

## Effective ventilation: The most critical intervention for successful delivery room resuscitation



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### ABSTRACT

Lung aeration is the critical first step that triggers the transition from fetal to postnatal cardiopulmonary physiology after birth. When an infant is apneic or does not breathe sufficiently, intervention is needed to support this transition. Effective ventilation is therefore the cornerstone of neonatal resuscitation. In this article, we review the physiology of cardiopulmonary transition at birth, with particular attention to factors the caregiver should consider when providing ventilation. We then summarize the available clinical evidence for strategies to monitor and perform positive pressure ventilation in the delivery room setting.

### 1. Introduction

Lung liquid clearance and aeration is the critical first step that initiates a series of cardiopulmonary events needed for successful newborn transition at birth [1]. When an infant is insufficiently breathing or apneic, this transition fails and prompt intervention is needed in order to avoid (further) hypoxia and ischemic insults. Thus, effective ventilation is the cornerstone of resuscitation after birth [2]. Whereas resuscitation is defined as the process of reviving someone from unconsciousness or apparent death, most infants only need to be stabilized with respiratory support to restore breathing. It is rare for newborns to require extensive resuscitation measures after birth, and in most cases this is because effective ventilation has not been established [3].

Although effective ventilation is the most critical step in newborn resuscitation, current recommendations are largely based on historical practice, evidence from animal models, and dogma. Very little clinical evidence exists to support the current approach to ventilation, in terms of inflation time and pressures used to clear lung liquid, aerate the lung, and establish gas exchange. Our understanding of the mechanisms regulating lung aeration and maintaining the functional residual capacity is largely informed by experimental studies of animal models using phase-contrast X-ray imaging [4]. This knowledge provides a physiologic rationale to approach respiratory support in newborn infants after birth.

In the first part of this review, we discuss the physiological mechanisms of cardiopulmonary transition that the caregiver should consider when providing ventilation at birth. We then review the existing clinical evidence for providing positive pressure ventilation (PPV)

in the delivery room setting.

### 2. The physiology of newborn transition and how this alters during neonatal resuscitation

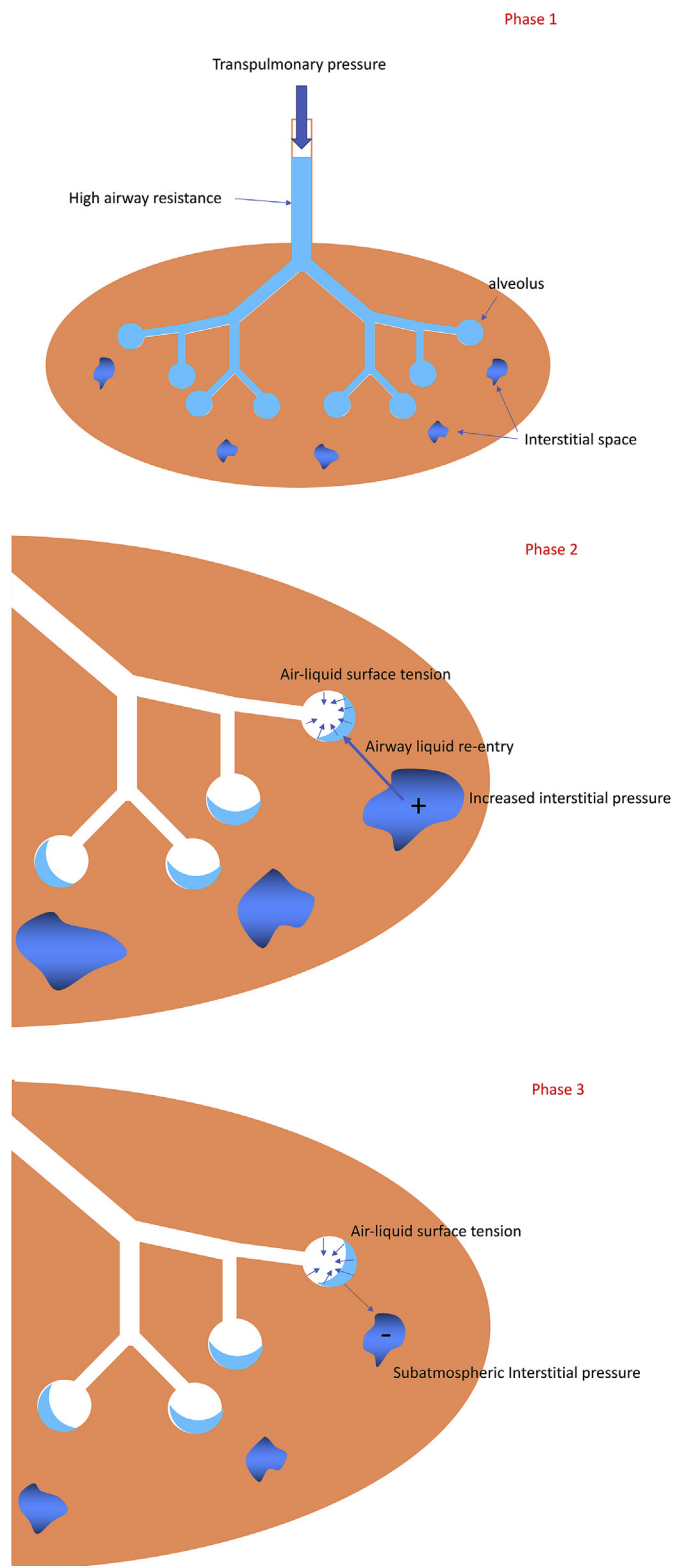
In the last decade, there has been renewed interest in performing experimental and observational human studies in neonatal transition and resuscitation at birth. Several recent reviews provide a comprehensive summary of the current knowledge [4–6]. For the purpose of this review we describe the most important features that caregivers need to take into account when an infant fails transition and requires intervention.

