety of manual bagging devices used for neonatal resuscitation. To our knowledge, there has been no comparison of the ability of different operators to utilize such devices for the delivery of predetermined inspiratory and end-expiratory pressures. In addition, the use of prolonged inflation may be of benefit for infants who require bag and mask ventilation, and there has been no evaluation of the ability of a variety of operators to reliably deliver such breaths using currently available equipment. **METHODS:** We utilized a neonatal manikin (Laerdal Armonk, NY) with a functional larynx and lungs, and a clear cushioned mask (Owens-BriGam, Morganton, NC). We studied a latex-free disposable anesthesia type bag (Model 5126 Vital Signs, Totawa, NJ), a Jackson-Rees (JR) type anesthesia bag (Model E191 Anesthesia Associates, San Marcos, CA) fitted with a Norman elbow and a flow-control tail-piece (Dupaco, Oceanside, CA), and the Neopuff (Fisher and Paykel, Auckland, New Zealand), an FDA approved mechanical device that is flow-controlled and pressure-limited, specifically designed to facilitate neonatal resuscitation. The ventilating pressures were continuously recorded throughout the process. We evaluated neonatal nurses, neonatal nurse practitioners, neonatal staff and fellows, pediatric residents and neonatal respiratory therapists. **RESULTS:** The peak inspiratory pressure (PIP) was significantly different between operators using either anesthesia bag,  $P < 0.001$ . Similar results were found for positive end-expiratory pressure (PEEP) with a significant difference among the operator groups,  $P < 0.001$ . All the differences in post hoc analysis were between the therapists and the other groups,  $P < 0.05$ . Therapists produced significantly higher pressures than the other groups for both PIP and PEEP ( $P < 0.001$ ). The PIP was similar for all groups using the Neopuff device. The PIP and PEEP delivered by the Neopuff differed from the other two devices independent of the operators ( $P < 0.05$ ). On post hoc analysis, there was a significant difference between the disposable anesthesia bag and Neopuff for both PIP and PEEP for the therapists, whereas among the non-therapists, there was a difference in PIP with the JR device producing a greater PIP ( $26.6 \pm 3.8$  cmH<sub>2</sub>O) compared with the Neopuff and disposable anesthesia bag ( $24.8 \pm 1.1$  cmH<sub>2</sub>O,  $24.8 \pm 4.3$  cmH<sub>2</sub>O). The level of PEEP was significantly different among all three devices for the non-therapists ( $1.3 \pm 1.6$  cmH<sub>2</sub>O, Disposable;  $2.9 \pm 1.2$  cmH<sub>2</sub>O, JR;  $4.7 \pm 0.5$  cmH<sub>2</sub>O, Neopuff;  $P < 0.05$ ). Only the therapists were able to consistently deliver PEEP with the anesthesia bags, whereas all operators could generate the target PEEP with the Neopuff ( $P < 0.05$ ). We compared the pressure delivered during the first second to the pressure delivered during the fifth second during prolonged 5-s inflations. The absolute differences between the first and fifth second for the Neopuff versus the anesthesia bags were significantly different with a median of 7.1 cmH<sub>2</sub>O for the anesthesia bags compared with 0.2 cmH<sub>2</sub>O for the Neopuff,  $P < 0.001$ , reflecting the difficulty in obtaining and maintaining the target inflation pressures. **CONCLUSIONS:** Our experience suggests that the Neopuff, a purpose-built neonatal resuscitator ventilator, facilitates the delivery of the desired airway pressures while maximizing the operators ability to obtain and maintain a patent airway, and facilitates the delivery of prolonged inflations. Further research is required to determine the clinical benefit of end-expiratory pressure and prolonged inflations in neonatal resuscitation.

