Chapter 5

Respiratory Distress Syndrome Management in Delivery Room

Gianluca Lista, Georg M. Schmölzer and Ilia Bresesti

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.73090

Abstract

The proper management of respiratory distress syndrome in the delivery room is a crucial step in the transition to extrauterine life, especially for preterm infants. In fact, it has been widely established that the optimization of the cardiovascular and the respiratory changes, which normally happen as soon as a term healthy baby is delivered, can have long-term effects. For this reason, every clinician approaching the delivery room should be aware of the consequences an inappropriate management could lead to and should know how to perform a proper resuscitation, using, where available, the most recent techniques. Regardless of the level of care provided by the hospital, there are some key interventions, which can be applied easily in every setting and are of crucial importance. In this chapter, we aim to provide a comprehensive overview of the most relevant measures to manage respiratory distress syndrome from the delivery room, starting from an explanation of the disease and moving toward the most recent evidence, from the basic concepts to the most advanced techniques to monitor fetal-neonatal transition.

Keywords: delivery room, respiratory distress syndrome, newborn, pathophysiology, gestational age

1. Introduction

The delivery room (DR) is the setting where the baby is given birth and where the neonatologist may have to assist the newly born infant in optimizing the transition from dependent fetal to independent neonatal life.

There is a wide consensus among clinicians about the importance of the DR management, especially regarding premature birth. In fact, the adequate management of unstable babies during the transition to extrauterine life can influence lifelong outcomes.

Providing optimal respiratory support is crucial to improve tissue oxygenation and guarantee normal gas exchanges. However, the physiological fetal-neonatal transition includes several crucial steps, which are difficult to achieve when the baby is extremely preterm. In fact, the lung and the chest wall of the preterm infants have essential characteristics making the newborn at the risk of developing respiratory distress syndrome (RDS).

1.1. Pathophysiology of RDS

The respiratory transition is usually recognized as a three-phase process, which reflects the three physiological status of the lung during the transition to extrauterine life.

In the first phase [1] of the respiratory transition, the lungs are fluid filled, and for this reason, no gas exchange can occur. Immediately after birth, with the first few deep breaths, a large tidal volume (V_T) is generated, followed by a cascade of physiological events, promoting the clearance of the fluid from the lungs and the establishment of pulmonary gas exchanges.

All these changes are critical for initiating postnatal circulation and for the achievement of an early and adequate functional residual capacity (FRC).

During the second phase, lung fluid should be prevented from re-entering the lung. In order to avoid the continuous opening and closing of the alveoli, endogenous surfactant and positive end-expiratory pressure (PEEP) play an important role in reducing surface tension and preventing alveoli collapse, respectively.

The third phase, then, is characterized by the initiation of gas exchange and the subsequent establishment of cardio-respiratory homeostasis.

While all these transitions are made by the healthy full-term newborn by himself within a few minutes after birth, preterm infants must deal with several physiological impairments to properly aerate the lung.

In fact, between the periods of viability (23 weeks' gestation) to 35 weeks' gestation, the preterm lung undergoes several complex anatomical and physiological changes, which include structural maturation, increase in surfactant production and storage, improved ability to clear fetal lung fluid, and enhanced epithelial barrier function. All these modifications progressively reduce the incidence of RDS, which falls to 5% when the baby is near term (> 36 weeks of GA).

RDS, also known as hyaline membrane disease, is the most frequent respiratory disorder in preterm infants. Over the last decades, the introduction of antenatal steroids and exogenous surfactant, besides significant improvements in ventilation strategies, have significantly improved survival rate, short-term complications, and long-term respiratory and neurodevelopmental outcomes of the preterm neonate.

RDS typically affects infants <35 weeks gestational age (GA) but older infants who have delayed lung maturation may be at risk as well. Low gestational age (GA) is the greatest risk factor for RDS (**Figure 1**), and its incidence varies inversely with birth weight among adequate for gestational age (AGA) infants (**Table 1**).

http://dx.doi.org/10.5772/intechopen.73090

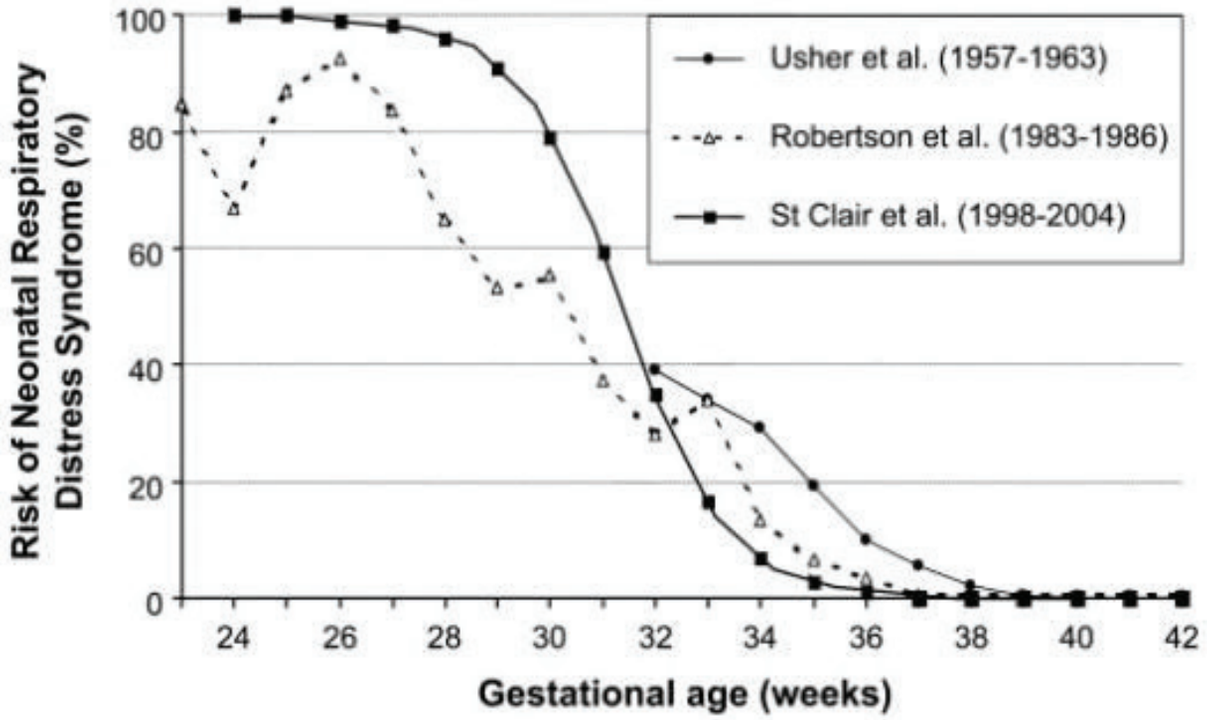

Figure 1. Risk of neonatal respiratory distress syndrome (RDS) as a function of gestational age and at different periods (current, from 1957–1963 prior to the introduction of antenatal steroids, and from 1983–1986 where ~40% of subjects received antenatal steroids). (da Caryn St. Clair "The Probability of Neonatal Respiratory Distress Syndrome as a Function of Gestational Age and Lecithin/Sphingomyelin Ratio", Am J Perinatol. 2008 September; 25(8): 473–480).