#### 2.1. The respiratory transition at birth passes through three distinct phases

When an infant is born, the lungs are filled with liquid, preventing pulmonary gas exchange. In this first phase the support should be entirely focused on clearing the lung liquid (Fig. 1). A trans-pulmonary pressure gradient plays a key role in driving the lung liquid towards the end-distal airways where it is cleared across the distal airway wall and enters the surrounding interstitial tissue space [7]. Lung liquid has a much higher resistance than air and therefore it is likely that the pressure needs to be higher or given for a longer period. There is very little gas exchange possible during this phase and it is a logical proposition that when an inflation is applied, a period of expiration in between is unnecessary.

After most of the lung liquid is cleared, the second phase commences and pulmonary gas exchange is possible. Between the air and

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**Fig. 1.** Phases of lung aeration during newborn transition. Phase 1: The airways are still fluid-filled, and the emphasis is to clear the fetal lung liquid and aerate the lung. Phase 2: Lung aeration has been achieved and gas exchange is now possible. The air–liquid surface tension is present, and fetal lung liquid (now in the interstitial tissue) increases perialveolar interstitial tissue pressures. The focus of respiratory support is minimizing alveolar collapse and/or reflooding during expiration. Phase 3: The lungs are aerated and liquid is cleared from the tissue. Ventilation is now focused on gas exchange and metabolic homeostasis.

the thin lining of liquid in the alveoli a tension force arises, the air–liquid surface tension, and depending on how much surfactant is present, the alveoli now have the tendency to collapse. In addition, the liquid cleared from the airways during the first phase accumulates and initially resides within the interstitial tissue, increasing perialveolar interstitial tissue pressures and posing the potential for liquid re-entry back into the airways [8,9]. In this second phase the focus of respiratory support should be on minimizing alveolar collapse and/or reflooding during expiration. Thus, adequate levels of positive end-expiratory pressure (PEEP) or continuous positive airway pressure should be applied [9].

In the third phase the infant has passed the immediate transition, the lungs are aerated, and the liquid is cleared from the tissue. Ventilation is now more focused on gas exchange and metabolic homeostasis, which depend on the functional and structural maturity of the lung, respiratory muscles, and chest wall.

