BPD ED
ENFISEMA BOLLOSO ACQUISITO:
Il danno polmonare e le strategie preventive

Dott. Oronzo Forleo
Pulmonary Injury Sequence

Immaturità polmonare

O2 tossicità

Fattori infiammatori

Volutrauma

Atelectrauma

Barotrauma

Biotrauma
Effect of 45 cmH₂O PIP

Control  5 min  20 min
Ventilator induced lung injury

Table 1  Goals of mechanical ventilation

- Overcome alveolar atelectasis
- Achieve adequate pulmonary gas exchange
- Decrease the patient work of breathing
- Maximise patient comfort
- Avoid ventilator induced lung injury

Minimising ventilator induced lung injury in preterm infants. Donn SM, Sinha SK. Arch Dis Child Fetal neonatal Ed 2006;91:F226-F230
Lung-Protective Ventilation

- Low tidal volumes: ~ 6 mL/kg of predicted body weight
- PIP not exceeding 30 cm H$_2$O
- Sufficient PEEP

*Using this approach mortality has been reduced*
Minimising ventilator induced lung injury in preterm infants. Donn SM, Sinha SK. Arch Dis Child Fetal neonatal Ed 2006;91:F226-F230

Figure 1 The pulmonary injury sequence. The diagram illustrates the effect of ventilator induced injury and other factors on lung development and their relation to chronic lung disease (CLD). Reproduced from Attar MA, Donn SM. Mechanism of ventilator-induced lung injury in premature infants. Semin Neonatol 2002;7:353-60, with permission from Elsevier.
Stress and Strain within the Lung

**Volutrauma**  
*Strain*: lung deformation or ratio of the change in lung volume to the resting volume due to VT

**Barotrauma**  
*Stress*: forces/pressure developing into the lung structure that react to the transpulmonary pressure

Neither VT/ideal body weight nor plateau pressure are adequate estimate of volutrauma and barotrauma, because of large individual variability in FRC and chest wall elastance respectively.
Ventilator Induced Lung Injury

Stretch Injury

Alveolar Space

A-C Membrane
Atelectrauma (Stress)

Forces/pressure developing into the lung structure that react to the transpulmonary pressure

The applied force are inhomogeneously distributed within the lung parenchyma and in the regions around lung collapse or consolidation stress is multiplied and pressure can be much higher than that applied to the airway.
Volutrauma (Strain)

Lung deformation, or ratio of the change in lung volume to the resting volume due to VT (VT/FRC)

When the strain is unphysiological, the cells anchored to the lung skeleton are abnormally stretched.

Edema/Inflammatory reaction

Lung fibrous skeleton (extracellular matrix)
Schematic representation of mechanisms of injury during tidal ventilation

- **A**: the aerated ventral regions (baby lung) have the highest compliance and are easily overdistended $V_t$ (volutrauma)

- **B**: regions of collapse (reversible lung closure) are prone to cyclic recruitment- derecruitment (atelectrauma)

- **C**: regions of consolidation and atelectasis (irreversible lung closure)
Sufficient PEEP (Recruitment)

- Airway collapse
- Atelectasis
- Open, stable alveoli
- Alveolar overdistension
- Impedance of pulmonary perfusion
- Impedance of venous return
- Poor right heart filling

- Practically... is the lowest pressure that, at a safe FiO₂, yields satisfactory oxygen delivery (PaO₂, SaO₂, lactates) with minimal cardiovascular compromise (BP, HR, SvO₂)
Maria

EG: 26 settimane
Nata da TC

Peso alla nascita: 650 gr
Recruitment maneuvers

- sustained inflation to high pressure
- intermittent sighs
- stepwise increases in PEEP (and PIP)

In presence of areas of stress raisers recruitment maneuvers are not without risks.
Caratteristiche cliniche della BPD

<table>
<thead>
<tr>
<th>OLD BPD</th>
<th>NEW BPD</th>
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<tbody>
<tr>
<td>No steroidi prenatali</td>
<td>Steroidi prenatali</td>
</tr>
<tr>
<td>Prematurità</td>
<td>Prematurità grave</td>
</tr>
<tr>
<td>Patologia respiratoria acuta grave (RDS o Polmonite)</td>
<td>Patologia respiratoria acuta lieve o assente</td>
</tr>
<tr>
<td>No surfactant esogeno</td>
<td>Surfactant esogeno</td>
</tr>
<tr>
<td>Ventilazione meccanica con pressioni di picco elevate ed alte FiO₂</td>
<td>Ventilazione meccanica con pressioni di picco basse e bassa FiO₂ per brevi periodi</td>
</tr>
<tr>
<td>Enfisema interstiziale, PDA, Edema polmonare, Infezioni</td>
<td>PDA e/o Infezioni virali o batteriche</td>
</tr>
<tr>
<td>Radiografia toracica tipica</td>
<td>Radiografia toracica aspecifica</td>
</tr>
<tr>
<td>Mortalità: 30-40%</td>
<td>Mortalità molto bassa o nulla</td>
</tr>
<tr>
<td>Funzione polmonare anormale per molti anni</td>
<td>Funzione polmonare normale al follow-up (??)</td>
</tr>
</tbody>
</table>
Lung Protective Strategies