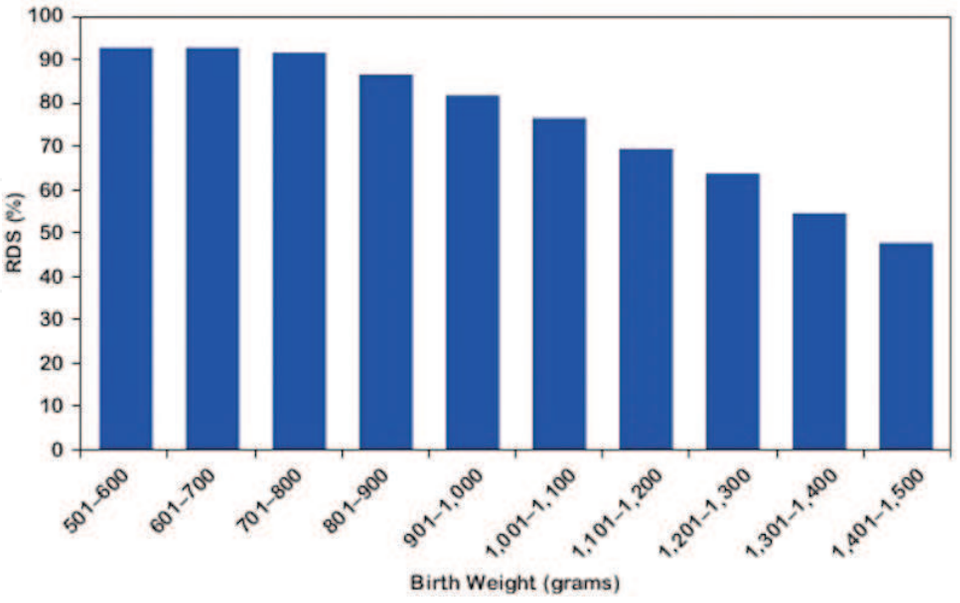

Table 1. Incidence of RDS by Birth Weight (BW) in the United States. Data from Vermont Oxford Network, 2003.

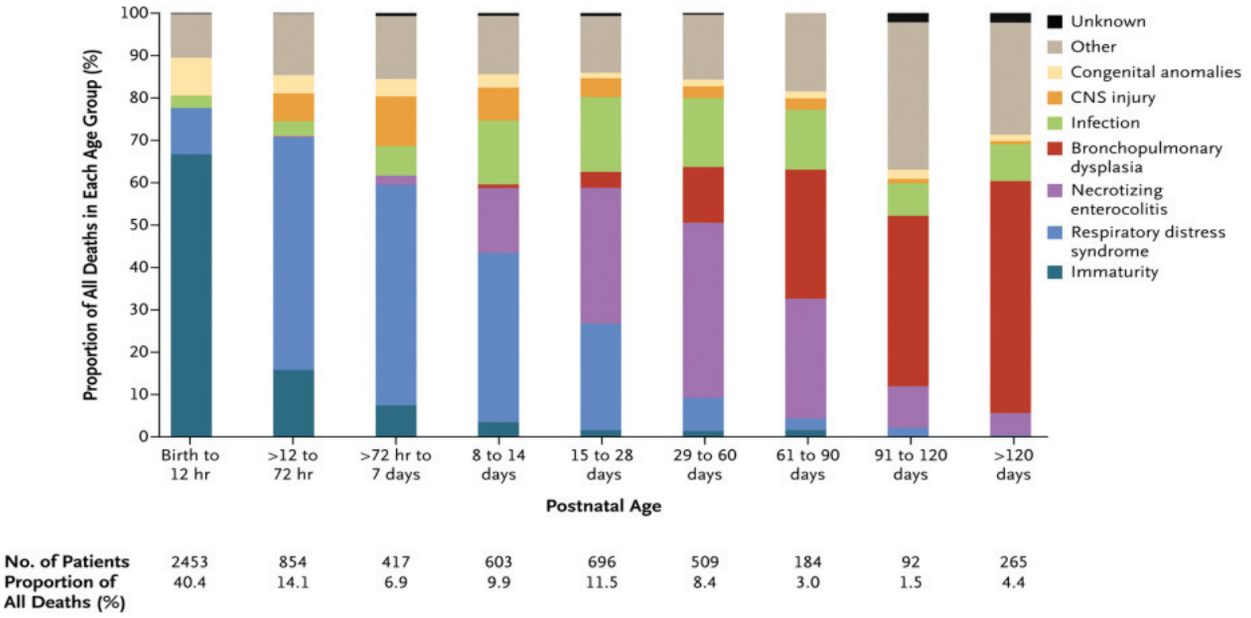

Figure 2. Proportionate mortality for major causes of death, According to postnatal age (da Ravi M. Patel et al, Causes and Timing of Death in Extremely Premature Infants from 2000 through 2011, N Engl J Med. 2015 January 22; 372(4): 331–340.).

The clinical diagnosis is made in preterm infants with respiratory difficulty, which includes tachypnoea, retractions of the rib bones, grunting respirations, nasal flaring, and increasing O_2 requirement. As shown in **Figure 2**, RDS plays a relevant role in premature infants' outcome in the first weeks of life, underlying how the proper ventilatory management is crucial for survival.

2. Interventions in the delivery room

2.1. Thermoregulation

Especially in preterm infants, maintenance of thermal homeostasis is crucial for the success of postnatal transition. This population, in fact, is particularly susceptible to cold stress and hypothermia, related to increased neonatal mortality [2–4].

Thermoregulation after birth is mainly dependent on the capacity of the neonate to activate thermogenesis using brown adipose tissue. Unfortunately, preterm infants lack sufficient brown fatty tissue deposition, and for this reason, they are highly exposed to an unequivocal tendency toward hypothermia once they leave maternal milieu.

The exact range within the newborn body temperature should be kept is not well defined, but using a target range of 36.5–37.5°C seems to be reasonable. On the contrary, mild neonatal hypothermia has been defined as mild when the body temperature is between 36.0 and 36.5°C, moderate at 32.0–35.9°C and severe below 32.0°C. There is a dose-related effect on mortality

with an increased risk of approximately 30% for each degree below 36.5°C body temperature at admission.

Both hypothermia and hyperthermia should be avoided during stabilization and upon admission to the neonatal intensive care unit. Of note, low temperature worsens the susceptibility of premature infants to hypoglycemia. Cold stress with following altered pulmonary vascular tone and metabolic acidosis can worsen respiratory transition and trigger respiratory failure onset.

Systematic monitoring of temperature during resuscitation (preferably skin and rectal) is therefore mandatory to prevent inappropriate uncontrolled temperature variations.

Strategies to minimize heat loss include occlusive wrapping, exothermic warming mattress, warmed humidified resuscitation gases, polyethylene caps, and adequate DR temperature.

It is recommended that DR should be maintained at a temperature ranging 23–26°C, to the upper limits when expecting the birth of a very preterm infant (<28 weeks' gestation) [5]. Then, all infants below 28 weeks' gestation or <1500 g should be wrapped in polyethylene or polyurethane bags [6] up to their necks as soon as they are delivered, without being previously dried, to reduce heat loss and keep an adequate humidity [7]. The head coverage is fundamental, regardless of the material used for the hats, for two main reasons: the brain is a primary heat-producing organ and the head represents an extensive component of the neonatal body surface area.

