Lung Protective Ventilation Strategies
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Respiratory Support in Neonatology:
State-of-the-Art 2012

Unique Challenges in NB Ventilation

- Children ≠ Small Adults!
- Newborns ≠ Small Children!
- Transitional circulation
- Compliant chest wall, stiff lungs
- Unfavorable chest wall mechanics
- Limited muscle strength and endurance
- Immature respiratory control
- Rapid RR, short time constants
- Small trachea, high ETT resistance
- Uncuffed ETT
- Tidal volume measurement

→ Need to understand the pathophysiology
Lung Injury: Strategies for Prevention
- Optimal DR stabilization
- Avoidance of mechanical ventilation
- Surfactant replacement
- Avoid excessive $V_T$
- Optimize lung volume / avoid atelectasis
- Permissive hypercapnia/lower $SPO_2$
- High-frequency ventilation
- Volume-targeted ventilation
- (?) Nitric oxide
- (?) Liquid ventilation

The Pathogenesis of BPD

- Chorioamnionitis
- Preterm Labor
- Initiation of air-breathing
- Mechanical Ventilation
- Oxygen
- Infusion
- PDA
- Fluid intake

- Antenatal Steroids
- Postnatal Steroids
- Nutrition, antioxidants, ??NO, ??

- Fetal Lung Development
- Postnatal Lung Growth and Development
- Pulmonary outcome
Why Volume-Targeted Ventilation?

✓ Volutrauma *not* Barotrauma
✓ Inadvertent hyperventilation is common
✓ Hypocarbia is bad for the brain and the lungs
✓ Adult-type volume controlled ventilation poses challenges in NB
Effect of Pressure v. Volume on Lung Injury


Capillary filtration coefficient: measure of acute lung injury

PIP is Excessive Relative to Compliance!

Ventilator-Induced Lung Injury: Volutrauma, not Barotrauma

Rodents ventilated with 3 modes:
- High pressure (45 cm H₂O), high volume
- Low (negative) pressure, high volume
- High pressure (45 cm H₂O), low volume (strapped chest & abdomen)

Hypocarbia in First 3 Days of Life
Proportion of infants with PaCO2 < 25 mm Hg
Luyt, et al  2001

Adverse Effects Associated with Maximally Low PaCO₂

Both High and Low PCO₂ Increase Risk of IVH

17 torr = 2.25 kPa ; 20 torr = 2.67 kPa. All differences < 0.01
Graziani Pediatrics '92
Limitations of Volume - Controlled Ventilation in Newborns

Actual tidal volume is influenced by:
1) Ratio of circuit compliance to respiratory system compliance
\[ V_{\text{T Lung}} = V_{\text{T set}} \times \frac{1}{1 + \frac{C_T}{C_{RS}}} \]

2) Compressible volume of the circuit, including humidifier

Modalities of Volume -Targeted Ventilation

<table>
<thead>
<tr>
<th>Controls</th>
<th>Adjusts</th>
<th>Based on</th>
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</thead>
<tbody>
<tr>
<td>Servo (PRVC)</td>
<td>( V_T ) to circuit</td>
<td>PIP Inspiratory ( V_T ) of last breath</td>
</tr>
<tr>
<td>VIP Bird (VAPS)</td>
<td>Minimum ( V_T ) to patient</td>
<td>Inspiratory time (†) Inspiratory ( V_T )</td>
</tr>
<tr>
<td>Bear Cub 750</td>
<td>Max. ( V_T ) to patient</td>
<td>Inspiratory time (††) Inspiratory ( V_T )</td>
</tr>
<tr>
<td>(Volume Limit)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avea (VAPS + VL)</td>
<td>Min/Max ( V_T ) to circuit/pt</td>
<td>Inspiratory time (††) Inspiratory ( V_T )</td>
</tr>
<tr>
<td>P. Bennett 840</td>
<td>( V_T ) to circuit</td>
<td>Inspiratory time / flow Inspiratory ( V_T )</td>
</tr>
<tr>
<td>(Volume Vent +)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Babylog, Evita</td>
<td>( V_T ) to patient</td>
<td>PIP Exhaled ( V_T ) of last breath</td>
</tr>
<tr>
<td>(VG, Neoflow)</td>
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</table>

PRVC Control Algorithm
Volume Limit

Pressure limited breaths

Decreased compliance or decreased patient effort

Increased compliance or increased patient effort

Volume Limit

Flow (L/min)

The PIP ("working pressure") is servo-regulated within preset limits ("pressure limit") to achieve $V_T$ that is set by the user. Regulation of PIP is in response to exhaled $V_T$ to minimize artifact due to ETT leak. Breath terminates if 130% of $TV_T$ reached. Separate algorithm for spontaneous and machine breaths.