1. Avoidance of the “mechanical” elements of VILI by ventilating the lung close to the normal functional residual capacity

2. Careful attention must be given to airway and circuit flow

3. Monitoring of tidal volume delivery

Experienced clinicians who continues to ask the right questions and seek the right answers

Minimising ventilator induced lung injury in preterm infants. Donn SM, Sinha SK. Arch Dis Child Fetal neonatal Ed 2006;91:F226-F230
Lung Protective Strategies

1. Antenatal corticosteroids
2. Surfactant replacement
3. Continuous Positive Airway Pressure
4. Permissive Hypercapnia
5. Conventional Mechanical Ventilation (PTV-VTV-PAV)
6. High Frequency Ventilation (HFJV-HFOV)
7. Continuous Monitoring Technique (pulmonary graphics and waveforms in real time)
La negazione del danno
**Immaturità polmonare**

Distress respiratorio grave

- Barotrauma
- Ossigenotossicità
- Flogosi
- Necrosi + Fibrosi

Distress respiratorio non grave

- Volutrauma
- Barotrauma
- Atelectrauma
- Rheotrauma
- Biotrauma
- Infiammazione
- Arresto sviluppo alveolo-capillare

OLD BPD

NEW BPD
<table>
<thead>
<tr>
<th>Severity-Based Diagnostic Criteria for BPD</th>
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<tbody>
<tr>
<td><strong>Gestational Age</strong></td>
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<tr>
<td><strong>Time point of Assessment</strong></td>
</tr>
<tr>
<td><strong>Mild BPD</strong></td>
</tr>
<tr>
<td><strong>Moderate BPD</strong></td>
</tr>
<tr>
<td><strong>Severe BPD</strong></td>
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</table>
DEFINIZIONE DI MALATTIA POLMONARE CRONICA

DBP di Northway ’67
(clinico-radiologica ed anatomo-patologica)

CLD - Tooley ’79
BPD e CLD tipo I - Edwards ’79
BPD tipo 1 e 2 - Hyde ’89
(clinico-radiologica)

O₂ dipendenza a 28 gg. - anni 90
O₂ terapia per 28 gg. - anni 90
O₂ dipendenza a 36 sett. e.p.c. - anni 90
(clinico-terapeutica non standardizzata)

New Definition of BPD - 2001

Physiologic definition - 2003
Physiologic definition

Diagnosis based on oxygen-saturation monitoring in selected infants in low oxygen $\gg \text{FiO}_2 < 0.30$ (hood or nasal cannula) at 36 ± 1 weeks pca

Diagnostic challenge

- 1 hour before: $\text{SpO}_2$ 90%-96% if Fio2 <0.30 and >96% if Fio2 ≥ 0.30

- Oxygen weaned in 2% increments every 10 minutes

- 30 minutes on room air:
  - Test passed if SpO2 >96% for 15 minutes or 90%-95% for 30 minutes
  - Failure if SpO2 80%-89% for 5 minutes or <80% for 15 seconds

- Return to usual oxygen

1. Criteria to assess need for oxygen therapy
2. Limits of oxygen-saturation
3. Methods for oxygen administration (hood, nasal cannula)
4. Oxygen administration for extrapulmonary indications
5. Adverse events during oxygen weaning (apnea, bradycardia)
6. Pharmacologic therapies (diuretics, methylxanthines, bronchodilators, corticosteroids)
ASISTENZA IN SALA PARTO

NEONATI CON E.G. > 28 SETTIMANE

- EUPNEA: NESSUNA ASISTENZA
- APNEA + F.C. > 50/min: VENTILAZIONE CON MASCHERA
- APNEA + F.C. < 50/min: INTUBAZIONE e VM
- SINTOMI DI RDS: VENTILAZIONE CON MASCHERA, poi NASOCANNULE (CPAP 4; FiO₂ 0.21-0.40)
  (TRANNE ERNIA DIAFRAMMATICA E SAM)