Exothermic mattresses and radiant heaters are also recommended, with an accurate control of the babies' temperature especially after the first 10 minutes after birth, when the risk of hyperthermia substantially increases [5, 8].

An attractive way to promote thermoregulation is the application of skin-to-skin contact as a means of preventing heat loss at birth. This alternative is obviously applicable only to infants requiring minimal stabilization at delivery, assuming that techniques of skin-to-skin contact are carefully performed.

2.2. Ventilatory strategies promoting airway liquid clearance and alveolar recruitment

As previously mentioned, the preterm neonate, particularly that of an extremely low gestational age (ELGAN), often has limitations in achieving and maintaining "adequate" lung volume, mainly because surfactant production and storage are not sufficient and the respiratory effort is not effective [9].

In a preterm infant, lung volume optimization from the first breath should lead to a more physiological transition to neonatal life while maintaining adequate gas exchange and preventing, or at least limiting, lung injury [10].

The achievement of an adequate FRC at birth seems to be a crucial point for noninvasive respiratory support success.

To facilitate this achievement, reduced lung damage and improved oxygenation, continuous positive airway pressure (CPAP) has been advocated as the optimal strategy for the initiation

of respiratory support [11–13]. If an infant fails to breathe spontaneously, current neonatal resuscitation guidelines recommend positive pressure ventilation (PPV) via a face mask [14].

Devices through which PPV can be applied are different according to the level of care provided by the unit.

Ventilation bags are the most easily found in the delivery room, and given the small V_T of neonates (4–8 mL/kg), they should not be larger than 750 ml to avoid excessive volume delivery and therefore volutrauma.

There are two types of ventilation bags: self-inflating bags and flow-inflating bags. The first one is relatively easier to use, and the recoil of the bags allows refilling even with no compressed gas source. Most self-inflating bags have a pressure release valve to prevent excessive pressure build-up and should release at approximately 30–35 cmH_2O. To deliver 100% oxygen, the bags must be connected to an oxygen reservoir. Otherwise, a maximum of 40% oxygen will be reached.

The flow-inflating bag only inflates when compressed gas is flowing into it, and the patient outlet is occluded. Proper use of flow-inflating bag requires a relative more training and practice.

Neither of these devices is optimal for the stabilization of preterm infants needing CPAP, because self-inflating bags cannot deliver positive pressure continuously, and on the other hand appropriate levels of CPAP are difficult to achieve and maintain with a flow-inflating bag. The T-piece resuscitator is the most widespread device in neonatal units, and like the flow-inflating bag, depends upon a compressed gas source and requires a tight face mask or endotracheal tube to inflate the lungs. With T-piece, it is easier to set and maintain PEEP and to administer PPV. One example of a T-piece resuscitator is the Neopuff™, which is flow-controlled and pressure-limited and specifically designed for application in neonatal settings. There is no wide consensus about which is the optimal PEEP to start resuscitation with. However, the latest ERC guidelines suggest a value around 5–6 cmH_2O [14], while the European Consensus recommends at least 6 cmH_2O to be individualized according to clinical condition, oxygenation, and perfusion [8].

Recent studies on preterm lamb have shown that a stepwise PEEP strategy at birth emphasizing time- and pressure-based recruitment and titrated to the subject's lung mechanics was feasible and demonstrated short-term beneficial results [15]. An observational study describing DR management with stepwise increments of PEEP (e.g., from 8 to 14 cmH_2O) plus surfactant administration among infants <26 weeks GA was shown to improve the rates of survival and morbidity, and reduce the need for mechanical ventilation (MV) [16]. However, since this approach included other interventions that may have interfere the final outcomes, there is a need for further evidence from a randomized trial before gaining wide acceptance.

There are several situations in which using bag and mask or a T-piece resuscitator is not sufficient to provide an efficient ventilation, which is the most important goal to achieve to guarantee normal perfusion and therefore normal gas exchange. The most likely cause for heart rate (HR) < 60 bpm, in fact, is deficient oxygenation of the cardiac tissue.

Tube size (internal diameter)	Birth weight (g)	Gestational age (weeks)
2.5	<1000	<26
3	1000–2000	27–34
3.5	2000–3000	35–40
3.5–4	>3000	>38

Table 2. Suggestions for ETT size (Wyllie P, Neonatal Endotracheal Intubation, Arch Dis Child Educ Pract Ed. 2008 Apr; 93(2):44-9).

When ventilation with these devices does not show effects on chest expansion, HR and/or saturation of peripheral oxygen (SpO_2) or when PPV mask ventilation is prolonged, endotracheal intubation must be considered.

Supplies and equipment for endotracheal intubation should be readily available in the DR.

Intubation can be performed orally or nasally, although the oral way is usually preferred in emergency intubation because it is faster and easier to perform. However, both these techniques have their unique complications and share a few as well.

The tube size should be usually chosen according to the estimated weight of the newborn and/or to gestational age. Suggestions are shown in **Table 2**. However, other clinical considerations must be taken into account (e.g., nares size, malformations, glottis dimension, etc.).

To properly insert the tube at the right depth, a practical rule can be used:

Weight of the baby (kg) + 6 = position of the tube (cm); for example, 2 (kg) + 6 = 8 cm

Another popular way to rapidly calculate the depth of the endotracheal tube insertion is the "7-8-9 rule," which is translated into a baby weighing 1 kg intubated to 7 cm, an infant of 2 kg to 8 cm and one of 3 kg to 9 cm. This method should not be applied in neonates < 750 g [17].

After having achieved alveolar recruitment in the DR, with the initiation of gas exchanges and clearance of lung fluid, is of great importance to maintain a constant distending pressure in the airway using CPAP or PPV, to avoid losing the acquired FRC. For this reason, transport to the neonatal unit must be done with extreme care and should aim at guaranteeing a reliable administration of pressure in the recently recruited lung, always trying to limit the risk of lung injury.

2.3. Heart rate and oxygen saturation

During resuscitation maneuvers, HR and SpO_2 are monitored continuously using pulse oximetry, because they reflect the efficacy of the fetal-neonatal transition process [5].

The pulse oximeter should be placed on the right hand or wrist of the infant as soon as the baby is placed on the resuscitation trolley.

During neonatal resuscitation, an increase in HR is an indicator for effective ventilation [5, 18].

For this reason, a quick and reliable detection of the cardio-respiratory parameters is crucial to optimize critical interventions [19]. In fact, it has been demonstrated that alternative methods such as evaluation of HR using the stethoscope or palpation of the umbilical cord are not as accurate, especially in extremely preterm infants and when the baby is bradycardic [20–23].

Recently, besides the use of pulse oximetry, ECG monitoring has been proposed as an alternative to display HR during resuscitation [24]. However, challenging ECG lead placement on the wet skin, epidermal loss at the site of leads placement, and overestimation of HR in the setting of potential pulseless electric activity need a particular skill by the clinician to avoid delay in resuscitation maneuver.

Since in utero, the fetus is exposed to low relative blood oxygen tension, and thus fetal life occurs in a hypoxic environment, defining specific ranges for normal HR and SpO_2 at birth has been a priority for a rational use of oxygen therapy in the DR.

Preterm infants, in fact, are at high risk for hyperoxia-induced damages due to the immaturity of the mechanism that protects against oxygen free radicals. For this reason, avoid inappropriate O_2 administration, and consequently useless interventions, are mandatory. With the aim of correctly titrating fraction of inspired oxygen ($FiO_{2)}$ in the DR, Dawson et al. have defined the range values for SpO_2 and HR in the newly born infants, which are now incorporated into resuscitation guidelines (**Figure 3**).

