

Chapter 8: Respiratory System

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A. Respiratory Distress in Newborn

- **Etiology**

pulmonary Causes

Transient tachypnea of newborn

- Hyaline membrane disease
- Meconium aspiration
- Air leak syndromes: Pneumomediastinum, pneumothorax, PIE, pneumopericardium, pneumoperitoneum
- Neonatal pneumonia
- Pulmonary hypoplasia: Idiopathic, agenesis of lung. Secondary to CDH, oligohydramnios, renal agenesis
- Congenital pulmonary lymphangiectasia

extrapulmonary causes

- Sepsis
- Cardiovascular disorders: Congenital heart disease, PPHN, Hypotension
- Metabolic disorders: Hypoglycemia, Hyperthermia, Metabolic acidosis
- Neuromuscular disorders

Brain: Asphyxia, hemorrhage, infection

Spinal cord: trauma, Werdnig-Hoffmann disease

Nerves: injury (Phrenic nerve)

Myasthenia gravis

- Mechanical-restrictive problems

Airway obstruction: Choanal atresia, micrognathia, laryngeal web, tracheomalacia, ascular ring, cystic hygroma, mediastinal masses

Rib cage anomalies: Thoracic dystrophies, generalized bone disease, skeletal dysplasia's

Diaphragmatic disorders: Phrenic nerve injury, CDH, abdominal distension

Pleural effusion or chylothorax

- Hematologic disorders: Polycythemia, anemia

B. Surfactant

Indication

- Respiratory Distress Syndrome
- Meconium Aspiration Syndrome
- Congenital Pneumonia

Mechanism of Action

- Reduces alveolar surface tension
- Decreases opening pressure
- Provides alveolar stability
- Enhances alveolar fluid clearance

Criteria

- Infants requiring > 30% oxygen delivered by positive pressure using either nasal CPAP or an ET tube.
- Diagnosis of RDS on CXR
- If you have a baby meeting these criteria at 6 hours, you should give surf within an hour meeting the criteria.

Dosage (Curosurf)

- 2.5 ml/kg/dose intratracheally for first dose. Subsequent doses 1.25 ml/kg q 12 hrs (maximum dosage 5 ml/kg)
- Repeat surfactant dose if ≥ 12 hours from first dose AND ≤ 48 hours of age AND 30% FiO_2

Initial management of Respiratory Distress in Delivery Room

<29 wks. Starting FiO_2 = 21-30%	29-34 6/7 wks. Starting FiO_2 = 21-30%	≥ 35 wks. Starting FiO_2 = 21%
Follow Micro preemie DR guidelines	Apply CPAP \pm rate in DR	Apply CPAP \pm rate in DR Interface: Mask
Give surfactant if Intubated	Give surfactant if Intubated and concerns for RDS	Give surfactant if Intubated and concerns for RDS

Meriter NICU: Oxygen Saturation Parameter

Patient Status	Oxygen Saturations Goals	Oxygen Saturation Alarm
Preterm <37 Wks.	90-94%	88-95%
Preterm ≥37 Wks.	≥95%	92-98%
All infants in room air	≥95%	92-100%

C. Ventilation Support

Ventilation types

- **High Flow Nasal Cannula**

- Delivers heated and humidified gas such as oxygen, air, or nitric oxide for infants requiring support with low positive airway pressure.
- Infants weaned from CPAP are typically started on heated humidified high flow cannula at 2 LPM and later weaned to room temperature humidified cannula when on ≤1 LPM
- Recommended flow rates should be initiated between 2-6 Lpm. The flow rate can be titrated to provide a variable level of positive distending pressures.
- Infants can PO feed on 2 LPM and lower respiratory support
- Indications: Bronchopulmonary Dysplasia, Respiratory Distress Syndrome, Transient Tachypnea of the Newborn, Apnea of prematurity, Failure to wean from NIV support (CPAP and/or NIPPV), Nasal and/or upper airway congestion/anomalies

- **Nasal Continuous Positive Airway Pressure (NCPAP)**

- Recommended intervention in delivery room for all infants <29 wks.
- For older infants, this is the first intervention for worsening respiratory distress despite nasal cannula oxygen.
- Start at 5-8 cm H₂O and adjust as needed

- **NIPPV (Nasal Intermittent Positive Pressure Ventilation)**

- Nasal ventilation with higher level of support
- Recommend in premature infants with apnea
- Initial settings: Rate 40, PIP 18-20, PEEP 5-8, IT 0.35