Volume “Guarantee”

Principles of Operation

$TV_T = V_T$ set by user
Benefits of VG

- Maintenance of (relatively) constant tidal volumes
- Prevention of overdistention and volutrauma due to
  - Surfactant administration
  - Lung volume recruitment
  - Clearance of lung fluid
- Automatic lowering of pressure support level during weaning
- Compensation for variable respiratory drive
  - Stabilization of tidal volume and minute ventilation due to changes of respiratory drive (periodic breathing)

The benefits of VTV cannot be realized without ensuring that the tidal volume is evenly distributed throughout an “open lung”!!!

Non-Homogenous Aeration in RDS

Recruitment/de-recruitment injury, Shear forces, “Atelectotrauma” Expiration

Ventilated Stable, Ventilated Unstable, Unventilated Inspiration
Adequate PIP, Adequate PEEP

Good oxygenation, low FiO2, minimal lung injury

CCP = critical closing pressure; COP = critical opening pressure

OLC Prevents Lung Injury

VG reduces markers of lung inflammation

- Two prospective randomized trials
- A/C vs. A/C + VG
- BAL on days 1,3,5
- VG @ 5 mL/kg reduced pro-inflammatory cytokine levels and decreased duration of ventilation
- VG @ 3 mL/kg increased pro-inflammatory cytokine levels
- Low PEEP (3-4 cm H₂O)
Proportion of Values Outside the Target Range

* p < 0.001  Keszler, et al. Ped Pulmonol '04

Spontaneous Hyperventilation and VG

Note the large \( V_T \), generated by the infant, while the PIP drops near the PEEP level as the ventilator in VG mode responds appropriately to the large \( V_T \) by reducing PIP.
Summary of VG Studies

- When compared to PLV, VG results in:
  - Same or lower PIP\(^1,2,3\)
  - More stable VT\(^1,3\)
  - Less hypocapnia\(^3\)
  - Faster recovery from forced exhalation episodes\(^3\)
  - Works better with A/C than SIMV\(^4\)
  - Faster recovery from suctioning\(^4\)
  - Pro-inflammatory cytokines decreased @ 5 ml/kg\(^5\)
  - Faster weaning from mechanical ventilation\(^5\)
  - Higher VT needed in RLBW* infants\(^6\)
  - Higher VT needed with advancing post-natal age\(^3\)

6 Montazami, et al
* RLBW = Ridiculously low birth weight infant (<600g)

VG-Clinical Caveats

- VG should be implemented immediately upon initiation of mechanical ventilation.
- The usual starting target VT is 4 - 5 mL/kg during the acute phase of the illness.
- Larger VT is needed in ELBW infants, those with MAS and older infants with chronic lung disease!
- PIP limit should be set 25% above the PIP currently needed to deliver the target VT and adjusted as needed.
- PIP will default to the limit if sensor is out or when giving a manual breath!
- If the low VT alarm sounds repeatedly, increase the pressure limit AND INVESTIGATE THE CAUSE

VT in infants with MAS

Sharma, et al ESPR 2011

<table>
<thead>
<tr>
<th></th>
<th>MAS (n=28)</th>
<th>Control (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT (ml/kg)</td>
<td>6.11 ± 1.05</td>
<td>4.86 ± 0.77</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MV (ml/kg/min)</td>
<td>371 ± 110</td>
<td>282 ± 63</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PaCO(_2) (mmHg)</td>
<td>41.0 ± 3.9</td>
<td>41.5 ± 3.12</td>
<td>0.56</td>
</tr>
</tbody>
</table>
Relationship of Birthweight and $V_T$
Montazami, et al, Ped Pulmonol 2009

![Graph showing the relationship between birthweight and VT.](graph.png)

$R = -0.563 \ p < 0.001$

Conventional Physiology
Anatomical dead-space = 2mL/kg. Instrumental dead-space is fixed.
Anatomical + Instrumental dead-space = 3mL in a typical 1 kg infant
Anatomical + Instrumental dead-space = 2.5mL in a typical 0.5 kg infant

