Noninvasive Ventilation in the Delivery Room for the Preterm Infant

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Education Gaps

The preterm lung is highly susceptible to injury from exposure to mechanical ventilation in the delivery room. It is important to use optimal noninvasive ventilation strategies and continuous positive airway pressure to establish functional residual capacity during resuscitation to avoid intubation and mechanical ventilation.

Abstract

A decade ago, preterm infants were prophylactically intubated and mechanically ventilated starting in the delivery room; however, now the shift is toward maintaining even the smallest of neonates on noninvasive respiratory support. The resuscitation of very low gestational age neonates continues to push the boundaries of neonatal care, as the events that transpire during the golden minutes right after birth prove ever more important for determining long-term neurodevelopmental outcomes.

Continuous positive airway pressure (CPAP) remains the most important mode of noninvasive respiratory support for the preterm infant to establish and maintain functional residual capacity and decrease ventilation/perfusion mismatch. However, the majority of extremely low gestational age infants require face mask positive pressure ventilation during initial stabilization before receiving CPAP. Effectiveness of face mask positive pressure ventilation depends on the ability to detect and overcome mask leak and airway obstruction. In this review, the current evidence on devices and techniques of noninvasive ventilation in the delivery room are discussed.

Objectives

After completing this article, readers should be able to:

1. Describe the fetal to neonatal transition in the lung.
2. Explain the importance of establishing functional residual capacity for successful noninvasive respiratory support.
3. Describe the modes of noninvasive respiratory support and list the devices used for premature infants at time of birth.
FETAL TO NEONATAL TRANSITION

The critical period of fetal lung development occurs during the canalicular to saccular stages. Premature infants are born in this critical period and therefore are at highest risk for lung underdevelopment and injury. For the lung to develop properly, the lung must be fluid-filled. In utero, the fetal lung epithelium secretes liquid, allowing for the lungs to be fluid-filled. (1)(2) With the help of a closed fetal larynx that prevents fluid from flowing out of the lung, the fluid creates lung expansion that is important for the normal development of the lung. During this time, fetal gas exchange relies solely on the placenta. (1)(2) The low oxygen tension in the alveoli results in a state of constant pulmonary vasoconstriction in the fetus, which diverts blood from the lungs to the systemic circulation.

As gestation advances, multiple changes prepare the fetal lung for an ex utero environment, including the differentiation of type I and II pneumocytes, the secretion of surfactant to reduce alveolar surface tension, and the modification of epithelial sodium channels. Signals around the time of birth lead to an increase in catecholamine release that downregulates fluid secretion by the lung epithelium and stimulates fluid resorption by the sodium channels, changing the lungs from fluid-filled to gas-filled. (1) Once the lung is gas-filled, the oxygen tension increases and leads to nitric oxide–mediated pulmonary vasodilation and gas exchange. At birth, all of these pulmonary changes help to facilitate the neonatal lung in establishing functional residual capacity (FRC). However, several factors impede the development of adequate FRC among preterm infants, including immature lung parenchyma, surfactant deficiency, a compliant chest wall, slower lung fluid clearance, weak respiratory muscle, poor laryngeal tone leading to decreased ability to grunt, and an immature respiratory drive. (3)(4)(5) Preterm infants often require positive pressure ventilation (PPV) soon after birth because of poor FRC and ineffective respiration that may be associated with bradycardia.

While the majority of preterm infants (65%–77%) born at less than 28 weeks’ gestational age (GA) require PPV in the delivery room (DR), (6)(7) they are also the most vulnerable to the adverse consequences that may arise from exposure to PPV. Even brief exposure to large tidal volume (VT) breaths can initiate an inflammatory cascade that alters lung architecture and contributes to the development of bronchopulmonary dysplasia (BPD). (8)(9)(10) Meta-analyses of large, multicenter, randomized controlled trials (RCTs) that evaluated invasive and noninvasive respiratory support in the DR show that avoiding intubation and stabilizing infants on continuous positive airway pressure (CPAP) decreases the composite outcome of death or BPD. (11)(12) DR management for the premature infant may have an extremely important effect on survival and survival without severe illness. (13)(14) These findings have resulted in a practice change, with an increasing number of infants in the DR being stabilized on CPAP. (15)(16)(17) The aim of this article is to provide an updated review of noninvasive devices and strategies used in the DR for premature infants (Table 1).