## 2.2. The pulmonary and hemodynamic transitions are intimately linked

Lung aeration plays a key role in the sudden increase in pulmonary blood flow (PBF) that is needed after birth. It has been shown in pre-term rabbit pups that aeration of the lung, even with 100% nitrogen, increases both PBF and heart rate [1]. The mechanism has not been elucidated yet, but the global increase in PBF is likely a vagal response to lung aeration [1,10]. Aerating the lungs indicates a rapid accumulation of liquid in the interstitium and could activate juxta-capillary receptors (J-receptors) [11]. It has been reported that in lung edema J-receptors are triggered by fluid accumulation and that via vagal C-fibers cause global pulmonary vasodilatation [12]. The increase in heart rate might be due to triggering of the J-receptors, but it could be also that the rapid increase in PBF, which increases pulmonary venous return and left atrial filling, may increase the heart rate by increasing left ventricular preload [1].

In asphyxiated near-term lambs, heart rate and PBF did not increase until oxygen was added to the gas mixture. However, only a small fraction was needed (5%) whereas increasing the oxygen to 100% did not have any additional effect [13]. This likely indicates that, once aerated, only a small amount of oxygen is needed in the inhaled gas to increase PBF and myocardial energetics. This is likely to result from a direct effect of increasing oxygen levels on both the myocardium and the pulmonary vasculature as well as the effect of lung aeration (irrespective of inspired oxygen level) on PBF [13].

Thus, it is clear that an increase in heart rate is an important indicator of effective ventilation, as it indicates that lung aeration has been successful. However, when the lungs are not uniformly aerated, the neural reflex will cause a prompt increase PBF in both the aerated and non-aerated part, which leads to a ventilation–perfusion mismatch [1]. This is clinically often compensated by increasing the oxygen concentration and thus increasing the alveolar–capillary partial pressure difference.

This also indicates that when lung aeration and thus increased PBF have not been established, the left ventricle output is still largely dependent on the venous return from umbilical venous flow, which flows via the foramen ovale directly into the left atrium [14]. When the umbilical cord is clamped before lung aeration, the loss of umbilical venous return leads to a sudden decrease in preload for the left ventricle. The lung must be aerated with resultant increased PBF in order to restore cardiac output [14].

## 2.3. The transition of the larynx

A patent larynx is required for effective breathing and ventilation at birth. At birth, laryngeal activity needs to change from a fetal to neonatal pattern. Before birth, the glottis is adducted during apnea. This provides a high resistance to liquid efflux from the trachea, promotes fetal lung expansion, and thereby regulates lung growth and

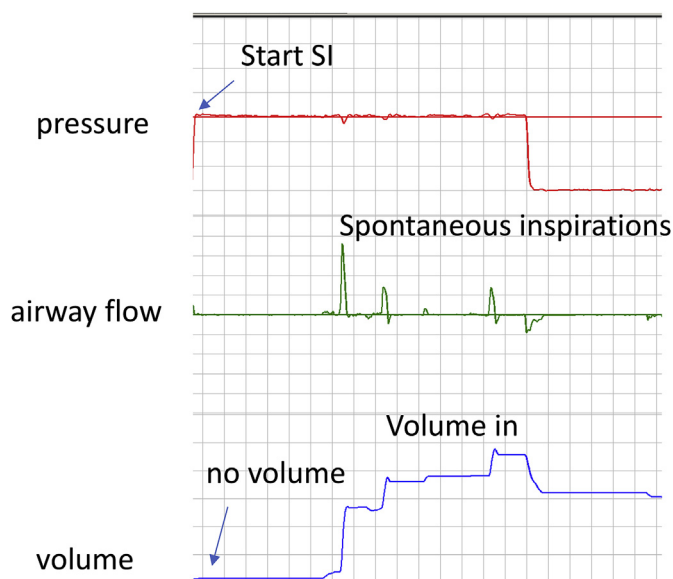


Fig. 2. Impact of closed glottis on tidal volume delivery during sustained inflation (SI). In this respiratory tracing, when the sustained inflation begins, the pressure rises but there is almost no positive flow and no volume enters the lung. When the infant starts spontaneously breathing (and opens the glottis), there is positive flow to the infant with improved tidal volume delivery.

development [15]. The glottis dilates phasically during fetal breathing movements, and the resistance to liquid efflux is temporarily reduced and liquid leaves the lung [16]. It was recently demonstrated that apneic preterm rabbit pups retain their fetal pattern of glottic activity at birth and the glottis is closed unless a breath is taken [17]. The glottis will also relax when an infant becomes severely hypoxic and asphyxiated [17].

