BASICS OF VENTILATION:
SPONTANEOUS BREATHING

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Disclosures

• Consultant for Xenios
• Speaker fees from Getinge
Outline

Scope of the problem
Pros & Cons of Spontaneous Breathing
Types of Asynchrony
Methods to Reduce Asynchrony
Summary
Evolution of Mortality Over Time in Patients Receiving Mechanical Ventilation

A Esteban, F Frutos Vivar, A Muriel, ND Ferguson, et al.

Am J Respir Crit Care Med 2013
Ventilator modes have 3 key elements

**PS - Pressure Support Ventilation**

**Trigger:** Patient

**Limit:** Pressure

**Cycle:** Flow (% Peak Insp V)
Outline

Scope of the problem
Pros & Cons of Spontaneous Breathing
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Methods to Reduce Asynchrony
Summary
FIFTY YEARS OF RESEARCH IN ARDS
Spontaneous Breathing during Mechanical Ventilation
Risks, Mechanisms, and Management

Takeshi Yoshida¹,²,³,⁴, Yuji Fujino⁴, Marcelo B. P. Amato⁵, and Brian P. Kavanagh¹,²,³
MECHANICAL VENTILATION TO MINIMIZE PROGRESSION OF LUNG INJURY IN ACUTE RESPIRATORY FAILURE

Laurent Brochard¹,², Arthur Slutsky¹,², Antonio Pesenti³,⁴

Initial Lung Injury → Capillary Leak → Lung Edema

P-SILI
↓ PaO₂
↑ Vt, Pendelluft
Increased Pes swings

Impaired Gas Exchange Mechanics

Increased Respiratory Drive
Acute respiratory failure following pharmacologically induce hyperventilation: an experimental animal study


RR 25 then 70/min
V_T 7 then 9-15ml/kg

Table 1. Gross pathologic findings

<table>
<thead>
<tr>
<th>Group</th>
<th>Normal lungs</th>
<th>Mild lesions</th>
<th>Severe lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2</td>
<td>5*a</td>
<td>9*</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Spontaneous Effort Causes Occult Pendelluft during Mechanical Ventilation

Takeshi Yoshida\(^1\), Vinicius Torsani\(^1\), Susimeire Gomes\(^1\), Roberta R. De Santis\(^1\), Marcelo A. Beraldo\(^1\), Eduardo L. V. Costa\(^1\), Mauro R. Tucci\(^1\), Walter A. Zin\(^3\), Brian P. Kavanagh\(^4,5\), and Marcelo B. P. Amato\(^1\)
The Comparison of Spontaneous Breathing and Muscle Paralysis in Two Different Severities of Experimental Lung Injury*

Takeshi Yoshida, MD; Akinori Uchiyama, MD, PhD; Nariaki Matsuura, MD, PhD; Takashi Mashimo, MD, PhD; Yuji Fujino, MD, PhD

Rabbits with mild (saline lavage) or severe (saline lavage + VILI) lung injury
Spontaneous Effort During Mechanical Ventilation: Maximal Injury With Less Positive End-Expiratory Pressure*

Takeshi Yoshida, MD, PhD1,2; Rollin Roldan, MD1,3; Marcelo A. Beraldo, PhD1,4; Vinicius Torsani, PhD1; Susimeire Gomes, PhD1; Roberta R. De Santis, MD1; Eduardo L. V. Costa, MD1,5; Mauro R. Tucci, MD1; Raul G. Lima, PhD6; Brian P. Kavanagh, MD7; Marcelo B. P. Amato, MD, PhD1

Crit Care Med 2016; 44:e678–e688
For tidal volume, data exclude patients weaning in pressure support mode, with FiO$_2 \leq 0.4$ and PEEP $\leq 10$. 

For tidal volume, data exclude patients weaning in pressure support mode, with FiO$_2 \leq 0.4$ and PEEP $\leq 10$. 