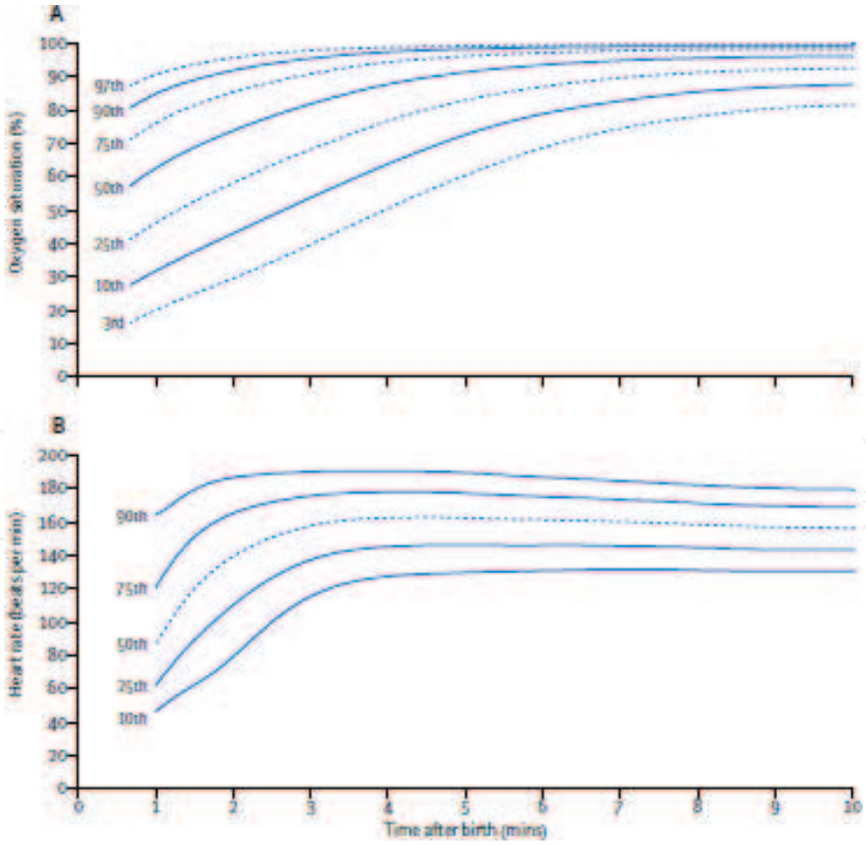

Figure 3. Normal ranges of heart rate and SpO_2 within the first 10 min of life in term and preterm infants who received no medical intervention at birth (Dawson et al.).

However, there is currently uncertainty about the optimal oxygen concentration at which starting resuscitation of preterm infants.

Considering what is shown in a meta-analysis by Saugstad et al. [25], resuscitation of term infants in air reduced mortality in comparison with resuscitation with 100% oxygen. Thus, babies born at term and near-term should initially be resuscitated with air (FiO_2 21%). On the other hand, very preterm infants who are initially resuscitated with air nearly always receive some supplemental oxygen in the subsequent minutes [18, 26]. Then, it seems that starting with intermediate FiO_2 titrating in the course of resuscitation is more appropriate for very preterm infants. Pending further evidence, the latest International guidelines on resuscitation [5] now strongly recommend initiating stabilization of preterm infants less than 35 weeks gestation with lower initial FiO_2 (21–30%). They also advocate against using high oxygen concentrations (65–100%), underlying instead the importance of not exposing these infants to additional oxygen without proven benefit.

2.4. Sustained inflation

Sustained inflation (SI) is defined as "a positive pressure inflation designed to establish FRC and applied over a longer period of time than would normally be used to deliver subsequent tidal inflations" [27].

The rationale behind SI relies on the concept that maintaining positive pressure for a prolonged time provides the lung with the necessary pressure gradient to drive the fluid along the airways distally and aiding transition in infants with inadequate respiratory effort.

For this reason, the SI maneuver is an intriguing approach to allow premature infants to achieve an FRC rapidly. This experimental maneuver has been successfully used to recruit the lung in the early transitional phase to extrauterine life and in preventing repeated collapse and the opening of alveoli preterm animal models [28]. Reports of prompt increases in HR, as well as cerebral and systemic oxygenation in preterm infants exposed to SI in the DR, are signs suggestive of a positive effect of this maneuver [29].

Studying the resuscitation of asphyxiated near-term infants, Vyas et al [30] observed that the first inflations considered at the end of a 1" inflation gas were still entering the lung. Hence, they speculated that a longer inflation time would increase the Vt. They showed that in maintaining the initial inflation for approximately 5", the Vt was doubled. According to these findings, the latest ERC neonatal guidelines recommend to maintain the initial pressure for 2–3" for the first five inflations [14].

Sustained inflation can be delivered with a face mask or through an endotracheal tube. However, effects on infants [31, 32] using face masks have shown to be less impressive than using a tube in animal models [33], probably because of the tendency toward active closure of the glottis in infants during apnea or hypoxia [34, 35].

Observational studies analyzing the effect of SI in the have reported a significant reduction in rates of intubation and MV, bronchopulmonary dysplasia (BPD), and use of oxygen [36],

which led to the design of several randomized controlled trials to compare SI with PPV alone [31, 37].

However, there is a lack of data regarding the optimal pressure to deliver and the best duration of the prolonged inflation. Thus, concerns regarding the safety of this technique still need to be clarified. A potential method could be end-tidal CO_2 ($ETCO_2$) monitoring, which have shown to be feasible to guide length of SI during resuscitation [38]. Also, the effectiveness of SI maneuver can be largely influenced by several factors, such as the different skill of the clinical team, interface through which a SI is delivered [39], the infant's respiratory effort [35] and mask leak [32]. Given these findings, SI might not be the optimal approach in all apneic infants.

This data, besides the paucity of large well-designed RCT on the routine use of SI, especially in the most premature infants, suggest that its application should be actually limited to research settings, in according with AAP [40] and ERC guidelines [14].

2.5. Surfactant administration

The introduction of surfactant replacement therapy in early 1990s was a milestone in the treatment of preterm babies, leading to a significant reduction in mortality and to a different approach in respiratory problems of premature neonates. In fact, exogenous surfactant is nowadays routinely used in clinical practice to treat RDS.

The types of surfactant currently commercialized are animal-derived and are obtained from either bovine or porcine lungs.

Due to its composition, surfactant can reduce surface tension on the inner surface of the alveoli, thus preventing alveoli from collapsing during expiration.

In the last decades, the use of surfactant has changed consistently, and recommendations for its administration have been modified. For decades, the standard stabilization method for very preterm infants <29 weeks GA was endotracheal intubation and surfactant replacement therapy in the DR. However, a recent Cochrane meta-analysis [41] concluded that thanks to the widespread use of antenatal steroids and noninvasive respiratory support, routine prophylactic surfactant treatment provides no advantage over selective surfactant administration. In fact, prophylactic intubation and surfactant administration, compared with early noninvasive CPAP therapy, does not reduce BPD risk in preterm infants [12, 42, 43].