Caregivers should be aware that in all infants a closed glottis will prevent facemask ventilation from inflating the lung (Fig. 2). Logically, the best way to open the larynx is to stimulate and support spontaneous breathing, which is also likely to be the most gentle and effective way of providing respiratory care without causing injury.

#### 2.4. Breathing at birth and oxygenation

For a successful pulmonary transition, the infant's respiratory drive has to change from fetal breathing movements, which are discontinuous and generate low transpulmonary pressures and small tidal volumes [18], to breathing after birth, which is regular and with large inspiratory efforts and tidal volumes. The factors that trigger the onset of large inspiratory efforts at birth are not clear but are thought to include activation of chemoreceptors, increased PaCO<sub>2</sub> levels, loss of inhibitory factors on respiratory center activity (prostaglandins, progesterone, adenosine) and physical stimuli (light, temperature, and handling).

Low oxygen level has a direct inhibitory neural input to the respiratory center in the upper lateral pons and suppresses the breathing effort [19]. Increasing the fetal oxygen level removes the inhibition and the fetus will breathe regularly and with large effort [20]. In contrast, hypoxia potentiates the inhibitory neural input and the fetus becomes apneic [21]. During parturition, the infant may become mildly hypoxic. Whereas hypoxia stimulates breathing effort later in life, immediately after birth hypoxia may inhibit respiratory drive, particularly in preterm infants where the maturation of the increase in O<sub>2</sub> sensitivity is delayed [22]. Then during the first few weeks after birth, hypoxia increasingly stimulates respiratory drive due a temporal change in O<sub>2</sub> sensitivity [22]. However, hyperoxia could also inhibit the chemoreceptors as a delay in onset of breathing was observed in asphyxiated infants and animals resuscitated with 100% oxygen [23].

Most preterm infants breathe at birth, but the effort is often insufficient to clear the lung liquid and to aerate the lung in an adequate manner [24]. The caregiver should be aware that breathing can be subtle and is often missed while positive pressure is applied. Because we now use a lower oxygen concentration in order to avoid hyperoxia, hypoxia may occur in the first minutes after birth [25,26], and this should also be avoided as it negatively influences the breathing effort.

### 3. Clinical evidence for the most effective methods to provide ventilation in the delivery room

Initial recommendations for PPV were grounded in historical practice, not clinical evidence. In recent years, many observational studies and clinical trials have focused on identifying the most effective methods to provide PPV in the delivery room setting. Here we discuss residual questions related to delivery room PPV and review the available clinical evidence for each.

#### 3.1. What are the targets for positive pressure ventilation in the delivery room?

The critical target values of key respiratory parameters (such as pressure, volume, and duration) during PPV remain poorly defined. In addition, the most appropriate targets for these parameters will depend on the infant's gestational age and what phase of transition the caregiver is supporting. If the lung is still liquid-filled, the first task is to clear the lung liquid and aerate the lung. Once this process is complete, the caregiver can focus on ventilating the lung with phasic ventilation [5]. Therefore, appropriate respiratory targets for PPV are dynamic, depending on the phase of transition.

##### 3.1.1. Peak pressure

Pressure is currently one of the only respiratory parameters monitored during resuscitation, as manometers are readily available in the delivery room. If the glottis is open, the critical opening pressure needed to achieve initial lung aeration is likely influenced by individual differences in physiology, such as the amount of lung liquid present and the size of the airways and cross-sectional surface area of the epithelium of alveoli [27]. These factors vary by gestational age, the mode of delivery, and whether the infant is apneic or has spontaneously breathed. As discussed in Section 3.1.2, the amount of pressure required to aerate the lung is also influenced by how long the pressure is held.

When term asphyxiated infants ( $n = 12$ ) were intubated during delivery room resuscitation in the 1970s, peak pressures of 13–20 cmH<sub>2</sub>O were necessary for functional residual capacity formation [28]. The critical peak pressures to aerate the lung in preterm infants are unknown but are likely higher as the narrower airways and smaller surface area of the epithelium lead to a higher resistance to move liquid distally and across the epithelium. In addition, surfactant deficiency and a distensible chest wall in the preterm infant lower lung compliance.