INTERFACES FOR DELIVERING NONINVASIVE PPV IN THE DR

Face Mask
Administration of noninvasive PPV via face mask is the current standard of care. Two different types of masks are available for use: an anatomic shaped mask and a round mask. Face mask PPV is dependent on achieving an adequate seal to avoid mask leak. Commercially available masks vary in shape and size (Fig 1). Palme et al compared 5 widely used round and triangular masks for mask leak in 44 newborns in the DR. (18) They assessed the percentage of leak by calculating the difference between set pressure and the average peak pressure. This study reported less leak with the use of the round silicone mask compared with the triangular mask. (18) However, O’Donnell et al compared round and anatomic masks using mannequins and found no difference in the air leak between the 2 different mask types. (19)

O’Shea et al evaluated the facial measurements of preterm infants born between 24 and 33 weeks’ GA and suggested that masks of 35-mm diameter are suitable for infants of less than 29 weeks’ GA and 42-mm diameter masks are suitable for infants between 27 and 33 weeks’ GA. Interestingly, the standard commercially available face mask measures 50 mm while small round face masks are available in 35-mm and 42-mm inner diameter sizes. (20) The correct mask size should be determined by placing the bottom of the mask on the tip of the chin to cover the mouth and the nose but the top of the mask not reaching the eyes. However, a recent RCT that measured the mask leak using respiratory function monitoring did not show any difference in the mask leak between standard and small round masks. (21)

There are several ways to hold the face mask (Fig 2). A recent study looking at corrective ventilation strategies for infants of less than 32 weeks’ GA in the DR found that the most frequent mask holds were 1-handed (95%), 2-handed (63%), stem hold (23%), and modified spider hold (6%). (22) The mask hold also depends on the face mask that is being...
used, because a different hold may be necessary for the silicone face mask versus the bubble face mask.

There is a theoretical concern that when the face mask is placed, it overlies the nasotrigeminal area and can influence ventilation by stimulating the trigeminal nerve, resulting in cessation of a normal breathing pattern, bradycardia, peripheral vasoconstriction, and closure of the larynx. (23) This further necessitates proper face mask positioning and size to limit stimulation of this nerve.

**Single Nasal Tube**

To overcome the shortcomings of the face mask, other interfaces such as nasal tubes and short binasal prongs are being studied for the delivery of noninvasive ventilation. A nasal tube is a single tube that enters one nare and ends in the nasopharynx and is used to deliver PPV. Van Vonderen et al, in their study of 43 infants, used nasal tubes as the primary mode to deliver noninvasive ventilation and found more leak and tube obstruction with the nasal tube compared with a face mask. (24) In addition, using the nasal tube delayed PPV initiation because of placement of the tube, and was also noted to be associated with inadequate \( V_T \). (24)

**Short Binasal Prongs**

Although binasal prongs are widely used to provide CPAP in the DR, the experience with its application for providing PPV in the DR is limited. To date, the RAM Cannula (Neotech, Valencia, CA) is the only nasal prong that is able to directly interface with the T-piece resuscitator. A single-center retrospective study reported a decrease in DR intubation rate after instituting these particular short binasal prongs to provide noninvasive ventilation compared with historical cohorts who were resuscitated with a face mask. (25) However, theoretical concerns exist including possible higher intrinsic resistance (26) and insignificant \( V_T \) delivery with ventilator-delivered noninvasive positive pressure breaths. (27)

In summary, there is no current evidence to suggest one mask is better than another for neonatal DR resuscitation, although mask size is important. Other interface options such as a single nasal tube and short binasal prongs need to be evaluated further in well-designed RCTs before being adopted for routine clinical practice. Simulation-based training has been shown to decrease mask leak and improve the effectiveness of face mask PPV.