<table>
<thead>
<tr>
<th>Variables</th>
<th>Lung Open Ventilation</th>
<th>Control</th>
<th>P Value</th>
<th>Lung Open Ventilation</th>
<th>Control</th>
<th>P Value</th>
<th>Lung Open Ventilation</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume, mean (SD), mL/kg predicted body weight</td>
<td>6.8 (1.4)</td>
<td>6.8 (1.3)</td>
<td>.76</td>
<td>6.9 (1.5)</td>
<td>6.7 (1.5)</td>
<td>.02</td>
<td>6.9 (1.3)</td>
<td>7.0 (1.6)</td>
<td>.53</td>
</tr>
<tr>
<td>No. of patients</td>
<td>436</td>
<td>469</td>
<td>.337</td>
<td>397</td>
<td>305</td>
<td>.001</td>
<td>255</td>
<td>281</td>
<td>.76</td>
</tr>
<tr>
<td>Total respiratory rate, mean (SD), /min</td>
<td>25.2 (6.6)</td>
<td>26.0 (6.5)</td>
<td>.08</td>
<td>25.1 (6.6)</td>
<td>27.1 (8.0)</td>
<td>&lt;.001</td>
<td>25.5 (8.0)</td>
<td>26.1 (7.6)</td>
<td>.26</td>
</tr>
<tr>
<td>No. of patients</td>
<td>471</td>
<td>507</td>
<td>.347</td>
<td>447</td>
<td>479</td>
<td>.001</td>
<td>316</td>
<td>351</td>
<td>.001</td>
</tr>
<tr>
<td>Plateau pressure, mean (SD), cm H$_2$O</td>
<td>30.2 (6.3)</td>
<td>24.9 (5.1)</td>
<td>&lt;.001</td>
<td>28.6 (6.0)</td>
<td>24.7 (5.7)</td>
<td>&lt;.001</td>
<td>28.8 (6.3)</td>
<td>25.1 (6.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of patients</td>
<td>435</td>
<td>424</td>
<td>.174</td>
<td>334</td>
<td>380</td>
<td>.001</td>
<td>174</td>
<td>232</td>
<td>.001</td>
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<tr>
<td>30.1-35.0</td>
<td>113</td>
<td>33</td>
<td>.037</td>
<td>76</td>
<td>38</td>
<td>.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35.1-40.0</td>
<td>86</td>
<td>4</td>
<td>22</td>
<td>17</td>
<td>.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;40.0</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>&lt;.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pco$_2$, mean (SD)</td>
<td>0.59 (0.16)</td>
<td>0.59 (0.17)</td>
<td>&lt;.001</td>
<td>0.41 (0.12)</td>
<td>0.52 (0.16)</td>
<td>&lt;.001</td>
<td>0.39 (0.12)</td>
<td>0.48 (0.17)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of patients</td>
<td>471</td>
<td>507</td>
<td>.319</td>
<td>447</td>
<td>482</td>
<td>.356</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set PEEP, mean (SD), cm H$_2$O</td>
<td>15.6 (3.9)</td>
<td>10.1 (3.0)</td>
<td>&lt;.001</td>
<td>11.8 (4.1)</td>
<td>8.8 (3.0)</td>
<td>&lt;.001</td>
<td>10.3 (4.3)</td>
<td>8.0 (3.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>All patients</td>
<td>471</td>
<td>507</td>
<td>.316</td>
<td>447</td>
<td>479</td>
<td>.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First 151 patients</td>
<td>15.3 (3.8)</td>
<td>10.6 (2.9)</td>
<td>&lt;.001</td>
<td>12.1 (4.1)</td>
<td>9.3 (3.0)</td>
<td>&lt;.001</td>
<td>10.4 (4.3)</td>
<td>8.2 (3.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of patients</td>
<td>77</td>
<td>82</td>
<td>.47</td>
<td>72</td>
<td>79</td>
<td>.63</td>
<td></td>
<td></td>
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<tr>
<td>Subsequent 922 patients</td>
<td>15.7 (4.0)</td>
<td>10.0 (3.0)</td>
<td>&lt;.001</td>
<td>11.8 (4.1)</td>
<td>8.7 (3.0)</td>
<td>&lt;.001</td>
<td>10.3 (4.3)</td>
<td>8.0 (3.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of patients</td>
<td>269</td>
<td>425</td>
<td>.269</td>
<td>278</td>
<td>385</td>
<td>.269</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I:E ratio, mean (SD)</td>
<td>0.62 (0.19)</td>
<td>0.56 (0.19)</td>
<td>&lt;.001</td>
<td>0.64 (0.21)</td>
<td>0.56 (0.21)</td>
<td>&lt;.001</td>
<td>0.64 (0.19)</td>
<td>0.59 (0.23)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of patients</td>
<td>410</td>
<td>420</td>
<td>.170</td>
<td>397</td>
<td>373</td>
<td>.312</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paco$_2$/Pco$_2$, mean (SD)</td>
<td>187.4 (68.6)</td>
<td>140.1 (60.6)</td>
<td>&lt;.001</td>
<td>196.8 (60.6)</td>
<td>164.1 (63.5)</td>
<td>&lt;.001</td>
<td>212.7 (70.5)</td>
<td>180.8 (73.9)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: Pco$_2$, fraction of inspired oxygen; I:E, inspiration/expiration; PEEP, positive end-expiratory pressure; Pa$_{aO2}$, partial pressure of arterial oxygen; Pa$_{aCO2}$, partial pressure of arterial carbon dioxide.