NEONATI CON E.G. < 28 SETTIMANE

- EUPNEA: NASOCANNULE (CPAP 4; FiO₂ 0.21)
- APNEA + F.C. > 50/min: VENTILAZIONE CON MASCHERA poi NASOCANNULE (CPAP 4; FiO₂ 0.21)
- APNEA + F.C. < 50/min: INTUBAZIONE e VM
- SINTOMI DI RDS: VENTILAZIONE CON MASCHERA, poi NASOCANNULE (CPAP 4; FiO₂ 0.21-0.40)
L’ingresso nella TIN: il comportamento assistenziale

A] NEONATO CHE ARRIVA DALLA SALA PARTO NON INTUBATO

<table>
<thead>
<tr>
<th>Silverman 4-6: NASOCANNULE</th>
<th>Silverman &gt;6 :IMV (PTV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP 4 cm H₂O</td>
<td>PIM 20 cm H₂O</td>
</tr>
<tr>
<td>FiO₂ 0,40</td>
<td>PEEP 4 cm H₂O</td>
</tr>
<tr>
<td></td>
<td>FR 40/m’</td>
</tr>
<tr>
<td></td>
<td>Ti 0,3”</td>
</tr>
<tr>
<td></td>
<td>FiO₂ 0,21</td>
</tr>
</tbody>
</table>

N.B.: Considerare HFOV e Trattamento precoce con Surfactant

B] GOALS DELL’ASSISTENZA RESPIRATORIA

<table>
<thead>
<tr>
<th>Obiettivi assistenziali</th>
<th>Riduzione rischio iatrogeno</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH 7,30 - 7,45</td>
<td>PIM &lt;15 cm H₂O</td>
</tr>
<tr>
<td>PaCO₂ 45 - 55 mmHg</td>
<td>Ti &lt; 0,4”</td>
</tr>
<tr>
<td>PaO₂ 50 - 70 mmHg</td>
<td>FiO₂ &lt; 0,40</td>
</tr>
<tr>
<td>SpO₂ 88 - 93 %</td>
<td>PEEP 4 - 6 cm H₂O</td>
</tr>
<tr>
<td></td>
<td>Intubazione &lt; 5gg</td>
</tr>
</tbody>
</table>
66 neonates with MAS randomized to receive either BAL with diluted surfactant in two large aliquots of 15 mL/Kg or standard care

Lavage led to a significant reduction (-21%) in mortality or need for ECMO and to a more rapid decrease in mean airway pressure, with no substantial adverse effects.

A higher fluid recovery is associated with shorter disease duration and greater reduction in mean airway pressure, thus the recovered volume seems to be a priority target while performing lavages.
Prone position: side effects

- accidental extubation
- facial oedema
- airway obstruction
- skin lesions
- transitory decrease in $\text{SaO}_2$
- difficulties with enteral feeding
- hypotension
- loss of venous accesses and probes
- loss of dialysis catheters
- apical atelectasis due to incorrect positioning of EET
- increased need for sedation
High-Frequency Oscillation for Acute Respiratory Distress Syndrome


METHODS

In a multicenter study, we randomly assigned adults requiring mechanical ventilation for ARDS to undergo either HFOV with a Novalung R100 ventilator (Metran) or usual ventilatory care. All the patients had a ratio of the partial pressure of arterial oxygen (PaO₂) to the fraction of inspired oxygen (FiO₂) of 200 mm Hg (26.7 kPa) or less and an expected duration of ventilation of at least 2 days. The primary outcome was all-cause mortality 30 days after randomization.

CONCLUSIONS

The use of HFOV had no significant effect on 30-day mortality in patients undergoing mechanical ventilation for ARDS. We recommend that this mode of ventilation not be used for routine care.
Should critically ill children with acute respiratory failure be treated with surfactant?

Zhi Min Ng, Nirmal Visrusthan Kavalloor and Jan Hau Lee

Arch Dis Child published online May 16, 2013

Clinical bottom line

The use of surfactant in critically ill children with acute respiratory failure may improve gaseous exchange but it has not been conclusively proven to shorten duration of mechanical ventilation, length of ICU stay and improve mortality.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Summary</th>
</tr>
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<tbody>
<tr>
<td>Jat and Chawla [1] (Cochrane review of three RCTs by Ludetti et al [2] Tibby et al [3] Wilton et al [4])</td>
<td>77 given surfactant, 75 were given air placebo OR equal volume of air placebo every 12 h for 1 to 2 doses</td>
</tr>
<tr>
<td>Moller et al, 2003 [5]</td>
<td>Lucinactant 175 mg/kg (5.8 ml/kg) OR sham air 6 ml/kg</td>
</tr>
<tr>
<td>Wilton et al [6] Thomas et al [7]</td>
<td>RCT (level 1b) Duration of MV No difference Duration of ICU stay No difference Mortality No difference Adverse events Incidence of desaturation (34/94 (40%) vs 4/81 (5%), p&lt;0.001) and bradycardia (19/84 (22%) vs 1/81 (1%), p=0.006) were significantly higher in surfactant group than in the placebo group</td>
</tr>
</tbody>
</table>