However, the efficacy of noninvasive respiratory support is closely related to GA. Among very low birth weight (VLBW) infants initially managed with N-CPAP about 50% of needs subsequent intubation and MV [11]. For this reason, in very preterm infants, *early rescue* surfactant therapy seems to be appropriate [36, 44] and should be considered early in the DR or immediately at NICU entry. According to the latest Consensus on the management of RDS [8], babies showing signs of RDS are recommended to be treated with early surfactant rescue therapy, and if the baby needs intubation surfactant should be given.

Providing early rescue surfactant (within the first 2 h of life) to mechanically ventilated preterm infants, as compared with delayed surfactant administration (after the second hour of life), reduces the risk of BPD and the composite of death or BPD (RR 0.83, 95% CI 0.75–0.91) [45].

As mentioned previously, prenatal history must be carefully considered among the criteria for surfactant administration (especially prenatal steroids which promotes lungs' maturation).

As it is noted from literature MV, especially when prolonged, has been widely shown to be associated with BPD onset, neurodevelopmental impairment and death [12, 46]. With the aim to reduce these risks, limiting endotracheal ventilation, the so-called INSURE procedure was introduced in clinical practice. It combines intubation, surfactant treatment, then rapid extubation back to noninvasive respiratory support.

Recently, other strategies to administer surfactant avoiding endotracheal intubation and subsequent MV are gaining in popularity [47–49]. They are commonly called "LISA" (Less Invasive Surfactant Administration) or "MIST" (Minimally Invasive Surfactant Therapy). Kribs et al. perform direct laryngoscopy and using a Magill forceps place a feeding tube in the trachea, with no premedication [50, 51]. Overall, the need for MV was reduced; however, no differences in BPD or death were observed. [47]

The MIST technique uses a narrow-bore tracheal catheter during direct laryngoscopy [48, 49] without using Magill forceps.

Observational studies using MIST reported a reduction in the need of MV in 25–28 weeks' gestation babies with a similar trend at 29–32 weeks' gestation.

Although these minimally invasive modes of administering surfactant are promising, their feasibility needs to be better established, especially in the periviable period.

2.6. Early use of caffeine

The early use of caffeine, which has been used for many years to treat apnea of prematurity, seems to be a promising approach. Early treatment (2 vs. 12 h of life) is associated with improved blood pressure and superior vena cava flow without any differences in need for intubation or vasopressors in a small cohort of preterm infants [52].

Moreover, when caffeine is administered early in the DR, it has shown to be effective in increasing spontaneous breathing. Moreover, Dekker et al have found that caffeine enhances the GA-related increase in minute ventilation, and that the stimulatory effect of caffeine on minute ventilation increases with GA [53].

To date, international guidelines do not suggest caffeine administration in the DR, due to lack of extensive studies. However, further evidence is needed to verify its efficacy and benefits when used earlier.

2.7. Practical suggestions:

1. Provide initial alveolar recruitment (using PEEP, short SI, prolonged SI in research setting)
2. Evaluate the presence and efficacy of spontaneous breathing and provide the ventilatory support accordingly:
   - CPAP: **PEEP** = 6 cmH_2O, FiO_2
   - PPV: peak inspiratory pressure (**PIP)** = 25–30 cmH_2O **PEEP** 6 cmH_2O **RR** 40–60 bpm
3. Evaluate response to mask ventilation and titrate support accordingly
   - HR (>100 bpm)
   - SpO_2 (consider postnatal range values)
   - If available, use $ETCO_2$ device and RFM to verify gas exchange and exhaled V_T (V_{Te})
4. Consider surfactant administration
5. Assure maintenance of recruitment during transport to NICU (PPV/CPAP delivered with mask or endotracheal tube or prongs)

2.8. Cord clamping

The current neonatal resuscitation guidelines recommend in term infants delayed cord clamping (DCC) for at least 30 s, although the optimal timing is poorly studied. DCC as opposed to early cord clamping is associated with increased birthweights, hemoglobin levels at 24–48 h, iron stores at 3–6 months [54] and reduced hospital mortality [55]. However, there are some areas of concern surrounding DCC.

Babies undergoing DCC seem to be more likely to need phototherapy for jaundice. It is hypothesized that DCC babies will have a greater incidence of hyperbilirubinemia due to increased iron stores. Pending further evidence, this is an important aspect to consider in settings where kernicterus is common.

Regarding the influence of DCC on respiratory mechanics, there is lack of evidence. A Cochrane review found that babies receiving DCC babies are no more at risk than ICC infants of developing RDS [56], despite limited numbers of studies included and the small size population.

When a baby requires resuscitation or shows clinical conditions, which suggest medical interventions, DCC is not recommended. Thus, under specific circumstances (severe respiratory failure, asphyxia, etc.) an alternative maneuver called "*cord milking*" has been proposed. It consists of stripping the umbilical cord approximately 20–40 cm once or several times (2–4) from the placental end toward the proximal site of the cord. It can be performed in few seconds either while the cord is still attached to the placenta or not.

Whether cord milking is a valid alternative to cord clamping is still under investigation. However, in a population of term infants, early cord clamping with cord milking has shown

to increase hemoglobin concentration and iron stores at 6 months of age [57]. The same procedure in late preterm infants is associated with improved iron stores at 6 weeks but also increases the risk of jaundice needing phototherapy [58].

There is paucity of evidence regarding the effects of cord milking on neurodevelopmental outcomes.

2.9. Monitoring during neonatal transition

Although the use of multiple devices monitoring resuscitation (pulse oximetry, ECG, respiratory function monitor-RFM, end-tidal CO_2, NIRS) is still challenging in the DR, there is an increasing interest in monitoring physiologic changes during neonatal transition [59–62].

When preterm infants need respiratory assistance in the delivery room, RFM is desirable to deliver adequate and gentle resuscitation maneuvers and to identify potential pitfalls during mask ventilation [63]. However, establishing this approach may be technically challenging.

Despite all the efforts to optimize resuscitation by the neonatologists, there are several situations in which the efficacy of PPV or CPAP mask ventilation is compromised.

Mask leaks, airways obstructions (e.g., laryngeal closure [64]), interruptions of ventilation due to drying or hat placing are just some examples of how the ventilation can lose efficacy and be suboptimal [65] to deliver a safe and appropriate Vt.

Moreover, the majority of VLBW infants often show a respiratory effort, which is difficult to evaluate, making the decision to start PPV or use CPAP only particularly tricky. Especially in these babies, delivering the adequate Vt is fundamental, because of the high risk of damaging the lung with volutrauma. Measuring the Vt, in fact, is not currently possible without specific devices.

The RFM (**Figure 4**) can integrate and show in real-time information about pulse oximetry and the main respiratory data, reflecting the efficacy of the resuscitation maneuvers. Particularly, a pneumotachometer connecting the resuscitator device and the patient interface provides data of delivered pressures and flows [66, 67] (**Figure 5**). Integration of the flow signal offers data on inspiratory and expiratory tidal volumes (Vti and V_{Te}). This information helps the neonatologist in changing the PIP level to achieve adequate ventilation (**Figure 2**). Moreover, real-time observation of the flow signal is useful to detect face mask leaks or obstructions, which significantly influence a successful mask ventilation. In addition, the flow signal can help in verifying the efficacy of endotracheal intubation.

Upon informed parental consent, RFM can also be used in debriefing sessions of the resuscitation team or for educational purposes, since it is able to video-record the DR stabilization process.