In the absence of high-quality evidence to guide starting pressures during PPV, it remains logical to initiate PPV with low pressures and subsequently titrate both peak inspiratory pressures and PEEP according to the infant's clinical response. It is also worth noting that after lung aeration is achieved, there are large and sudden changes in lung characteristics. Thus, the same pressures required to first aerate the lung will likely result in excessive tidal volumes during phasic ventilation.

##### 3.1.2. Duration

As described above, the newly born infant must first clear the lung of residual lung fluid in order to recruit and aerate the lung in the first phase of newborn transition. One method to support lung liquid clearance is to increase peak inflation pressures, but this causes heterogeneous lung recruitment and can induce acute lung injury within

regions of the lung that are already aerated. An alternative strategy is to apply pressure for a longer duration, i.e. a “sustained inflation”. The available preclinical and clinical evidence for sustained inflation have been extensively reviewed [29]. In brief, some of the available randomized controlled trial (RCT) evidence from preterm infants suggests that sustained inflation improves short-term outcomes, such as need for mechanical ventilation in the first 72 h after birth [30]. However, most trials of sustained inflation were not designed to assess the impact of sustained inflation on clinically relevant outcomes, such as bronchopulmonary dysplasia. Until safety and long-term outcome data are available from sufficiently powered trials, such as the ongoing Sustained Aeration of Infant Lungs trial [31], sustained inflation is not currently recommended for routine clinical practice [2].

### 3.1.3. Tidal volume (TV)

In a historic study of spontaneously breathing full-term infants ( $n = 16$ ), the inspiratory TV of initial inflations was the parameter most closely associated with establishment of the functional residual capacity [32]. The mean inspiratory TV required to form the functional residual capacity was 37.7 mL, well over 12 mL/kg for a typical term infant with a birth weight of 3 kg. Many studies of preterm infants have defined an ‘appropriate’ exhaled TV range of 4–8 mL/kg during phasic PPV [33,34], which is largely extrapolated from physiologic data in infants with an aerated lung [35]. However, the tidal volume needed to displace the fetal lung fluid and initially aerate the preterm lung is unknown.

### 3.2. What are the obstacles to performing effective PPV?

PPV is the most important intervention performed during neonatal resuscitation, but it is technically challenging to perform. In preterm infants, there is a narrow therapeutic TV range needed to sufficiently aerate the lung without inducing acute lung injury from overdistention and subsequent brain injury from a systemic inflammatory cascade [36].

To minimize injury, empiric intubation and mechanical ventilation are now avoided, and the focus of respiratory care is non-invasive PPV. Whereas mask ventilation is the first choice of respiratory support after birth, mask technique is more difficult than assumed, even for experienced caregivers. As detailed in other reviews, major obstacles to performing effective ventilation include mask leak and airway obstruction [37,38].

Mask leak is typically caused by a poor-fitting mask or poor mask position or hold. Airway obstruction can be iatrogenic from incorrect head position, insufficient chin lift, or applying the mask to tightly to the face. In addition, a closed larynx can also cause airway obstruction, especially in preterm infants [17]. Finally, if the lung is not yet aerated, there may be a residual liquid column in the airways that needs to be displaced distally; this causes a functional airway obstruction.

Recognizing these common impediments, newborn resuscitation algorithms recommend ventilation corrective steps if the heart rate does not rise in response to initial PPV. Corrective steps include actions to address mask leak (mask adjustment) and physical or functional airway obstruction (repositioning the airway, opening and suctioning the mouth, and increasing peak pressure) [39,40]. These ventilation corrective steps are necessary skills for providers to learn as part of neonatal resuscitation education and training.

Lastly, appropriate recognition of spontaneous breathing is difficult during resuscitation of preterm infants, especially when the infant is wrapped in plastic for thermoregulation. Whereas PPV is recommended for apneic or gasping infants, continuous positive airway pressure and stimulation are appropriate alternative strategies when breathing is present. Observational studies have demonstrated that preterm infants often breathe between and during the inflations given during PPV, which could be counterproductive and potentially lead to injury [41,42].