**Critique:** *PIP is higher with bag devices than with the Neopuff device.*

Hird M.F.	<p>M. F. Hird, A. Greenough, and H. R. Gamsu. Inflating pressures for effective resuscitation of preterm infants. <i>Early Hum.Dev.</i> 26 (1):69-72, 1991.</p> <p>Abstract: The magnitude of inflating pressure necessary for effective resuscitation was examined in 70 preterm infants. The median pressure to cause clinically acceptable chest wall expansion was 22.8 cmH<sub>2</sub>O; no infant required a peak inflating pressure greater than 30 cmH<sub>2</sub>O. No further increase in inflation pressure was used during resuscitation and the median 5- and 10-min Apgar scores were 8 and 9, respectively</p> <p><b>Critique</b> <i>One of 3 papers describing inflation pressures required by preterm infants. Median was 22.8 cmH<sub>2</sub>O.</i></p>
Howard-Glenn L	<p>L. Howard-Glenn and D. Koniak-Griffin. Evaluation of manometer use in manual ventilation of infants in neonatal intensive care units. <i>Heart Lung</i> 19 (6):620-627, 1990.</p> <p>Abstract: Variations exist in the techniques used to perform manual ventilation in neonates and in the proficiency levels of nurses in neonatal intensive care units (NICU) who perform the procedure. <b>Objective</b> This study was undertaken to determine (1) whether significant differences exist in nurses' ability to control prescribed peak inspiratory pressure (PIP) accurately when manometers are used, as compared with when they are not used, during manual ventilation in NICU infants; and (2) whether the number of years of work experience nurses have in the NICU is related to manometer use and success in controlling prescribed PIP. The sample included 60 professional nurses whose experience ranged from 1 to 26 years. <b>Results</b> A statistically significant difference was found in nurses' ability to control PIP successfully when manometers were used as compared with when they were not used (t = 12.04, p = 0.001). Nurses with more experience tended to rely less on manometers to guide their manual ventilation techniques, but were also less accurate in controlling the delivery of PIP without the devices. We provide recommendations for clinical practice based on these findings</p> <p><b>Critique:</b> <i>PIP control is easier with a manometer, regardless of the healthcare provider's experience.</i></p>

Hoskyns E.W.

E. W. Hoskyns, A. D. Milner, A. W. Boon, H. Vyas, and I. E. Hopkin. Endotracheal resuscitation of preterm infants at birth. *Arch Dis Child* 62 (7):663-666, 1987.

**Abstract:** The adequacy of initial ventilation in 21 preterm babies (25-36 weeks' gestation), who required endotracheal intubation and positive pressure ventilation, were studied. **Methods** Pressure and flow were measured at the proximal end of the endotracheal intubation tube and expiratory volume calculated from the flow trace. The results were compared with those from a group of 26 term infants who also required resuscitation. Five of 21 preterm babies (24%) had adequate tidal ventilation with the first inflation. This rose to seven of 21 (33%) by the third inflation. This was significantly less than the results in the term infants (chi 2 = 4.38 p less than 0.05). Respiratory reflex responses to resuscitation were seen in 41% of inflations in preterm and 56% of inflations in term infants. There was a significant correlation between reflex activity and adequate ventilation in the preterm group (chi 2 = 11.83, p less than 0.001) but not in the term group (chi 2 = 0.212, p = NS). No correlation was seen between initial ventilation and outcome.

**Critique:** *Mean inflation pressure given to these preterm infants was 27 cmH<sub>2</sub>O.*

Ingimarsson J.

Ingimarsson J, Bjorklund LJ, Curstedt T, Gudmundsson S, Larsson A, Robertson B, Werner O. Incomplete protection by prophylactic surfactant against the adverse effects of large lung inflations at birth in immature lambs. *Intensive Care Med.* 2004 30(7):1446-53

Abstract: **OBJECTIVE.** To investigate whether preceding surfactant instillation prevents the harmful effect of large lung inflations at birth in immature lambs, and, if not, to find out for how long the immature lung remains sensitive to large inflations. **DESIGN.** In an exploratory study, 12 preterm lambs given surfactant at birth were randomized to receive five large lung inflations at four different times: at birth just before or immediately after surfactant treatment; at 10 min; or at 60 min of age. In a confirmatory study, 10 pairs of preterm lamb twins were all given surfactant before the first breath. One lamb in each pair was randomised to receive large lung inflations immediately after surfactant while the other twin underwent similar inflations at 10-15 min of age. **SETTING.** Animal laboratory. **EXPERIMENTAL ANIMALS.** Anaesthetized lambs delivered by cesarean section at a gestational age of 127 days. **INTERVENTIONS.** Surfactant supplementation at birth. Five sustained lung inflations of 16 ml/kg at different times in relation to surfactant instillation. Pressure-limited mechanical ventilation for 4 h. **MEASUREMENTS AND RESULTS.** The response to surfactant was assessed by ventilator settings, lung mechanics and lung histology. Preceding surfactant supplementation did not prevent the adverse effect of large lung inflations at birth on ventilatory efficiency and lung mechanics, but seemed to protect against severe lung injury. No adverse effect was seen from large lung inflations given at 10 min of age or later. **CONCLUSION.** Prophylactic surfactant supplementation does not fully protect against the harmful effect of large lung inflations during a short sensitive period immediately after birth