However, RFM does not provide information about the success of lung aeration.

Carbon dioxide (CO_2) levels are good indicators of efficacy in gas exchange [68], and for this reason, colourimetric CO_2 detector is currently used to detect the correct placement of the endotracheal tube [69–71].

Figure 4. Resuscitation setting with RFM.

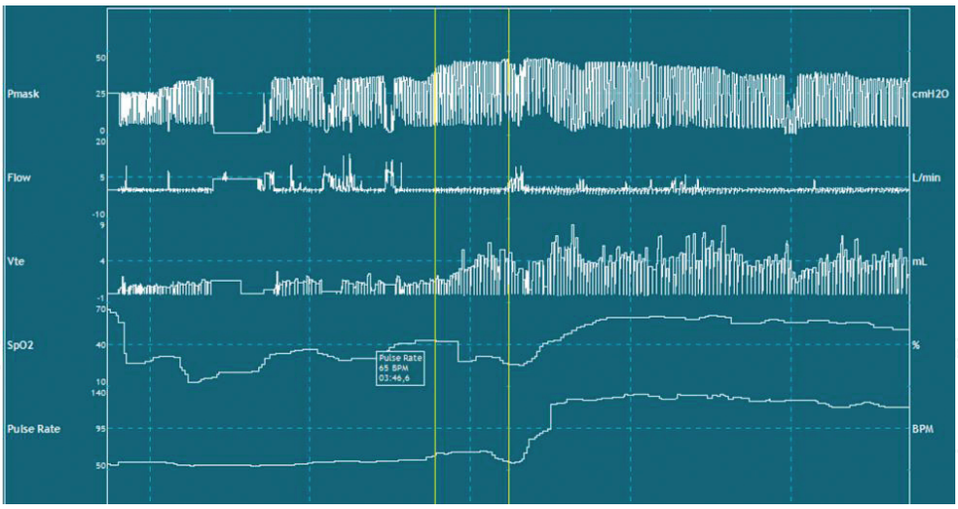

Figure 5. The picture describes the signals recorded by an RFM during stabilization of a preterm infant in the DR. The signal of pressures delivered during mask PPV is indicated as Pmask, expired tidal Volume calculation (V_{Te}), flow signal, pulse rate, and oxygen saturation (SpO_2) are recorded concurrently. Pulse rate and SpO_2 raise in this example is clearly related to raise in peak pressures during mask PPV with a following increase in V_{Te}.

To date, several observational studies have reported the value of using exhaled CO_2 measurement to assess lung aeration and guide respiratory support in the DR [59, 68].

Even if it is a new technique, which must be further investigated to be standardized as a routine practice in the DR, $ETCO_2$ monitoring has been recently shown to be a promising

measurement to evaluate the degree of lung aeration and the onset of gas exchange. Moreover, it has been successfully used to monitor SI maneuver during resuscitation [38].

While peripheral oxygen saturation is easily monitored by pulse oximetry and is routine in the DR, Near-infrared spectroscopy (NIRS) allows noninvasive continuous real-time measurement of the regional tissue oxygen saturation. Hence, using NIRS has the potential to monitor cerebral oxygen delivery [72]. Having this information during resuscitation of preterm babies with RDS, could optimize the use of oxygen in the DR and reduce its potential damages.

All the techniques described are potentially intriguing, but further evidence is needed to apply them into routine clinical practice in the DR.

3. Summary

Preterm infants at birth have to face with several limitations, which are inversely proportional to their gestational age. Moreover, prenatal factors play a crucial role in the prognosis and can guide the clinicians in the decision-making process, as early as in the DR.

Antenatal steroids prophylaxis, maternal complications (e.g., diabetes or gestosis) or intrauterine growth restriction may influence surfactant synthesis and storage, mode of delivery and use of general anesthesia may interfere in fetal-neonatal transition and therefore must be considered when the baby is about to be delivered and when resuscitation starts. If RDS signs are already present at birth, several interventions can be adopted to optimize cardiorespiratory management, to improve gas exchange and therefore oxygenation.

An appropriate management from birth, in fact, should lead to the achievement of an early FRC and the following steps should aim at maintaining an adequate lung volume facilitating a more stable systemic and cerebral hemodynamics.

Literature underlines the importance of a tailored respiratory management of preterm infants from birth and during the whole NICU stay to reduce mortality rate and occurrence of severe respiratory (e.g., BPD) and neurological sequelae (e.g., intraventricular hemorrage and periventricular leukomalacia).

Author details

Gianluca Lista[1], Georg M. Schmölzer[2,3]* and Ilia Bresesti[1]

*Address all correspondence to: georg.schmoelzer@me.com

1 Division of Neonatology, "V.Buzzi Children's Hospital", ASST-FBF-Sacco, Milan, Italy

2 Centre for the Studies of Asphyxia and Resuscitation, Royal Alexandra Hospital, Edmonton, Canada

3 Division of Neonatology, Department of Pediatrics, University of Alberta, Edmonton, Canada

References

[1] Hooper SB, Te Pas AB, Kitchen MJ. Respiratory transition in the newborn: A three-phase process. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2016;**101**:F266-F271

[2] Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: Outcomes to discharge from hospital for infants born at the threshold of viability. Pediatrics. 2000;**106**:659-671

[3] Laptook AR, Salhab W, Bhaskar B. Admission temperature of low birth weight infants: Predictors and associated morbidities. Pediatrics. 2007;**119**:e643-e649

[4] Silverman WA, Fertig JW, Berger AP. The influence of the thermal environment upon the survival of newly born premature infants. Pediatrics. 1958;**22**:876-886

[5] Wyllie J, Perlman JM, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, Kim HS, Liley HG, Mildenhall L, Simon WM, Szyld E, Tamura M, Velaphi S. Part 7: Neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation. 2015;**95**: e169-e201

[6] Trevisanuto D, Doglioni N, Cavallin F, Parotto M, Micaglio M, Zanardo V. Heat loss prevention in very preterm infants in delivery rooms: a prospective, randomized, controlled trial of polyethylene caps. The Journal of Pediatrics. 2010;**156**:914-917, 917.e911

[7] McCall EM, Alderdice F, Halliday HL, Jenkins JG, Vohra S. Interventions to prevent hypothermia at birth in preterm and/or low birthweight infants. Cochrane Database of Systematic Reviews. 2010 Mar 17;(3):CD004210

[8] Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R, Saugstad OD, Simeoni U, Speer CP, Vento M, Visser GH, Halliday HL. European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2016 Update Neonatology. Basel, Switzerland: S. Karger AG; 2017. pp. 107-125

[9] Jobe AH. Lung maturation: The survival miracle of very low birth weight infants. Pediatrics and Neonatology. 2010;**51**:7-13

[10] Lista G, Maturana A, Moya FR. Achieving and maintaining lung volume in the preterm infant: From the first breath to the NICU. European Journal of Pediatrics. 2017

[11] Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet JM, Carlin JB. Nasal CPAP or intubation at birth for very preterm infants. The New England Journal of Medicine. 2008; **358**:700-708

[12] Schmölzer GM, Kumar M, Pichler G, Aziz K, O'Reilly M, Cheung PY. Non-invasive versus invasive respiratory support in preterm infants at birth: Systematic review and meta-analysis. BMJ. 2013;**347**:f5980