### 3.3. How should we monitor PPV in the delivery room?

Limited methods exist to monitor the safety and efficacy of PPV in the delivery room setting. Rise in heart rate is considered the best indication of effective ventilation. However, in the absence of rise in heart rate, clinicians have few tools to objectively identify technical impediments or measure the quality of delivered ventilation. In addition, rise in heart rate alone will not identify excessive ventilation, which predisposes the preterm infant to lung and systemic inflammation [36,43]. Potential methods to monitor delivery room PPV include visual assessment of chest rise, exhaled CO<sub>2</sub> detection (both qualitative and quantitative), and respiratory function monitoring.

#### 3.3.1. Chest rise

Visual assessment of chest rise is currently recommended to guide ventilation and indicate ventilation corrective steps [39,40]. However, clinicians' subjective assessment of chest rise during PPV is poorly associated with measured TV delivery [44]. Further, although mask leak and airway obstruction are common during delivery room PPV [45], providers' subjective assessment of mask leak is inaccurate [46]. Importantly, providers are more likely to underestimate than overestimate the delivered TV [44,46], suggesting that reliance on chest rise alone may contribute to excessive TV delivery during PPV.

#### 3.3.2. Exhaled CO<sub>2</sub>

Continuous CO<sub>2</sub> measurements are widely used to monitor ventilation in the neonatal intensive care unit (NICU) setting. In contrast, absolute exhaled CO<sub>2</sub> levels do not reflect arterial CO<sub>2</sub> levels immediately after birth, due to partially fluid-filled lungs, reduced pulmonary blood flow, dead space in the respiratory circuit, and re-breathing CO<sub>2</sub>. In addition, exhaled CO<sub>2</sub> values are typically lower in apneic infants, compared with infants who spontaneously breathe [47,48].

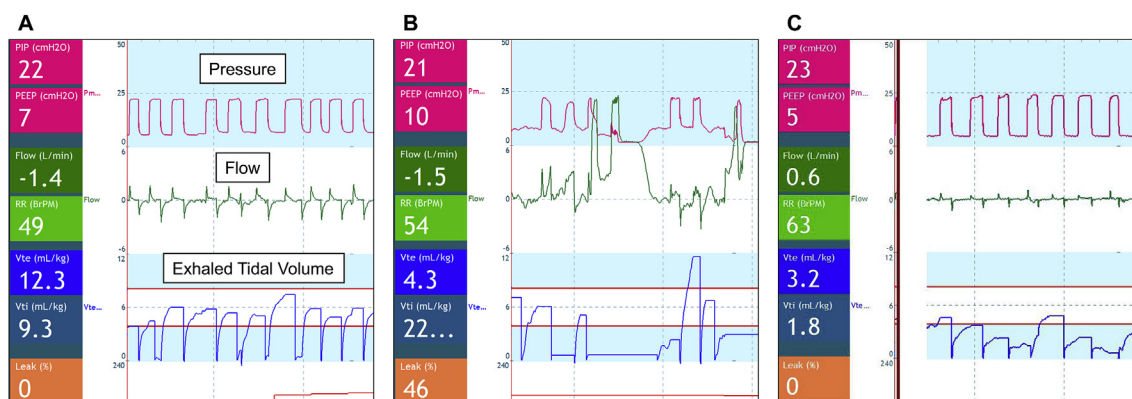
Qualitative exhaled CO<sub>2</sub> detection and rising trends in CO<sub>2</sub> precede rise in heart rate during PPV [49,50] and likely reflect lung aeration [48,51–53]. Whereas many observational studies have demonstrated that exhaled CO<sub>2</sub> monitoring is feasible during delivery room PPV [54], there are limited data suggesting that CO<sub>2</sub> monitoring in the delivery room improves clinical outcomes.