**Critique:** *Large sustained inflations immediately after birth, without intervening PEEP caused lung injury whether given before or after surfactant. The same inflations were not injurious if preceded by surfactant and pressure controlled ventilation with peep for 10 minutes or 60 minutes. The lungs seem to be most prone to injury during their initial recruitment.*

Kendig J.W.

J. W. Kendig, R. M. Ryan, R. A. Sinkin, W. M. Maniscalco, R. H. Notter, R. Guillet, C. Cox, H. S. Dweck, M. J. Horgan, L. J. Reubens, H. Risemberg, and D. L. Phelps. Comparison of two strategies for surfactant prophylaxis in very premature infants: a multicenter randomized trial. *Pediatrics* 101 (6):1006-1012, 1998.

**Abstract:** **INTRODUCTION:** Previous trials of surfactant therapy in premature infants have demonstrated a survival advantage associated with prophylactic therapy as an immediate bolus, compared with the rescue treatment of established respiratory distress syndrome. The optimal strategy for prophylactic therapy, however, remains controversial. When administered as an endotracheal bolus immediately after delivery, surfactant mixes with the absorbing fetal lung fluid and may reach the alveoli before the onset of lung injury. This approach, however, causes a brief delay in the initiation of standard neonatal resuscitation, including positive pressure ventilation, and is associated with a risk for surfactant delivery into the right main stem bronchus or esophagus. As an alternative approach, surfactant prophylaxis may be administered in small aliquots soon after resuscitation and confirmation of endotracheal tube position. Although this strategy has substantial logistical advantages in clinical practice, its efficacy has not been established. **OBJECTIVE:** The purpose of this study was to determine whether the established benefits of the immediate bolus strategy for surfactant prophylaxis could still be achieved using a postventilatory aliquot strategy after initial standard resuscitation and stabilization. **DESIGN:** Multicenter **randomized** clinical trial with patients randomized before delivery to immediate bolus or postventilatory aliquot therapy. **PARTICIPANTS:** Inborn premature infants delivered to mothers at an estimated gestational age of 24[0/7] to 28[6/7] weeks. **INTERVENTIONS:** Those infants who were randomized to the immediate bolus strategy were intubated as rapidly as possible after birth, and a 3-mL intratracheal bolus of calf lung surfactant extract (Infasurf) was administered before the initiation of positive pressure ventilation. Those infants who were randomized to the postventilatory aliquot strategy received standard resuscitation measures with intubation by 5 minutes of age, if not required earlier. At 10 minutes after birth, 3 mL of surfactant was administered in 4 divided aliquots of 0.75 mL each. Patients in both groups were eligible to receive up to three additional doses of surfactant as rescue therapy in the neonatal intensive care unit, if needed. **OUTCOME MEASURES:** The primary outcome variable was survival to discharge to home. Secondary variables included neonatal complications and requirement for oxygen therapy at 36 weeks' postmenstrual age. **RESULTS:** Among three centers, 651 infants were enrolled and randomized before delivery. Survival to discharge to home was similar for the two strategies for surfactant therapy as prophylaxis: 76% for the immediate bolus group and 80% for the postventilatory aliquot group. In a secondary analysis, the rate of supplemental oxygen administration at 36 weeks' postmenstrual age was 18% for the immediate bolus group and 13% for the postventilatory aliquot group. **CONCLUSIONS:** Survival to discharge to home was similar with immediate bolus and postventilatory aliquot strategies for surfactant prophylaxis. Because of its logistical advantages in the delivery room and its beneficial effects on prolonged oxygen requirements, we recommend the postventilatory aliquot strategy for surfactant prophylaxis of premature infants delivered before 29 weeks' gestation.