[13] Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, Ferrelli K, O'Conor J, Soll RF. Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics. 2011;**128**:e1069-e1076

[14] Wyllie J, Bruinenberg J, Roehr CC, Rudiger M, Trevisanuto D, Urlesberger B. European Resuscitation Council Guidelines for Resuscitation 2015: Section 7. Resuscitation and support of transition of babies at birth. Resuscitation. 2015;**95**:249-263

[15] Tingay DG, Bhatia R, Schmölzer GM, Wallace MJ, Zahra VA, Davis PG. Effect of sustained inflation vs. stepwise PEEP strategy at birth on gas exchange and lung mechanics in preterm lambs. Pediatric Research. 2014;**75**:288-294

[16] Mehler K, Grimme J, Abele J, Huenseler C, Roth B, Kribs A. Outcome of extremely low gestational age newborns after introduction of a revised protocol to assist preterm infants in their transition to extrauterine life. Acta Paediatrica. 2012;**101**:1232-1239

[17] Peterson J, Johnson N, Deakins K, Wilson-Costello D, Jelovsek JE, Chatburn R. Accuracy of the 7-8-9 Rule for endotracheal tube placement in the neonate. Journal of Perinatology. 2006;**26**:333-336

[18] Yam CH, Dawson JA, Schmölzer GM, Morley CJ, Davis PG. Heart rate changes during resuscitation of newly born infants <30 weeks gestation: An observational study. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2011;**96**:F102-F107

[19] Perlman JM, Wyllie J, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP, Guinsburg R, Hazinski MF, Morley C, Richmond S, Simon WM, Singhal N, Szyld E, Tamura M, Velaphi S. Part 11: Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation. 2010;**122**:S516-S538

[20] Chitkara R, Rajani AK, Oehlert JW, Lee HC, Epi MS, Halamek LP. The accuracy of human senses in the detection of neonatal heart rate during standardized simulated resuscitation: Implications for delivery of care, training and technology design. Resuscitation. 2013; **84**:369-372

[21] Mizumoto H, Tomotaki S, Shibata H, Ueda K, Akashi R, Uchio H, Hata D. Electrocardiogram shows reliable heart rates much earlier than pulse oximetry during neonatal resuscitation. Pediatrics International. 2012;**54**:205-207

[22] Voogdt KG, Morrison AC, Wood FE, van Elburg RM, Wyllie JP. A randomised, simulated study assessing auscultation of heart rate at birth. Resuscitation. 2010;**81**:1000-1003

[23] Kamlin CO, O'Donnell CP, Everest NJ, Davis PG, Morley CJ. Accuracy of clinical assessment of infant heart rate in the delivery room. Resuscitation. 2006;**71**:319-321

[24] Kamlin CO, Dawson JA, O'Donnell CP, Morley CJ, Donath SM, Sekhon J, Davis PG. Accuracy of pulse oximetry measurement of heart rate of newborn infants in the delivery room. The Journal of Pediatrics. 2008;**152**:756-760

[25] Saugstad OD, Ramji S, Soll RF, Vento M. Resuscitation of newborn infants with 21% or 100% oxygen: an updated systematic review and meta-analysis. Neonatology. 2008; **94**:176-182

[26] Wang CL, Anderson C, Leone TA, Rich W, Govindaswami B, Finer NN. Resuscitation of preterm neonates by using room air or 100% oxygen. Pediatrics. 2008;**121**:1083-1089

[27] McCall KE, Davis PG, Owen LS, Tingay DG. Sustained lung inflation at birth: What do we know, and what do we need to know? Archives of Disease in Childhood. Fetal and Neonatal Edition. 2016;**101**:F175-F180

[28] te Pas AB, Siew M, Wallace MJ, Kitchen MJ, Fouras A, Lewis RA, Yagi N, Uesugi K, Donath S, Davis PG, Morley CJ, Hooper SB. Establishing functional residual capacity at birth: The effect of sustained inflation and positive end-expiratory pressure in a preterm rabbit model. Pediatric Research. 2009;**65**:537-541

[29] Fuchs H, Lindner W, Buschko A, Trischberger T, Schmid M, Hummler HD. Cerebral oxygenation in very low birth weight infants supported with sustained lung inflations after birth. Pediatric Research. 2011;**70**:176-180

[30] Vyas H, Milner AD, Hopkin IE, Boon AW. Physiologic responses to prolonged and slow-rise inflation in the resuscitation of the asphyxiated newborn infant. The Journal of Pediatrics. 1981;**99**:635-639

[31] Lista G, Boni L, Scopesi F, Mosca F, Trevisanuto D, Messner H, Vento G, Magaldi R, Del Vecchio A, Agosti M, Gizzi C, Sandri F, Biban P, Bellettato M, Gazzolo D, Boldrini A, Dani C. Sustained lung inflation at birth for preterm infants: A randomized clinical trial. Pediatrics. 2015;**135**:e457-e464

[32] van Vonderen JJ, Hooper SB, Hummler HD, Lopriore E, te Pas AB. Effects of a sustained inflation in preterm infants at birth. The Journal of Pediatrics. 2014;**165** 903-908.e901

[33] Sobotka KS, Hooper SB, Allison BJ, Te Pas AB, Davis PG, Morley CJ, Moss TJ. An initial sustained inflation improves the respiratory and cardiovascular transition at birth in preterm lambs. Pediatric Research. 2011;**70**:56-60

[34] Harding R, Bocking AD, Sigger JN. Influence of upper respiratory tract on liquid flow to and from fetal lungs. Journal of Applied Physiology. (1985) 1986;**61**:68-74

[35] Lista G, Cavigioli F, La Verde PA, Castoldi F, Bresesti I, Morley CJ. Effects of breathing and apnoea during sustained inflations in resuscitation of preterm infants. Neonatology. 2017;**111**:360-366

[36] Lindner W, Vossbeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weight infants: Spontaneous breathing or intubation? Pediatrics. 1999;**103**:961-967

[37] te Pas AB, Walther FJ. A randomized, controlled trial of delivery-room respiratory management in very preterm infants. Pediatrics. 2007;**120**:322-329

[38] Ngan AY, Cheung PY, Hudson-Mason A, O'Reilly M, van Os S, Kumar M, Aziz K, Schmölzer GM. Using exhaled CO2 to guide initial respiratory support at birth: A randomised controlled trial. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2017;**102**:F525-f531

[39] Keszler M. Sustained inflation during neonatal resuscitation. Current Opinion in Pediatrics. 2015;**27**:145-151

[40] Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, Simon WM, Weiner GM, Zaichkin JG. Part 13: Neonatal Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;**132**:S543-S560

[41] Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database of Systematic Reviews. 2012 Mar 14;(3):CD000510

[42] Subramaniam P, Ho JJ, Davis PG. Prophylactic nasal continuous positive airway pressure for preventing morbidity and mortality in very preterm infants. Cochrane Database of Systematic Reviews 2016 Jun 14;(6):CD001243

[43] Fischer HS, Buhrer C. Avoiding endotracheal ventilation to prevent bronchopulmonary dysplasia: A meta-analysis. Pediatrics. 2013;**132**:e1351-e1360

[44] Finer NN, Carlo WA, Duara S, Fanaroff AA, Donovan EF, Wright LL, Kandefer S, Poole WK, Network NIoCHaHDNR. Delivery room continuous positive airway pressure/positive end-expiratory pressure in extremely low birth weight infants: A feasibility trial. Pediatrics. 2004;**114**:651-657