Kong et al. randomly assigned preterm infants who required PPV after birth to have resuscitation guided by exhaled CO<sub>2</sub> monitoring versus clinical assessment alone. In that trial, there were no significant differences in median PCO<sub>2</sub> levels at the end of the resuscitation or upon NICU admission between groups. In addition, the proportion of normocarbic infants at both time-points was not significantly different [55]. Hawkes et al. randomized preterm infants to undergo resuscitation with qualitative CO<sub>2</sub> detector versus colorimetric CO<sub>2</sub> detector. There was no significant difference between groups with regards to the primary outcome, normocarbica on first blood gas, or other clinically relevant clinical outcomes [56].

#### 3.3.3. Respiratory function monitoring

A respiratory function monitor (RFM) uses an in-line flow transducer between the gas flow and facemask to instantaneously calculate and display spirometric data [57]. Displayed inflation parameters include peak pressures, PEEP, expiratory TV, flow patterns, and mask leak (Fig. 3). The RFM provides the potential for volume-targeted delivery room PPV, as opposed to reliance on subjective assessment of chest rise to titrate peak pressures. In addition, the numeric data and respiratory waveforms can be used to identify common impediments to PPV, such as mask leak or airway obstruction (Fig. 3), which would allow a more targeted approach to ventilation corrective steps.

In preliminary manikin studies, use of an RFM improved PPV performance [58–60]. Few studies have investigated the impact of RFM on provider performance and patient outcomes in the clinical environment. In Schmolzer's single-site feasibility RCT, providers performed



**Fig. 3.** Respiratory function monitor display during positive pressure ventilation (PPV). In each display, respiratory data are presented numerically on the left side and with waveforms displayed centrally, as labelled on panel A. (A) Successful PPV: Unobstructed air flow, exhaled tidal volume between 4 and 8 mL/kg, and there is no leak. (B) PPV with consistent mask leak. Air flow is consistently positive, exhaled tidal volumes are inconsistent and often low, and calculated leak is displayed numerically in the bottom left corner. (C) PPV with anatomic or functional airway obstruction. Peak pressures are consistent, minimal positive and negative air flow, exhaled tidal volumes are low, and there is no leak.

PPV for preterm infants with either a visible or masked RFM display; RFM data were recorded in all cases. The median facemask leak was significantly lower in the visible RFM group. In addition, the proportion of infants intubated during PPV – a secondary outcome – was significantly lower in the RFM-visible group [61]. The ongoing MONITOR trial is a multi-site RCT of infants < 28 weeks gestation receiving PPV after birth designed to determine whether a masked versus visible RFM display results in a significantly increased proportion of inflations delivered within a targeted range of exhaled TV [33].

### 3.4. How should we deliver PPV?

Historically, PPV has been applied via facemask and bag in the delivery room setting. Recognition of the technical impediments to safe and effective facemask ventilation have prompted interest in alternative devices and interfaces.

#### 3.4.1. Respiratory devices

Recommended respiratory devices to deliver PPV include a self-inflating bag, flow-inflating bag, and the T-piece resuscitator. These devices all have benefits and pitfalls, and there are insufficient data to identify any one of these as the optimal device for delivery room PPV. In manikin studies, providers deliver PPV with lower and more consistent pressures using the T-piece resuscitator [62,63], prompting an interest in the clinical effectiveness of this device. Guinsburg et al. published a large ( $n = 1962$ ) cohort study of preterm infants < 33 weeks who underwent resuscitation with either T-piece resuscitator or self-inflating bag. After adjusting for important maternal and infant demographic characteristics, infants who received PPV with the T-piece were significantly more likely to survive to discharge without bronchopulmonary dysplasia or severe intraventricular hemorrhage, or periventricular leukomalacia [64].

In by far the largest randomized trial of resuscitation devices, Szylt et al. performed a cluster-randomized crossover trial comparing the T-piece resuscitator with the self-inflating bag among 1027 infants  $\geq 26$  weeks gestation who required PPV after birth [65]. There was no significant difference in the primary outcome of heart rate  $\geq 100$  beats/min at 2 min of life. However, peak pressures delivered with the T-piece were significantly lower and less variable, fewer infants in the T-piece group were intubated in the delivery room, and, in a post-hoc analysis of very low birth weight infants, significantly fewer infants in the T-piece group developed bronchopulmonary dysplasia.