**MODES OF NONINVASIVE RESPIRATORY SUPPORT IN THE DR**

**Positive Pressure Ventilation**

The Neonatal Resuscitation Program (NRP) currently recommends initiating PPV in the DR for bradycardia (HR<100) and/or when respiratory effort by the neonate is inadequate. (28) The recommended initial settings are an

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**TABLE 1. Delivery Room Interfaces and Devices for Resuscitation**

<table>
<thead>
<tr>
<th>Interfaces for delivering positive pressure ventilation</th>
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<tbody>
<tr>
<td>• Face mask (anatomical shaped vs round)</td>
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<tr>
<td>• Single nasal tube</td>
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<tr>
<td>• Short binasal prongs</td>
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<table>
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<tr>
<th>Pressure delivery devices for delivering positive pressure ventilation</th>
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<tbody>
<tr>
<td>• T-piece resuscitator</td>
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<tr>
<td>• Flow-inflating bag</td>
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<td>• Self-inflating bag</td>
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**Figure 1.** Examples of face masks. A. The top row demonstrates anatomic face masks. The bottom row demonstrates round face masks. B. Anatomic masks (mask at far right) have an air-filled balloon whereas round masks (mask at far left and in the middle) have a silicone flap to promote adherence to the face without excessive downward pressure.
inflation pressure of 20 cm H₂O, and positive end-expiratory pressure (PEEP) of 5 cm H₂O at a rate of 40 to 60 breaths/ min, with the pressure being adjusted depending on the patient’s response. Response to PPV can be evaluated by improvement in heart rate which can be monitored using electrocardiographic waveforms or pulse oximetry.

There are 3 modes to deliver PPV: a T-piece resuscitator, a self-inflating bag, or a flow-inflating bag (Fig 3), which are all approved by NRP to be used for resuscitation in the DR, depending on resources available at the hospital. It should be noted that only the flow-inflating bag and T-piece resuscitator can be used to provide PPV and CPAP. Use of a T-piece is gaining favor for DR use because of its ability to deliver controlled pressures. However, 3 RCTs comparing the use of a T-piece resuscitator versus a self-inflating bag for ventilation of extremely preterm infants in the DR did not show improvement in long-term outcomes. (29)(30)(31) A single-center observational study comparing the self-inflating bag to the T-piece resuscitator in very-low-birthweight neonates showed that the latter modality had an increased hospital survival rate without BPD, intraventricular hemorrhage (IVH), and periventricular leukomalacia. (32)

It is difficult for practitioners to estimate the V₉ being delivered during PPV despite the use of advanced resuscitation devices such as the T-piece resuscitator. One study showed that of 218 neonates born at less than 29 weeks’ GA resuscitated in the DR, with the T-piece resuscitator set at a peak inspiratory pressure (PIP) of 24 and PEEP of 6 cm H₂O, 75% of patients received ventilation with V₉ greater than 6 mL/kg, which can injure the lungs and contribute to IVH. (33) Fifty-one percent of infants who received ventilation with large V₉ were diagnosed with IVH compared with a 13% rate of IVH in the group with a V₉ less than 6 mL/kg. (33) Hinder et al investigated T-piece devices on mannequins and showed that despite a set PEEP and PIP, the pressure being delivered to the individual neonate varied, depending on the changes in lung compliance. (34) Hinder et al also found that T-piece devices delivered inadvertent PEEP above the set value, possibly because of a number of factors, including accidental rotation of the PEEP knob, finger distance over the PEEP valve, presence of an endotracheal tube, use of surfactant, high airway resistance, and low delivery gas flowrate. (34) Further studies are needed to verify these findings.

**Sustained Lung Inflation**

Sustained lung inflation (SI) is the use of distending pressure PIP applied for a certain duration with the goal of establishing FRC. In animal models, SI performed during the first inflations after birth helped to clear liquid from the airways and helped in establishing FRC. To date, 5 RCTs have investigated the use of SI in preterm infants using different durations and SI pressures. A meta-analysis comparing all patients from these trials showed no significant difference in the rate of BPD or death. (35) Recently, the Sustained Inflation of Infant Lung (SAII) trial randomized 426 extremely preterm infants with bradycardia with inadequate respiratory effort in 9 countries to either 2 sustained inflations to maximal peak pressure of 25 cm H₂O for 15 seconds or standard bag and mask. (36) The trial was stopped early because of increased death in the first 48 hours after birth in the sustained inflation group. (36) Currently, there is not enough evidence to recommend
routine SI in the DR, and one RCT suggests potential harm with this approach.