- **NAVA and NIV NAVA (Neurally Adjusted Ventilatory Assist)**

- NAVA deliveries assist in proportion to and in synchrony with the baby's respiratory efforts, specifically depolarization of the diaphragm. These efforts are reflected by the Edi (electrical activity of the diaphragm) signal.
- A low or absent Edi signal may be due to hyperventilation, sedation, muscle relaxants, neural disorders or the catheter being too deep
- Edi max = force of the diaphragm contraction during inspiration
- Edi min = force required to maintain FRC at the end of exhalation
- Peak Pressure = NAVA level x (Edi peak – Edi Min) + PEEP
- Initial NAVA settings
 - Initial NAVA level of 1.5-2 cmH₂O/μV – Optimize the NAVA level according to Edi Max which is targeted between 5-15 uV. Max NAVA level 4 cmH₂O/μV.
- Management of Infants on NAVA
 - If Edi max is < 5 uV, decrease the NAVA level
 - If Edi max is > 15 uV, increase the NAVA level
 - If Edi min is > 2 uV, increase PEEP
 - Initially set the same PEEP as the previous ventilator settings.
 - Initial apnea time is set for 5 seconds. If baby is apneic or desaturating, decrease the apnea time to 2-3 seconds.
 - Initial Backup settings: PC 10 above PEEP, PEEP 6-8, Rate 40, It 0.35s
- NIV NAVA: Consider increasing the PEEP when transitioning from invasive to NIV NAVA to maintain adequate MAP.
- Contraindications: insufficient/absent respiratory effort, anomaly (atresia, severe CDH), phrenic nerve injury, congenital myopathy, MRI scanning (remove catheter before scan)

• Conventional Ventilation

Indications

- Persistent respiratory acidosis with pH ≤ 7.10 and PaCO₂ > 60
- Severe hypoxemia (arterial PaO₂ < 50-60) despite a high FiO₂ (40-70%)
- Significant apnea or increasing work of breathing

Volume ventilation mode: APV/CMV (Adaptive Pressure Ventilation/Controlled Mandatory Ventilation)

Initial Ventilator Settings

Volume	4-6 ml/kg
PEEP	5-6
I-time	0.35
RR	30-50

- APV should be combined with CMV because this mode supports all spontaneous breaths. APV/CMV is associated with more stable expired VT, better oxygenation and reduced tachypnea when compared with synchronized intermittent mandatory ventilation APV/SIMV.
- If ETT leak > 50% consider larger ETT
- APV mode not recommended if ETT leak > 40%. Consider changing to Pressure ventilation mode.
- May set upper PIP limit
- As the infant improves the PIP will gradually go down while the targeted tidal volume stays the same. Thus, infant weans naturally. When PIP is low (14-16), consider extubation.
- A trial of extubation may be considered when the patient is consistently over breathing the set ventilator rate without increased work of breathing and both MAP & FiO₂ have dropped to acceptable levels.
MAP 8-10 & FiO₂ < 35%.

ressure ventilation mode: P-SIMV (Pressure-Synchronized Intermittent Mandatory Ventilation)

Initial Ventilator Settings

	RDS	Normal Lung
PIP	18-20	12-16
PEEP	5-6	4-5
I-time	0.35	0.3
RR	30-40	20-40
Pressure Support (PS)	8-10	6-8

evaluate chest rise and increase PIP if chest rise is inadequate

ventilation Goals Based on Disease Process

	pH	pCO ₂
RDS	≥ 7.25	45-55 (60)
BPD/Air leak	≥ 7.25	50-65 (<7d) 55-70 (≥7d)
PPHN	≥ 7.40-7.55	35-50

Management for infants on ventilator:

o Improve Ventilation (\downarrow PaCO₂)

Action	Effect	Risk
\uparrow RR	\uparrow Minute ventilation, \uparrow MAP	\downarrow PaO ₂
\uparrow PIP or \uparrow Volume	\uparrow FRC, \uparrow TV, \uparrow MAP,	Air leaks, BPD
\downarrow IT	\uparrow ET	\downarrow PaO ₂

o improve Oxygenation (increase PaO_2)

Action	Effect	Risk
$\uparrow FiO_2$	$\uparrow PaO_2$	BPD with prolonged exposure, ROP
$\uparrow PEEP$ or $\uparrow CPAP$	\uparrow Intrapulmonary shunt, $\uparrow FRC$, $\uparrow MAP$	Hyperinflation with $\uparrow CO_2$ Air leaks \downarrow Venous return and cardiac output
$\uparrow PIP$ or \uparrow Volume	$\uparrow FRC$, $\uparrow MAP$, $\uparrow PIP$	Air leaks; BPD
$\uparrow T$	$\uparrow MAP$	Air leaks; BPD \downarrow Venous return and cardiac output $\uparrow CO_2$ retention 2° to $\downarrow E$ time

ulmonary functions and equations

- Tidal Volume (TV): Amount of gas inspired in a single spontaneous breath or delivered through an endotracheal tube during a single cycle of the ventilator.
- Minute Ventilation = Rate (IMV) x Tidal Volume (TV)
- Rate is affected by IT and ET
- Tidal Volume is influenced by PIP, PEEP, pulmonary resistance and pulmonary compliance
- Oxygenation Index (OI) = $(MAP \times (FiO_2 \times 100)) / PaO_2$
- $MAP = \frac{(IT \times PIP) + (ET \times PEEP)}{IT + ET}$