Similarly, Thakur et al. reported that infants resuscitated with the T-piece received PPV for a significantly shorter duration and were less likely to be intubated in the delivery room compared with infants

resuscitated with the self-inflating bag in their quasi-randomized trial of 90 infants > 26 weeks gestation [66]. In contrast, Dawson et al. compared oxygenation parameters among 80 infants < 29 weeks gestation resuscitated with the T-piece resuscitator versus the self-inflating bag [67]. In that RCT, there was no significant difference in median SpO<sub>2</sub> levels at 5 min of life between groups (primary outcome) or delivery room intubation (secondary outcome).

Thus, while the T-piece resuscitator is not necessarily a more effective ventilation device than the self-inflating bag, the more consistent pressures delivered with the T-piece resuscitator may make it a safer device for populations at risk for acute lung injury after birth, such as preterm infants.

#### 3.4.2. Interface

Although PPV is most usually delivered via facemask, alternative interfaces include nasal prongs or a nasal tube, and the laryngeal mask airway (LMA).

Two RCTs compared nasal tube with facemask for PPV in preterm infants. Kamlin et al. randomized 363 infants < 30 weeks gestation to undergo PPV with either single nasal tube or facemask [68]. There was no significant difference in the primary outcome of intubation in the first 24 h of life or any of the short-term secondary clinical outcomes. RFM recordings analysed from 43 infants enrolled in the Kamlin trial demonstrated that airway obstruction and leak were significantly more likely in inflations delivered via nasal tube than facemask [69]. Similarly, McCarthy et al. randomized 144 infants < 31 weeks gestation to receive PPV delivered via nasal tube or facemask. The primary outcome, delivery room intubation, was not significantly different between groups [70].

A laryngeal mask airway (LMA) is inserted orally with the laryngeal mask lumen sitting directly over the supraglottic airway. The LMA is easily placed without laryngoscopy [71], making it ideal for inexperienced providers. Current guidelines recommend the use of LMA as an alternative to endotracheal intubation when facemask ventilation is unsuccessful [39,40]. However, the LMA is also a potential alternative device to the facemask for initiation of PPV. A recent systematic review included four clinical trials comparing LMA to facemask ventilation for primary delivery room PPV [72]. These trials varied in design but all demonstrated that LMA is a safe and feasible method to deliver PPV in infants > 34 weeks gestation. In one RCT in that review, LMA significantly reduced the time to spontaneous breathing during PPV, compared with facemask [73]. In two of the additional trials, infants who received LMA PPV were significantly less likely to be intubated for ineffective ventilation compared with infants who received facemask PPV [74,75].

Thus, there is convincing preliminary evidence that PPV delivered via LMA may be more effective than facemask PPV. However, all infants in these trials were > 34 weeks gestation. There is insufficient evidence to assess the safety and efficacy of LMA in preterm infants < 34 weeks gestation, who are at highest need for PPV in the delivery room.

#### 4. Conclusion

Establishing lung aeration and ventilation is the most critical phase of newborn transition after birth. Respiratory interventions to support this transition should be individualized based on several factors, such as the infant's underlying physiology, the phase of lung aeration, and the infant's response to resuscitation. As there are limited data to identify one best method of providing PPV, providers should be aware of the strengths and limitations of the available techniques, monitoring, and equipment for delivery room PPV.

##### 4.1. Practice points

- Lung aeration triggers the cardiorespiratory adaptation to the post-uterine environment after birth.
- Effective ventilation is the most critical intervention for newborns who need support during neonatal transition.
- Lung aeration occurs in distinct phases, and the focus of respiratory support varies based on the phase of transition.

##### 4.2. Research directions

- To identify the impact of respiratory function monitoring and continuous CO<sub>2</sub> monitoring on providers' PPV performance and clinically relevant outcomes in the newborn.
- To characterize the safety and clinical effectiveness of sustained inflation for lung aeration after birth.
- To determine the safest and most effective devices and interfaces to provide delivery room positive pressure ventilation.

#### Conflicts of interest

The authors are both investigators on the ongoing SAIL trial (Sustained Aeration of Infant Lungs), [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02139800) Identifier NCT02139800 and MONITOR trial (Monitoring Neonatal Resuscitation) trial, [Clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03256578) Identifier NCT03256578.

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