**Intervention to Overcome Mask Leak and Airway Obstruction**

The best evidence that a neonate is receiving effective ventilation after initiation of PPV is a rising heart rate. Most premature infants will receive PPV in the DR. (6) When the heart rate fails to increase, the first step in troubleshooting is to address mechanical issues such as airway obstruction and mask leak. Premature infants are placed in plastic bags for thermoregulation and it is often difficult to assess chest rise through the bag. (37) To diagnose the potential issue leading to ineffective PPV, some studies suggest that the use of colorimetric end-tidal carbon dioxide (EtCO₂) detection during face mask ventilation may be beneficial. Using a disposable EtCO₂ detector attached to a face mask during PPV, providers can assess the patency of the airway. (38)(39)(40)(41) In one observational study using EtCO₂ detectors, 18 infants received a median of 14 obstructed breaths defined by no color change on the EtCO₂ despite reaching a target pressure. (38) The authors concluded that airway obstruction is extremely common in very-low-birthweight infants and that EtCO₂ detectors can help recognize this obstruction. (38) In addition, in the neonate undergoing PPV with good chest rise, but continued bradycardia leading to poor cardiac output and insufficient carbon dioxide delivery to the lungs, EtCO₂ detectors may not change. This was found in a piglet model in which low quantitative EtCO₂ values were directly related to low cardiac output states, leading to decreased pulmonary blood flow. (42) Figure 4 describes an algorithm for the practical use of EtCO₂ detectors in the DR. Importantly, when a target pressure cannot be obtained despite colorimetry change, this most likely represents mask leak. Of note, when using a T-piece device with a face mask, significant leak can occur while still visualizing the pressure reading on the manometer. Therefore, visualization of manometry pressures cannot be used to ensure reliable mask seal; practitioners must consider mask leak as a possible cause of ineffective PPV whether or not target pressure readings are obtained on the T-piece resuscitator.

After recognition of ineffective ventilation, NRP advises the use of the “MRSOPA” mnemonic to further correct ventilatory steps in a neonate with a decreasing heart rate. (28) Mask adjustment, repositioning the airway, opening the mouth, increasing inspiratory pressure, and alternate airway (MRSOPA) are the most important steps in correcting ventilation. One observational study on the frequency and use of MRSOPA strategies in the DR found that infants less than 32 weeks’ gestation who received more MRSOPA interventions were more likely to be intubated. (22) However, a quality improvement project reported decreased DR intubation rates and improved outcomes with simulation-based peer-to-peer training on MRSOPA strategies by using small round masks, EtCO₂ detectors, increasing pressure, and increasing inspiratory time to 1 second when indicated. (43) Such interventions to improve ventilation via corrective steps conducted in individual centers can help decrease the need for intubation and increase stabilization of infants receiving noninvasive respiratory support in the DR.
CPAP for DR Resuscitation

CPAP has been widely used for the respiratory support of preterm infants in the NICU over the last 5 decades. (28)(44) CPAP increases FRC, (44) decreases airway resistance, (45) decreases thoracoabdominal asynchrony, (46) and decreases intrapulmonary shunting, (44) thus leading to better oxygenation and ventilation in spontaneously breathing preterm infants. In addition, CPAP helps decrease obstructive apnea (47) and augments surfactant production. (48) The devices and interfaces of CPAP use in the DR are listed in Table 2.

**Constant-Flow CPAP Devices.** T-piece resuscitator use with a face mask is recommended by NRP for CPAP delivery in the DR. (49) The desired PEEP level can be adjusted at the PEEP valve. The T-piece is used with a face mask, single nasal tube, or specific type of short binasal prongs (RAM cannula). Bubble CPAP uses the water column at the end of the expiratory limb to generate pressure in the CPAP circuit. CPAP level is determined by the immersion length of the expiratory tubing. (50) The gas exiting from the underwater tubing creates bubbles. Bubbling may provide additional benefits with mechanisms such as stochastic resonance (51) and high-frequency oscillatory waveforms (52) in improving gas exchange and lung recruitment. CPAP can also be delivered in the DR using an adjustable PEEP valve connected to the expiratory limb of the CPAP circuit. The inspiratory limb is connected to the gas source from the blender, usually set at a flow rate of 8 to 10 L/min. Both bubble CPAP and the adjustable PEEP valve can be used with binasal prongs of many different types or small nasal masks. Ventilators are commonly used for CPAP delivery during transport and in the NICU rather than in the DR.