*Data shown were derived from the average value obtained for each patient over 3 measurements each day. Values were recorded on days 1, 3, and 7 after enrollment. For tidal volume and plateau airway pressure measurements, data exclude patients weaning in pressure support mode, with FiO$_2$ less than or equal to 0.4 and PEEP less than or equal to 10 cm H$_2$O.
Evolution of Diaphragm Thickness during Mechanical Ventilation

Impact of Inspiratory Effort

Ewan C. Goligher\textsuperscript{1,2,3,4}, Eddy Fan\textsuperscript{1,2,4,5}, Margaret S. Herridge\textsuperscript{1,2,4,6}, Alistair Murray\textsuperscript{1,4}, Stefannie Vorona\textsuperscript{1,4}, Debbie Brace\textsuperscript{1,4}, Nuttapol Rittayamai\textsuperscript{1,7}, Ashley Lanys\textsuperscript{1,4,7}, George Tomlinson\textsuperscript{2}, Jeffrey M. Singh\textsuperscript{1,2,4}, Steffen-Sebastian Bolz\textsuperscript{3}, Gordon D. Rubenfeld\textsuperscript{1,2,5,8}, Brian P. Kavanagh\textsuperscript{1,3,9,10}, Laurent J. Brochard\textsuperscript{1,2,7}, and Niall D. Ferguson\textsuperscript{1,2,3,4,5,6}

Am J Respir Crit Care Med Vol 192, Iss 9, pp 1080–1088, Nov 1, 2015

510 repeated measurements in 107 subjects

Adjusted for:
- Age
- Sex
- SAPS II
- Sepsis
- SOFA

Thickening fraction modifies the rate of change in thickness (interaction p=0.04)
Spontaneous Breathing in ARDS

When to allow any?

How much to allow?

Consider maintaining normal effort levels – implies measuring effort
Spontaneous Breathing in ARDS

**PRO**
- Prevent diaphragm atrophy (overassist myotrauma)
- Improved hemodynamics
- Less sedation and associated adverse effects
- Progress patients towards liberation

**CONs**
- Direct overdistention injury
- Pendelluft injury
- Increased lung perfusion
- Dyssynchrony – double-trigger
- Expiratory muscle activation leading to decreased EELV

**Effect Modifiers:**
ARDS Severity; Smaller Baby Lung; High Drive; Injurious Setting
Esophageal and transpulmonary pressure in the clinical setting: meaning, usefulness and perspectives
Airway Occlusion Pressure as an Estimate of Respiratory Drive and Inspiratory Effort During Assisted Ventilation
Telias I, et al. AJRCCM 2020 In Press
End-Expiratory Exclusion Manoeuvre

Perform 3 single breath end-expiratory airway occlusions to measure $\Delta P_{occ}$ every 4-8 hours

Estimate $P_{mus}$
If $\Delta P_{occ} < 0 \text{ cm H}_2\text{O}$, estimate $\Delta P_L$

Predicted $P_{mus} > 13-15 \text{ cm H}_2\text{O}$
OR
Predicted $\Delta P_L \geq 16-17 \text{ cm H}_2\text{O}$

Yes
Consider $P_{es}$ monitoring to guide clinical management
or
consider modifying sedation and ventilation to achieve predicted $P_{mus}$ and $\Delta P_L$
within acceptable limits

No

Target achieved

Predicted $P_{mus} = -0.7 \times \Delta P_{occ}$
Predicted $\Delta P_L = (\text{Peak Paw} - \text{PEEP}) - 0.6 \times \Delta P_{occ}$
Bedside Adjustment of Proportional Assist Ventilation to Target a Predefined Range of Respiratory Effort

Guillaume Carteaux, MD; Jordi Mancebo, MD, PhD; Alain Mercat, MD, PhD; Jean Dellamonica, MD, PhD; Jean-Christophe M. Richard, MD, PhD; Hernan Aguirre-Bermeo, MD; Achille Kouatchet, MD; Gaetan Beduneau, MD; Arnaud W. Thille, MD, PhD; Laurent Brochard, MD