**Critique:**

*More chronic lung disease was seen after immediate surfactant than after treatment at 10 minutes. The immediate group were bagged from birth and received surfactant bagged in as a single bolus. The 10 minute group were only bagged in the first 10 mins as required and received their surfactant bagged in as 4 smaller aliquots several minutes apart. Given that other trials of surfactant have not had an impact on the incidence of chronic lung disease, do these results reflect an adverse outcome from more vigorous early bagging as suggested by the animal studies above?*

Klopping-  
Ketelaars  
WA

Klopping-Ketelaars WA, Maertzdorf WJ, Blanco CE .Effect of sustained inflations applied directly after cord clamping on lung function in premature newborn lambs. Acta Paediatr. 1994;83:1017-21.

**Abstract:** We studied the possibility of improving lung volume and therefore clinical outcome in premature newborn lambs by increasing the inspiratory volumes during the first minute after birth. Sixteen lambs from eight were delivered by hysterotomy after 130-131 days' gestation. In eight lambs the lungs were inflated with a bag with a sustained inspiratory inflation (SI) of 5 s and expiratory time of 5 s during the first four inflations after cord clamping and then mechanically ventilated. Their siblings did not receive SI and served as a control group. At 8 h postnatally, the SI and control groups showed the following results (mean +/- SEM): mean airway pressure 14.8 +/- 1.8 cmH<sub>2</sub>O versus 11.9 +/- 1.1 cmH<sub>2</sub>O, PaO<sub>2</sub> 41.5 +/- 7.3 kPa versus 31.3 +/- 7.7 kPa, alveolar-arterial oxygen gradient 359 +/- 55 mmHg versus 437 +/- 58 mmHg. Clinical course, incidence of pneumothorax, oxygenation index, total static compliance, parenchymal-alveolar air area ratio or mortality rate were not different. There was no significant difference between the two groups at this time or at any other time during the experiments

**Critique:** *Preterm lambs given sustained inflations with PEEP followed by pressure controlled ventilation with PEEP for 8 hours were not significantly different from those just given pressure controlled ventilation with PEEP. Surfactant treatment was not given. Difficult to interpret as neither group received surfactant and both had lung disease and injury.*

Lindner W

Lindner W, Vossbeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weight infants: spontaneous breathing or intubation? *Pediatrics*.1999;103:961-7.

**Abstract:** Objective. 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,  $\geq 24$  weeks). **Methods.** Retrospective cohort study of 123 inborn ELBWIs born in 1994 and in 1996. DR policies have changed. Until 1994, ELBWIs were intubated immediately after delivery when presenting the slightest signs of respiratory distress or asphyxia after initial resuscitation using a face mask and a handbag. During 1995, the guidelines for respiratory support were changed. In 1996, continuous (15 to 20 seconds), pressure controlled (20 to 25 cm H<sub>2</sub>O) inflation of the lungs using a nasal pharyngeal tube, followed by continuous positive airway pressure (CPAP; 4 to 6 cm H<sub>2</sub>O) was applied to all ELBWIs immediately after delivery to establish a 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, primarily because of respiratory distress syndrome (RDS). Initial ventilator settings, ventilator days, mortality, and morbidity were not different between ELBWIs with EI/MV in the DR and infants with 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 (ie, 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 like feeding intolerance or necrotizing enterocolitis was not increased in 1996. PaCO<sub>2</sub> was significantly higher at admission to the neonatal unit in ELBWIs with CPAP in 1996 (54  $\pm$  15 mm Hg, 7.2  $\pm$  2.0 kPa) compared with infants with EI/MV in 1994 (38  $\pm$  11 mm Hg, 5.1  $\pm$  1.5 kPa). A total of 26% of spontaneously breathing infants had hypercapnia (PaCO<sub>2</sub>  $\geq$ 60 mm Hg [8.0 kPa]), compared with 7% of infants with EI/MV in 1994. Within the first few hours of life, PaCO<sub>2</sub> decreased to 46 (32 to 57) mm Hg (6.1 [4.3 to 7.6] kPa) in never intubated ELBWIs (n = 17), but increased to 70 (57 to 81) mm Hg (9.3 [7.6 to 10.8] kPa) in ELBWIs (n = 14) with RDS and secondary EI/MV (age 5.5 [1 to 44] hours). **Conclusions.** In our setting, the individualized intubation strategy in the DR restricted EI/MV to those ELBWIs who ultimately needed it, without increasing morbidity or mortality in infants with 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.