**Interfaces.** Although the face mask was routinely used to administer CPAP to infants with respiratory distress syndrome in the 1970s, it fell out of favor because of the difficulty in maintaining a proper seal. (53) However, CPAP is commonly administered with the T-piece resuscitator with the face mask in the DR because of the ability to provide PPV when indicated. As discussed before, maintaining a proper seal is important to provide the desired CPAP level. In addition, the increased dead space of the face mask may also decrease the effectiveness of CPAP delivery. (54)

Binasal prong CPAP has been effectively used since 1973. (50)(55) De Paoli et al demonstrated that short binasal prongs offered the lowest resistance to flow compared with the single nasal tube. (56) Prong size is an important consideration because the smaller prongs may generate higher resistance to flow. (56)(57) Small nasal masks can be used as an alternative to binasal prongs. Recently, Green et al reported that these small nasal masks pose less intrinsic resistance compared with short binasal prongs. (26)

**CPAP Delivery in the DR.** Face mask CPAP provided at 5 cm H₂O using a T-piece generator should be initiated at...
Birth for all spontaneously breathing infants. Face PPV should be provided when the infant has bradycardia, poor respiratory effort, or both. CPAP should be restarted when the infant shows spontaneous respiratory effort and a stable heart rate. Manometer reading and EtCO2 detectors can help in identifying mask leak while administering CPAP. Fraction of inspired oxygen is titrated using the NRP algorithm. (49) Although the titration of CPAP level in DR resuscitation has not been evaluated in clinical trials, one large RCT that routinely used 8 cm H2O reported a higher rate of pneumothoraces. (58) Subsequent trials that used CPAP levels of 5 to 7 cm H2O did not report higher rates of pneumothorax. (6) Higher CPAP levels can help achieve higher FRC. (44)(59) Therefore, CPAP level may be titrated higher—up to 7 cm H2O for infants requiring higher supplemental oxygen in the DR. When the infant demonstrates regular respiration, stable heart rate, and stable oxygen saturation, the infant can be transitioned to either binasal prong or small nasal mask for transport to the NICU. CPAP can be provided during transport in multiple ways, including bubble CPAP, an adjustable PEEP valve using gas flow, or ventilator CPAP. When using binasal prongs, it is important to use the binasal prong with the largest inner diameter that can snugly fill the nares.

**High-Flow Nasal Cannula**

High-flow nasal cannula (HFNC) delivers heated and humidified gas that aids in gas exchange by minimizing dead space. (60) The pressure that is generated by HFNC is determined by the flow rate, size of the nasal cannula, and amount of leak from the nose and mouth. (61)(62) Only 1 study has demonstrated the feasibility of using HFNC in the DR for infants between 23 and 29 weeks’ GA. (63) HFNC in the DR is not recommended before well-designed RCTs.

**SUMMARY**

During the delivery of premature infants, the DR can often be chaotic, given that premature deliveries could happen unexpectedly. A skilled resuscitation team is necessary to provide initial lifesaving breaths to this vulnerable population to quickly and effectively establish FRC. After establishment of FRC, maintaining neonates on CPAP to prevent lung injury with mechanical ventilation is well-studied. However, providing noninvasive ventilation can have challenges including mask leak, incorrect mask size, and airway obstruction. Use of a properly sized mask with a colorimetric EtCO2 detector provides early feedback for airway obstruction and mask leak, though RCTs are still needed. Performing MRSOPA in the event of ineffective ventilation is the most important step to ensure the successful transition from PPV to CPAP in the DR.

**TABLE 2. CPAP Devices and Interfaces for DR Resuscitation**

<table>
<thead>
<tr>
<th>Constant flow CPAP generators</th>
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<tbody>
<tr>
<td>• T-piece resuscitator</td>
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<tr>
<td>• Bubble CPAP</td>
</tr>
<tr>
<td>• Adjustable PEEP valve</td>
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<tr>
<td>• Ventilator</td>
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**Interfaces**

| • Face mask                  |
| • Single nasal tube          |
| • Binasal prongs             |
| • Small nasal masks          |

CPAP = continuous positive airway pressure; PEEP = positive end-expiratory pressure.