**INITIATION OF PAV+**

**VENTILATORY PARAMETERS SETTINGS**
- Gain: 50%
- Inspiratory trigger: 11/min

**ALARMS SETTINGS**
- $P_{peak}$ max: 40 cmH$_2$O
- RR max: 40 cycles/min
- $V_{te}$ max: 10 ml/kg of TBW
- $V_{te}$ min: 0 ml
- $V_{e}$ max: 20 l/min
- $V_{e}$ min: 7 l/min

**ALGORITHM TO ADJUST THE GAIN**

1. **CALCULATE $P_{mus,Peak}$**
2. **DECREASE THE GAIN IN STEPS OF 10% until $P_{peak}$ reaches the target range**
3. **TARGET RANGE ACHIEVED: NO ACTION, unless one of the followings occurs**
4. **INCREASE THE GAIN IN STEPS OF 10% until $P_{peak}$ reaches the target range**
Pressure Support Ventilation

Ventilator’s mission is to regulate pressure
• Set PS level; $C_{RS}$; AND Patient Effort determine $V_T$

PS 8; PEEP 5
$V_T = 750 \text{ mL}$
How do control $V_T$ in this patient???
Decreasing spontaneous effort levels

Increase inspiratory assist – but be careful with $V_T$
Increase PEEP
Consider NMB – but trade Under for Over-assist
Consider partial NMB
Consider ECLS
Outline

Scope of the problem
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Methods to Reduce Asynchrony
Summary
Patient-ventilator asynchrony during assisted mechanical ventilation

<table>
<thead>
<tr>
<th></th>
<th>Asynchrony index &lt; 10% (n = 47)</th>
<th>Asynchrony index ≥ 10% (n = 15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of mechanical ventilation (days; IQR)</td>
<td>7 (3–20)</td>
<td>25 (9–42)</td>
<td>0.005</td>
</tr>
<tr>
<td>Duration of mechanical ventilation ≥ 7 days</td>
<td>23 (49%)</td>
<td>13 (87%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>2 (4%)</td>
<td>5 (33%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Mortality</td>
<td>15 (32%)</td>
<td>7 (47%)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

25% of patients showed significant asynchrony
Asynchronies during mechanical ventilation are associated with mortality

<table>
<thead>
<tr>
<th></th>
<th>Al ≤ 10 % (n = 44)</th>
<th>Al &gt; 10 % (n = 6)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of MV (days)</td>
<td>6 [5.0; 15.0]</td>
<td>16 [9.7; 20.0]</td>
<td>0.061</td>
</tr>
<tr>
<td>Reintubation</td>
<td>9 (20 %)</td>
<td>0 (0 %)</td>
<td>0.57</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>14 (32 %)</td>
<td>2 (33 %)</td>
<td>0.999</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>6 (14 %)</td>
<td>4 (67 %)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>10 (23 %)</td>
<td>4 (67 %)</td>
<td>0.044*</td>
</tr>
</tbody>
</table>
Types of Asynchrony

Ineffective Efforts / Delayed Triggering
• Trigger too insensitive / weak efforts
• Auto PEEP
• Cycle-off Asynchrony (prolonged inspiration)

Double Triggering
• High respiratory drive / Short set inspiratory time

Cycle-off Asynchrony
• Prolonged inspiration
• Premature termination

Reverse Triggering

Auto Triggering
• Cardiac oscillations / Trigger too sensitive
Ineffective Efforts

![Graphs showing ineffecive efforts](image)
Delayed Triggering
Cycle-off Asynchrony (and others)
Cycle-off Asynchrony – Premature Termination
Spontaneous Breathing during Mechanical Ventilation
Risks, Mechanisms, and Management

Takeshi Yoshida\textsuperscript{1,2,3,4}, Yuji Fujino\textsuperscript{4}, Marcelo B. P. Amato\textsuperscript{5}, and Brian P. Kavanagh\textsuperscript{1,2,3}
Outline

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28-day Mortality:  
24% - Nimbex  
33% - Placebo  
p=0.05
Avoiding Asynchrony

Monitor and treat / match AutoPEEP
Avoid Volume A/C
Using Pressure Support
  • Decrease PS level
  • Increase cycle-off trigger
Advanced modes
Partial Neuromuscular Blockade during Partial Ventilatory Support in Sedated Patients with High Tidal Volumes