Alveolar ventilation = (tidal volume – dead-space volume) x RR

<table>
<thead>
<tr>
<th>VT (mL)</th>
<th>DS (mL)</th>
<th>Alveolar Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>3</td>
<td>X</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0.9 X</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Exponential Decline in ETCO$_2$

![Graph showing the exponential decline in ETCO$_2$.](graph2.png)
Time to Eliminate CO₂ from Test Lung
2.5 mm ETT, DS = 3.5 ml

- CO₂ Elimination Time (seconds)
- Added Dead Space (mL)

Keszler, et al. ADC FN in print

Gas Flow Through Narrow ETT

- Fresh gas inflow spikes through DS gas
- Mixing when flow abruptly stops
- Exhaled gas spikes through mixed DS gas

Henderson’s Experiment 1915
Relationship of Post-Natal Age and $V_T$ (mL/Kg)

<table>
<thead>
<tr>
<th>Day</th>
<th>VT (mL/kg)</th>
<th>PCO$_2$ (torr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>5.15 ± 0.6</td>
<td>44.0 ± 5.4</td>
</tr>
<tr>
<td>5-7</td>
<td>5.24 ± 0.7</td>
<td>46.3 ± 5.2</td>
</tr>
<tr>
<td>14-17</td>
<td>5.63 ± 1.0</td>
<td>53.9 ± 7.3</td>
</tr>
<tr>
<td>18-21</td>
<td>6.07 ± 1.4</td>
<td>53.9 ± 6.2</td>
</tr>
</tbody>
</table>

Keszler et al. Arch Dis Child '09

MV and Anatomical Dead Space in ELBW Infants

- As gas is delivered under pressure to the newborn lung, the airway expands in proportion to its compliance.
- Over time, elasticity is lost and airway becomes larger than normal.
- Preterm infants who are mechanically ventilated have larger tracheal widths than nonventilated neonates.


Herber-Jonat, Ped Crit Care Med 2008

Corrected VT
**VG Clinical Caveats: Weaning**

- If target VT is set at low normal (usually 4 mL/kg in first few days, higher later on) and PaCO₂ is allowed to rise to the mid- to high 40s (pH <7.35), weaning occurs automatically (“self-weaning”).
- If VT is set too high and/or the pH is too high, the baby will not have a respiratory drive and will not “self-wean”.
- If the VT is set too low, there will be excessive WOB!
- If significant oxygen requirement persists, PEEP may need to be increased to maintain mean airway pressure as PIP is automatically lowered.
- Most infants can be extubated when they consistently maintain VT at or above the target value with working PIP < 10-12 cm H₂O (< 12-15 cm H₂O in infants > 1 kg) with FiO₂ < 0.35 and good sustained respiratory effort.

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**Work of Breathing @ Different VT target**

*Patel, et al Pediatrics 2009*

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>PTPdi Results According to VT Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT, mL/kg</td>
<td>4 mL/kg</td>
</tr>
<tr>
<td>Baseline</td>
<td>158 ± 7°</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>VT, Inflation Time, Peak Inspiratory Pressure, and Minute Volume According to VT Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT, mL/kg</td>
<td>5.5 ± 0.8</td>
</tr>
<tr>
<td>Inflation time, s</td>
<td>0.24 ± 0.09</td>
</tr>
<tr>
<td>Peak inspiratory pressure, cm H₂O</td>
<td>10.8 ± 3.6</td>
</tr>
<tr>
<td>Infant respiratory rate, breaths per min</td>
<td>60 ± 16</td>
</tr>
</tbody>
</table>

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**VG-SIMV: Minute Ventilation**

*Herrera, et al Pediatr 2002*
Troubleshooting

- There will be more alarms (interactive mode, gives useful information, pay attention to it)
- Avoid excessive alarms (they get ignored!
- Common causes:
  - Limits are too tight (most often pressure limit)
  - Excessive ETT leak (change ETT if leak > 40% (Less of a problem with the VN 500)
  - Forced exhalation episodes
  - Agitation
    - Excessive noise
    - Handling
    - Lack of boundaries

What’s Next?

- Define optimal settings/weaning in BPD
- Randomized trial to show the impact of VG in the immediate post-intubation period.
- Long-term studies with important clinical endpoints: BPD, duration of mech. vent.
- Comparison with other volume-targeted modes

Thank You

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