**Critique** *Preterm infants were resuscitated using a ventilator with a sustained inflation of either 20 or 25 cmH<sub>2</sub>O before being put on CPAP. Those that did not breathe adequately got IPPV. Mean initial pressure requirement for ventilated infants was 25 cmH<sub>2</sub>O.*

Nilsson R

Nilsson R, Grossmann, G, Robertson B. Bronchiolar epithelial lesions induced in the premature rabbit neonate by short periods of artificial ventilation. Acta Path Microbiol Scand 1980;88:359-367

**Abstract:** Premature newborn rabbits were ventilated with standardized tidal volume (10 ml/kg) or standardized insufflation pressure (35 cm H<sub>2</sub>O) for 1--30 min. The lungs of the experimental fetuses were fixed by perfusion of the pulmonary artery and examined by light and electron microscopy, with particular reference to the prevalence and ultrastructure of bronchiolar epithelial lesions. Necrosis and desquamation of bronchiolar epithelium were constant findings in fetuses ventilated for 5 min. or more, and were also present in some of the fetuses ventilated for only 1 min. Since the light microscopic and ultrastructural appearance of these bronchiolar lesions is similar to early stages of human neonatal hyaline membrane disease, we conclude that artificially ventilated pre-term newborn rabbits might serve as a useful model of this disease.

**Critique:** *Early demonstration of the rapid onset of lung injury after ventilation in the pre-surfactant era.*

Palme-  
Kilander C.

Palme-Kilander C, Tunell R, Chiwei Y. Pulmonary gas exchange immediately after birth in spontaneously breathing infants. Arch Dis Child. 1993;68:6-10.

**Abstract:** The rate of carbon dioxide production ( $VCO_2$ ), heart rate, and oxygen saturation were recorded during resuscitation in 30 newborn infants. Twenty eight infants were ventilated through a facemask only and two were intubated after initial facemask ventilation. Five neonates were born at full term, eight had a gestational age of 32-36 weeks, and 17 of 27-31 weeks. Towards the end of the five minute study period, the  $VCO_2$  in ventilated infants, born after 32 weeks or more, was not different from that of spontaneously breathing infants. Neonates with a gestational age of 27-31 weeks showed a low  $VCO_2$ , particularly when no reflex response from the baby was recorded, with a significant increase if a reflex response was elicited. Ventilation was found to be satisfactory if the heart rate increased to 130 beats/min or more within 5-15 seconds or if the oxygen saturation, measured in the right hand, was 70% or more

**Critique:** *Heart rate rose rapidly with adequate ventilation, whilst SaO<sub>2</sub> was still around 70%.*

Spears R.S.

R. S. Spears, A. Yeh, D. M. Fisher, and M. S. Zwass. The "Educated Hand". Can Anesthesiologists Assess Changes in Neonatal Pulmonary Compliance Manually? *Anesthesiology* 75:693-696, 1991.

**Abstract:** 24 To determine whether anesthesiologists can manually detect significant changes in pulmonary compliance in neonates using an "educated hand," the authors tested whether clinicians could detect clamping of an endotracheal tube connecting a neonatal lung model to one of three anesthesia breathing circuits. The test lungs corresponded to the lung of a full-term neonate (large lung) or a premature neonate (small lung), and the circuits were a disposable Mapleson D and a disposable pediatric circle system with and without a humidifier. Clinicians having four levels of expertise (inexperienced anesthesia residents, experienced anesthesia residents, faculty not specializing in pediatric anesthesia, and specialized pediatric anesthesia faculty) were permitted to choose fresh gas flows, ventilatory pattern, and rate. After an acclimation period, the endotracheal tube connecting the test lung to the circuit was occluded once for 30 s. Clinicians were credited with a successful detection if they reported the occlusion within 15 s and had fewer than one false positive per minute. With the large lung model, only 4 of 24 clinicians detected occlusion with the Mapleson D circuit; similar results were obtained with the other circuits. With the small lung model, the only successful detection occurred with the Mapleson D circuit. Success at detecting occlusion was similarly low for clinicians with different levels of expertise. The authors conclude that the commonly held belief that the "educated hand" permits clinicians to detect subtle changes in pulmonary compliance in neonates during anesthesia (necessitating manual rather than mechanical ventilation) is not true.