T = Expiratory time IT = Inspiratory time

High Frequency Oscillatory Ventilation (HFOV)

- Uses small tidal volumes (usually less than anatomic dead space) and rapid respiratory rates at frequencies between 400 to 2400 breaths/min
- High frequency oscillators are air vibrators with piston pumps or vibrating diaphragms with active inspiration and expiration phase.
- Pressure oscillations within airway produce tiny tidal volumes around a constant mean airway pressure, maintaining lung volume.
- Advantages-delivers lower proximal airway pressures and possibly reduces ventilator related lung injury
- TV is determined by the amplitude (ΔP) of the airway oscillations, which in turn is determined by stroke of the device producing oscillations.

- Hz = number of oscillations/min,
1 Hz = 60bpm
- Decreasing Hz prolongs inspiratory time, thereby increasing TV **MAP**
- Oxygenation is controlled by MAP, FiO_2
- Ventilation is controlled by ΔP , Hz

Indications

- Respiratory failure unresponsive to conventional ventilation
 1. Inadequate oxygenation despite high FiO_2 and MAP
 2. Inadequate ventilation despite high PIP
- Air Leak Syndromes: pneumothorax, pulmonary interstitial emphysema
- Atelectasis

Improve oxygenation	Improve ventilation
$\uparrow FiO_2$	\uparrow Amplitude
\uparrow MAP (in increments of 1-2)	\downarrow Hertz

Complications of HFOV

- Hyperinflation and barotraumas
- \downarrow venous return \rightarrow \downarrow cardiac output \rightarrow hypotension \rightarrow \downarrow renal perfusion (\downarrow UOP)
- Edema
- \uparrow need for sedation
- Difficult to perform physical exam

High Frequency Jet Ventilation (HFJV)

- HFJV is pressure-limited, and time cycled with adjustable PIP and Rate
- Inspiratory Time (IT) is kept as short as possible (0.02 sec.)
- Exhalation is passive
- Delivers small tidal volumes (V_t) (1-2 ml/kg) at rapid rates (240-600 bpm) via special Et tube adaptor (Lifeport adaptor) with built-in nozzle.
- Connecting the Lifeport adaptor to a patient's ET tube enables tandem use of

conventional mechanical ventilation (CMV) (Hamilton G5 vent)

- Monitored Servo-controlled driving pressure (Servo Pressure) is used to detect changes in lung compliance and resistance.
- Jet rate changes are made in increments of 60 bpm and is independent of the Jet Vt. Lowering Jet rate allows for a longer expiratory time and helps avoid gas trapping.
- Jet PIP primarily regulates PaCO₂
- CMV vent PEEP is the main contributor to mean airway pressure (MAP).
- CMV vent rate (sigh breaths) reverse atelectasis.

Indications

- Preventative lung protection strategy in infants < 25 weeks or < 500 grams.
- Strongly consider Jet ventilation for infants < 26 weeks or < 750 grams.
- Rescue therapy for air leak syndromes such as pulmonary interstitial emphysema, pneumothorax, lung hyperinflation, & air trapping.

Recommended Initial HFJV Settings

Pt Population	Jet Rate	Jet PIP	Jet I.T.	PEEP
22-23 wk GA	300 bpm	24-26	0.02 seconds	5
24-25 wk GA	360 bpm	22-24	0.02 seconds	5

Management Strategies

- HFJV delta P (PIP-PEEP) is the primary determinant of PaCO₂. HFJV I-time and Rate are secondary.
- Resting lung volume (FRC supported by set PEEP) and mean airway pressure (MAP) are crucial determinants of PaO₂

Settings	When to Raise	When to Lower
HFJV PIP	To decrease PaCO ₂	To increase PaCO ₂
HFJV Rate	To decrease PaCO ₂	To eliminate inadvertent PEEP or hyperinflation
PEEP	To improve oxygenation	When oxygenation is adequate

Complication of HFJV

- Atelectasis → Add sigh breaths or increase PEEP
- Hypotension → Decrease PEEP and PIP to decrease MAP
- Hyperinflation → Decrease PEEP and PIP or decrease Jet rate