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**American Board of Pediatrics Neonatal-Perinatal Content Specifications**

- Know the indications for assisted ventilation, including continuous positive airway pressure, immediately after birth and how to assess its effectiveness.
- Understand how to use self-inflating and flow-inflating bags or T-piece resuscitators to provide assisted ventilation immediately after birth.
- Know the mechanism of production and factors affecting the clearance of fetal lung liquid, its contribution to amniotic fluid, and its importance to fetal lung development.
- Know the effects of surface tension on alveolar and airway stability and lung mechanics (LaPlace law).
- Know factors that determine residual lung volume, functional residual capacity, and tidal volume, and how they change with various pulmonary disorders.
- Know the clinical features of an infant with airway obstruction.
- Know the indications for and techniques of continuous positive airway pressure (CPAP).
- Know the effects and risks of CPAP.
References


1. The team is preparing for the delivery of an infant at 25 weeks’ gestational age. Which of the following statements regarding anticipation of respiratory management for this infant is correct?
   A. With optimal care including antenatal steroids and cesarean delivery, less than 20% of infants at this gestational age will require positive pressure ventilation in the delivery room.
   B. Brief exposure to large tidal volume breaths, even immediately after birth, can initiate an inflammatory cascade that alters lung architecture and contributes to the development of bronchopulmonary dysplasia.
   C. Even if it is not absolutely needed, the delivery of 10 to 20 carefully adjusted positive pressure ventilation breaths in a prophylactic fashion for all newborns in this circumstance will lead to decreased need for intubation and reduced incidence of respiratory distress syndrome and bronchopulmonary dysplasia.
   D. Continuous positive airway pressure should be avoided until stabilization has progressed in the NICU to avoid pneumothorax.
   E. The main factor that will drive respiratory management in the first few minutes, particularly in the decisions surrounding positive pressure ventilation, is oxygen saturation measurement.

2. A male infant born at 26 weeks’ gestational age is handed to the pediatrics team after 60 seconds of delayed cord clamping. The infant has spontaneous respirations at first, but proceeds to have apnea and bradycardia. The patient is given positive pressure ventilation. Which of the following statements regarding the interface for delivering positive pressure ventilation is correct?
   A. The first-line treatment for this patient should be endotracheal intubation.
   B. Nasal prongs have proven more effective than face mask for positive pressure delivery in this population.
   C. Triangular face masks have consistently been shown to have less air leak than circular masks in this population.
   D. For face masks, the correct size should be determined by placing the bottom of the mask on the tip of the chin to cover the mouth and nose, but with the top of the mask not reaching the eyes.
   E. The optimal “hold” of a face mask for preterm infants is to place in the correct position on the face, but actually not to hold it in place and let it lie there gently.

3. A female infant born at 27 weeks’ gestational age is delivered vaginally and is handed to the pediatrics team after 60 seconds of delayed cord clamping. The infant has spontaneous respirations before cord clamping. At the radiant warmer, the infant is gasping and is determined to have inadequate respirations. The team initiates positive pressure ventilation. Which of the following parameters for initial support for this patient is most appropriate?
   A. Inflation pressure of 30 cm H₂O.
   B. No positive end-expiratory pressure for the first few minutes.
   C. A rate of 40 to 60 breaths/min.
   D. Oxygen concentration of 60%.
   E. Sustained inspiratory time of 10 seconds.

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4. The pediatrics team is preparing for the delivery of an infant at 27 weeks’ gestational age for worsening preeclampsia in the mother. Several choices for delivering positive pressure ventilation are available to the team. Which of the following are advantages of a T-piece resuscitator over a self-inflating bag?

A. The ability to accurately detect tidal volumes.
B. Several studies showing improved neurodevelopmental outcomes at 2 years of age.
C. Easier to deliver controlled positive pressure ventilation and continuous positive airway pressure.
D. Safeguard mechanism to ensure that an exact positive end-expiratory pressure never exceeds 5 mm H₂O.
E. Capacity to work without a gas source.

5. A newborn infant delivered at 28 weeks’ gestational age is receiving positive pressure ventilation by T-piece and mask at 2 minutes of age for apnea and heart rate of 60 beats/min. Which of the following is the best indicator of the effectiveness of positive pressure ventilation?

A. A rising heart rate.
B. Increasing pink color of the extremities.
C. Manometry pressures indicating a peak inspiratory pressure greater than 20 cm H₂O.
D. Oxygen saturation reading greater than 90%.
E. Consistent positive end-expiratory pressure reading of 5 cm H₂O.
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