**Critique:** *Experienced clinicians cannot judge lung compliance manually*

Stenson B.J.	<p>B. J. Stenson, R. A. Wilkie, I. A. Laing, and W. O. Tarnow-Mordi. Reliability of clinical assessments of respiratory system compliance (Crs) made by junior doctors. <i>Intensive Care Med.</i> 21 (3):257-260, 1995.</p> <p>Abstract: <b>OBJECTIVE:</b> To assess the reliability of estimates of static respiratory system compliance (Crs) made by junior hospital doctors caring for ventilated newborn infants. <b>DESIGN:</b> A prospective comparison of junior doctors' estimates of Crs to the Crs measured immediately afterwards. <b>SETTING:</b> A regional neonatal intensive care nursery in Edinburgh, Scotland. <b>PATIENTS:</b> 46 ventilated newborn infants. <b>MEASUREMENTS AND RESULTS:</b> Crs was estimated by three grades of junior doctor (Senior House Officer, Registrar and Research Fellow) using two different methods, (i) based on visual assessment of tidal volume in relation to inflation pressure (optical Crs) and (ii) directly using a visual analogue scale (analogue Crs). The Crs was then measured immediately afterwards using the single breath passive expiratory flow technique. The differences between the estimates and the measurements were calculated for each grade of observer and plotted against the corresponding measurements. The relationship between estimates and measurements was also expressed in terms of the coefficients of determination <math>r^2</math> calculated by least squares regression. With both methods of estimation observers tended to overestimate the Crs of infants with lower measured Crs and underestimate that of infants with higher measured Crs with many estimates differing from the measurements by more than 50%. Values of <math>r^2</math> ranged from 0.086 to 0.481 indicating a weak relationship between the estimates and the measurements. <b>CONCLUSIONS:</b> Junior doctors' estimates of Crs were unreliable and did not represent a useful method of assessing respiratory function. The clinical use of compliance measurements merits wider evaluation</p> <p><b>Critique:</b> <i>Clinical assessments of chest wall movement may be unreliable</i></p>
Wada K	<p>K. Wada, A. H. Jobe, and M. Ikegami. Tidal volume effects on surfactant treatment responses with the initiation of ventilation in preterm lambs. <i>J Appl. Physiol</i> 83 (4):1054-1061, 1997.</p> <p><b>Abstract:</b> We hypothesized that initiation of ventilation in preterm lambs with high volumes would cause lung injury and decrease the subsequent response to surfactant treatment. <b>Methods</b> Preterm lambs were randomized to ventilation for 30 min after birth with 5 ml/kg (VT5), 10 ml/kg (VT10), or 20 ml/kg (VT20) tidal volumes and then ventilated with approximately 10 ml/kg tidal volumes to achieve arterial PCO<sub>2</sub> values of approximately 50 Torr to 6 h of age. <b>Results</b> VT20 lambs had lower compliances, lower ventilatory efficiencies, higher recoveries of protein, and lower recoveries of surfactant in alveolar lavages and in surfactant that had decreased compliances when tested in preterm rabbits than VT5 or VT10 lambs. Other lambs randomized to treatment with surfactant at birth and ventilation with 6, 12, or 20 ml/kg tidal volumes for 30 min had no indicators of lung injury. An initial tidal volume of 20 ml/kg decreased the subsequent response to surfactant treatment, an effect that was prevented with surfactant treatment at birth</p> <p><b>Critique:</b> <i>Work from this group also shows dose (tidal volume) dependent lung injury associated with initial ventilation strategy after birth.</i></p>



\*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 Enter to move down to start a new paragraph.