Complications of ALL Assisted Ventilation

- Air leak: Pneumomediastinum, pneumothorax, PIE, pneumopericardium, pneumoperitoneum
- ETT complications: displacement, dislodgement, obstruction, atelectasis, palatal grooves, subglottic stenosis
- Tracheal lesions: erosion, granuloma, perforation, necrotizing tracheobronchitis
- Infection: pneumonia, septicemia
- Impaired cardiac function
- CLD/BPD
- Oxygen toxicity
- Miscellaneous: Intracranial hemorrhage, PDA, ROP, delay in enteral feedings, complications of parenteral nutrition

Inhaled Nitric Oxide (iNO):

- Pulmonary vasodilator that facilitates perfusion of alveoli and can improve gas exchange and oxygenation.
- Indications: hypoxic respiratory failure despite optimal ventilator management, PPHN, meconium aspiration syndrome, pneumonia, and idiopathic pulmonary hypertension, differential pre and post SpO₂

- Inhaled nitric oxide can be given in conjunction with any oxygen system having 2 liters of oxygen or greater including: high flow nasal cannula, CPAP, NIPPV, conventional ventilation, and HFOV.
- Initial setting: 20 ppm of iNO
- Weaning: Can decrease nitric oxide by 5 ppm when FiO_2 is within a desired range. Once weaned to 5 ppm, then wean by 1 ppm.
- Due to the short half-life, nitric oxide should never be abruptly stopped. Wean slowly and be aware of a rebound effect.
- Consider monitoring methemoglobin levels daily while on iNO

Extubation Checklist:

Infants must meet following criteria

- Minimum Ventilator settings:
 - Volume: $FiO_2 \leq 0.3$, Rate ≤ 25 , VT ≤ 6 ml/kg, PEEP ≤ 6
 - Pressure: $FiO_2 \leq 0.3$, Rate ≤ 25 , PIP ≤ 18 , PEEP ≤ 6
 - NAVA level < 0.5 , $FiO_2 \leq 0.3$, PEEP ≤ 6
 - HFJV: Jet PIP ≤ 20 , Jet Rate 240-300, Jet MAP 7-8, FiO_2 0.03
- Safe airway
- $pH \geq 7.25$, $pCO_2 \leq 55$

Peri-Extubation Dexamethasone for Neonates

- To assist in success of extubation for infants at high risk for airway edema and obstruction and prevent reintubation
- Recommended regimen:
 - 0.1-0.25 mg/kg/dose IV q8h x 3 doses - begin 4 hr. prior to extubation
 - Infant must be ≥ 7 days of age
- Data not supportive of use for:
 - Low risk for airway edema and obstruction
 - Subglottic stenosis
 - Post-extubation atelectasis
- Use with caution in patients with respiratory or systemic infection

Management of Bronchopulmonary Dysplasia (BPD)

- Permissive hypercapnia (pH \geq 7.25 and pCO₂ 55-70)
- Ensure adequate caloric intake for weight gain-infants with BPD have increased basal metabolic rates: May need 130-150 kcal/kg/day
- Fluid restriction:130-150 ml/kg/day
- Diuretics
- Bronchodilators
- Systemic steroid: DART protocol
 - Use to facilitate extubation in vent-dependent infants
 - Do not use in infants less than 2 weeks of age
 - Dosing regimen: (IV or PO)
 - 0.075 mg/kg/dose q12h x 6 doses, THEN
 - 0.05 mg/kg/dose q12h x 6 doses, THEN
 - 0.025 mg/kg/dose q12h x 4 doses, THEN
 - 0.01 mg/kg/dose q12h x 4 doses, THEN STOP
 - Inhaled steroid options:
 - Budesonide 0.25-0.5 mg BID by nebulization
 - Fluticasone 110 mcg BID by inhalation
- Possible adverse effects: hyperglycemia, hypertension, hypokalemia, hypocalcemia, cessation of linear growth

Pulmonary Hypertension Screening Guidelines for Preterm Infants

(see Cardiology section for algorithm)

References:

1. Kair LR, Leonard DT, Anderson JM and Med. **Bronchopulmonary Dysplasia**. *Pediatrics in Review* 2012;33;255. DOI: 10.1542/pir.33-6-255
2. Bestic ML and Reed MD. **Common Diuretics Used in the Preterm and Term Infant: What's Changed?** *Neoreviews* 2012;13:e410. DOI: 10.1542/neo.13-7-e410
3. Doyle LW, et al. **DART Study Investigators**. Low-dose dexamethasone facilitates extubation among chronically ventilator-dependent infants: a multicenter, international, randomized, controlled trial. *Pediatrics*. 2006;117
4. Schmidt B, Whyte R, Asztalos E, Moddemann D, Poets C, et al (COT Group). **Effects of Targeting Higher vs Lower Arterial Oxygen Saturations on Death or Disability in Extremely Preterm Infants**. *JAMA*. 2013;309(20):2111-2125