[45] Bahadue FL, Soll R. Early versus delayed selective surfactant treatment for neonatal respiratory distress syndrome. Cochrane Database of Systematic Reviews. 2012;**11**:CD001456

[46] Walsh MC, Morris BH, Wrage LA, Vohr BR, Poole WK, Tyson JE, Wright LL, Ehrenkranz RA, Stoll BJ, Fanaroff AA. Extremely low birthweight neonates with protracted ventilation: Mortality and 18-month neurodevelopmental outcomes. The Journal of Pediatrics. 2005;**146**:798-804

[47] Gopel W, Kribs A, Ziegler A, Laux R, Hoehn T, Wieg C, Siegel J, Avenarius S, von der Wense A, Vochem M, Groneck P, Weller U, Moller J, Hartel C, Haller S, Roth B, Herting E. Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): An open-label, randomised, controlled trial. Lancet. 2011;**378**:1627-1634

[48] Dargaville PA, Aiyappan A, De Paoli AG, Kuschel CA, Kamlin CO, Carlin JB, Davis PG. Minimally-invasive surfactant therapy in preterm infants on continuous positive airway pressure. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2013;**98**:F122-F126

[49] Dargaville PA, Aiyappan A, Cornelius A, Williams C, De Paoli AG. Preliminary evaluation of a new technique of minimally invasive surfactant therapy. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2011;**96**:F243-F248

[50] Kribs A, Pillekamp F, Hunseler C, Vierzig A, Roth B. Early administration of surfactant in spontaneous breathing with nCPAP: feasibility and outcome in extremely premature infants (postmenstrual age </=27 weeks). Paediatric Anaesthesia. 2007;**17**:364-369

[51] Kribs A, Vierzig A, Hunseler C, Eifinger F, Welzing L, Stutzer H, Roth B. Early surfactant in spontaneously breathing with nCPAP in ELBW infants–A single centre four year experience. Acta Paediatrica. 2008;**97**:293-298

[52] Katheria AC, Sauberan JB, Akotia D, Rich W, Durham J, Finer NN. A pilot randomized controlled trial of early versus routine caffeine in extremely premature infants. American Journal of Perinatology. 2015;**32**:879-886

[53] Dekker J, Hooper SB, van Vonderen JJ, Witlox RSGM, Lopriore E, Te Pas AB. Caffeine to improve breathing effort of preterm infants at birth: A randomized controlled trial. Pediatric Research. 2017

[54] McDonald SJ, Middleton P, Dowswell T, Morris PS. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. Evidence-Based Child Health. 2014;**9**:303-397

[55] Fogarty M, Osborn DA, Askie L, Seidler AL, Hunter K, Lui K, Simes J, Tarnow-Mordi W. Delayed versus early umbilical cord clamping for preterm infants: A systematic review and meta-analysis. American Journal of Obstetrics and Gynecology. 2017

[56] Rabe H, Diaz-Rossello JL, Duley L, Dowswell T. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. Cochrane Database of Systematic Reviews. 2012 Aug 15;(8):CD003248

[57] Bora R, Akhtar SS, Venkatasubramaniam A, Wolfson J, Rao R. Effect of 40-cm segment umbilical cord milking on hemoglobin and serum ferritin at 6 months of age in full-term infants of anemic and non-anemic mothers. Journal of Perinatology. 2015;**35**:832-836

[58] Kumar B, Upadhyay A, Gothwal S, Jaiswal V, Joshi P, Dubey K. Umbilical cord milking and hematological parameters in moderate to late preterm neonates: A randomized controlled trial. Indian Pediatrics. 2015;**52**:753-757

[59] van Os S, Cheung PY, Pichler G, Aziz K, O'Reilly M, Schmölzer GM. Exhaled carbon dioxide can be used to guide respiratory support in the delivery room. Acta Paediatrica. 2014;**103**:796-806

[60] Mian QN, Pichler G, Binder C, O'Reilly M, Aziz K, Urlesberger B, Cheung PY, Schmölzer GM. Tidal volumes in spontaneously breathing preterm infants supported with continuous positive airway pressure. The Journal of Pediatrics. 2014;**165**:702-706.e701

[61] Pichler G, Cheung PY, Binder C, O'Reilly M, Schwaberger B, Aziz K, Urlesberger B, Schmölzer GM. Time course study of blood pressure in term and preterm infants immediately after birth. PLoS One. 2014;**9**:e114504

[62] Baik N, Urlesberger B, Schwaberger B, Schmölzer GM, Mileder L, Avian A, Pichler G. Reference ranges for cerebral tissue oxygen saturation index in term neonates during immediate neonatal transition after birth. Neonatology. 2015;**108**:283-286

[63] Lista G, Schmölzer G, Colm OD. Improving assessment during noninvasive ventilation in the delivery room. NeoReviews. 2012;**13**:e364-e371

[64] Crawshaw JR, Kitchen MJ, Binder-Heschl C, Thio M, Wallace MJ, Kerr LT, Roehr CC, Lee KL, Buckley GA, Davis PG, Flemmer A, Te Pas AB, Hooper SB. Laryngeal closure impedes non-invasive ventilation at birth. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2017 Oct 20. pii: fetalneonatal-2017-312681. DOI: 10.1136/archdischild-2017-312681

[65] Schmölzer GM, Dawson JA, Kamlin CO, O'Donnell CP, Morley CJ, Davis PG. Airway obstruction and gas leak during mask ventilation of preterm infants in the delivery room. Archives of Disease in Childhood. Fetal and Neonatal Edition. 2011;**96**:F254-F257

[66] Schmölzer GM, Morley CJ, Wong C, Dawson JA, Kamlin CO, Donath SM, Hooper SB, Davis PG. Respiratory function monitor guidance of mask ventilation in the delivery room: A feasibility study. The Journal of Pediatrics. 2012;**160**:377-381.e372

[67] Verbeek C, van Zanten HA, van Vonderen JJ, Kitchen MJ, Hooper SB, Te Pas AB. Accuracy of currently available neonatal respiratory function monitors for neonatal resuscitation. European Journal of Pediatrics. 2016;**175**:1065-1070

[68] Hooper SB, Fouras A, Siew ML, Wallace MJ, Kitchen MJ, te Pas AB, Klingenberg C, Lewis RA, Davis PG, Morley CJ, Schmölzer GM. Expired CO_2 levels indicate degree of lung aeration at birth. PLoS One. 2013;**8**:e70895

[69] Leone TA, Lange A, Rich W, Finer NN. Disposable colorimetric carbon dioxide detector use as an indicator of a patent airway during noninvasive mask ventilation. Pediatrics. 2006;**118**:e202-e204

[70] Schmölzer GM, O'Reilly M, Davis PG, Cheung PY, Roehr CC. Confirmation of correct tracheal tube placement in newborn infants. Resuscitation. 2013;**84**:731-737

[71] Schmölzer GM, Roehr CC. Techniques to ascertain correct endotracheal tube placement in neonates. Cochrane Database of Systematic Reviews. 2014 Sep 13;(9):CD010221

[72] Pichler G, Cheung PY, Aziz K, Urlesberger B, Schmölzer GM. How to monitor the brain during immediate neonatal transition and resuscitation? A systematic qualitative review of the literature. Neonatology. 2014;**105**:205-210

IntechOpen