Jonne Doorduin¹, Joike L. Nollet¹, Lisanne H. Roesthuis¹, Hieronymus W. H. van Hees², Laurent J. Brochard³,⁴, Christer A. Sinderby³,⁴, Johannes G. van der Hoeven¹, and Leo M. A. Heunks¹

1. Baseline
   VCV (10 min): $V_T = 6$ ml/kg

2. Titration
   Bolus rocuronium 2–5 mg
   if $V_T >$

Am J Respir Crit Care Med Vol 195, Iss 8, pp 1033–1042, Apr 15, 2017

start phase 2: rocuronium titration
Extracorporeal life support for adults with severe acute respiratory failure

Lorenzo Del Sorbo, Marcelo Cypel, Eddy Fan

ECCO₂R

- Circuit/hypoxia: Venous bypass or arteriovenous bypass
- Blood drainage: From central vein (IJV, FV, SV) or femoral artery in arteriovenous configuration
- Blood return: Into central vein (IJV, FV, SV)
- Cannula dimension: 8-29 Fr
- Intravenous access: Single or double
- Cannula type: Two single cannulas or dual-lumen cannula
- Pump: Centrifugal or peristaltic (absent in arteriovenous configuration)
- Extracorporeal blood flow: 0.2-2.0 L/min
- CO₂ clearance: 30-100% VO₂, dependent mainly on sweep-gas flow
- Oxygen delivery capacity: Not significant
- Anticoagulation target: ACT 1.5 times normal, aPTT 1.5 times normal
Laboratory Report

Control of Breathing Using an Extracorporeal Membrane Lung

Theodor Kolobow, M.D.,* Luciano Gattinoni, M.D.,* Timothy A. Tomlinson, B.S.,* Joseph E. Pierce, D.V.M.†

7 lambs
No anaesthesia or sedation
ECCO₂R

CO₂ Removal Increases with Blood Flow 200-1000 mL
Low-Frequency Positive-Pressure Ventilation With Extracorporeal CO₂ Removal in Severe Acute Respiratory Failure (JAMA 1986;256:881-886)

Luciano Gattinoni, MD; Antonio Pesenti, MD; Daniele Mascheroni, MD; Roberto Marcolin, MD; Roberto Fumagalli, MD; Francesca Rossi, MD; Gaetano Iapichino, MD; Giuliano Romagnoli, MD; Liji Uziel, MD; Angelo Agostoni, MD; Theodor Kolobow, MD; Giorgio Damia, MD
Opinion Based Medicine…

Set $V_T = 6$ ml/kg (or lower)
Control breath size if mod-severe ARDS

Set $V_T = 6-8$ ml/kg
Tolerate larger spontaneous breaths
Consider check for pendeluft
Take Home Points

- Impact of spontaneous breathing during ARDS depends on timing and severity
- Measuring patient effort is important
- Asynchrony is common and MAY impact outcomes
- When allowing spontaneous breathing – consider normalizing efforts to protect both lung and diaphragm
- Pay attention to flow and pressure–time waveforms!
ECMO for ARDS: from salvage to standard of care?

Darryl Abrams, Niall D Ferguson, Laurent Brochard, Eddy Fan, Alain Mercat, Alain Combes, Vin Pellegrino, Matthieu Schmidt, Arthur S Slutsky, *Daniel Brodie

Treat underlying cause of ARDS
Standard lung-protective ventilation strategy
Diuresis or resuscitation as appropriate

\[ \text{PaO}_2: \text{FiO}_2 < 150 \text{ mmHg} \]

Strongly recommend:
- Prone positioning (unless contraindicated)
Recommend:
- NMBA
- High PEEP strategy
May also consider:
- Inhaled pulmonary vasodilators
- Recruitment maneuvers

\[ \text{PaO}_2: \text{FiO}_2 \geq 150 \text{ mmHg} \]

Is the pH < 7.25 with PaCO\(_2\) ≥ 60 mmHg > 6hrs\(^a\)?

Yes\(^b\)
- Contraindication to ECMO?\(^d\)

Yes
- Consider adjunctive therapies,\(^d\) as appropriate

No
- Recommend ECMO?\(^e\)

Are any of the following criteria met?
- PaO\(_2\):FiO\(_2\) < 80 mmHg for > 6hrs
- PaO\(_2\):FiO\(_2\) < 50 mmHg for > 3hrs
- pH < 7.25 with PaCO\(_2\) ≥ 60 mmHg > 6hrs\(^a\)

No
- Continue current management