ARDS, acute respiratory distress syndrome; ICU, intensive care unit; MV, mechanical ventilation; RCT, randomised control trial; RSV, respiratory syncytial virus.
Potential therapeutic options according to the severity of ARDS: boxes in yellow represent therapies that still require confirmation in prospective clinical trials.
Prone position

In patients with severe ARDS the prone position provides a significant survival advantage.
Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure: impact and clinical fallout through the following 20 years

The primary mechanism of oxygenation improvement appears to depend on dorsal recruitment being greater than ventral de-recruitment.
Disruption of the alveolar-capillary barrier

- V/Q mismatch
- Alveolar-capillary injury
- Protein-rich edema fluid
- Inactivation of surfactant
- Platelet aggregation
- Neutrophil aggregation
- Vessel lumen
- Injured Epithelium
- Injured Endothelium
Therapeutic strategies

- Protective ventilation (A)
- Sufficient PEEP (B)
- Prone position (C)
Morfologia alveolare

Struttura sacculare

BPD

Controllo
To avoid atelectrauma, PEEP is kept above the lower inflection point (LIP).

Peak inflation pressure (PIP) is chosen to generate a tidal volume (TV) of 6 ml/kg to avoid volutrauma beyond the upper inflection point (UIP).
La gentle ventilation: una necessaria filosofia assistenziale

dott. Oronzo Forleo

Struttura Complessa di Patologia e Terapia Intensiva Neonatale
Azienda Ospedaliera "SS. Annunziata" TARANTO
La Patologia Polmonare Cronica del Neonato

La Storia

1967 Northway Displasia Broncopolmonare
1979 Edwards Type 1 CLD of Prematurity
1979 Tooley CLD
1989 Hyde DPB tipo 1
      DPB tipo 2

Workshop NICHD on PPC
DPB mild
      moderate
      severe
Pulmonary Injury Sequence
Ventilator Induced Lung Injury
Chronic Lung Disease

*Definizioni*

- Neonato con necessità di ventilazione meccanica e/o O₂ terapia a 28 giorni di vita
- Neonato con necessità di ventilazione meccanica e/o O₂ terapia al compimento della 36ᵃ settimana di età post-concezionale
Immaturità polmonare

- Distress respiratorio grave
  - Barotrauma
  - Ossigenotossicità
  - Flogosi
  - Necrosi + Fibrosi

- Distress respiratorio non grave
  - Volutrauma
  - Barotrauma
  - Atelectrauma
  - Rheotrauma
  - Biotrauma
  - Infiammazione
  - Arresto sviluppo alveolo-capillare

OLD BPD
NEW BPD
Chronic Lung Disease

Il quadro clinico è quello di una patologia cronica che fa seguito ad una patologia acuta.

Unresolved neonatal acute lung injury
(O’Brodovich)
Pulmonary Injury Sequence

Immaturità polmonare

O₂ tossicità

Fattori infiammatori

Volutrauma

Atelectrauma

Barotrauma
Morfologia alveolare

Struttura sacculare

Controllo

BPD
Rischio di danno polmonare da ventilazione!

✓ Dilatazione ultime vie aeree

✓ Alterazione dell’epitelio con accumulo di fluidi e proteine negli alveoli

✓ Attivazione della cascata infiammatoria
Rapporto compliance - CFR
Legge di Laplace

Equazione di Laplace

\[ P = \frac{2T}{r} \]

+ Surfattante

- Surfattante

Surfattante
Parete alveolare
Diagramma pressione volume

\[ C = \frac{V}{P} \]

RDS
Figure 1  The pulmonary injury sequence. The diagram illustrates the effect of ventilator induced injury and other factors on lung development and their relation to chronic lung disease (CLD). Reproduced from Altar MA, Donn SM. Mechanism of ventilator-induced lung injury in premature infants. Semin Neonatol 2002;7:353–60, with permission from Elsevier.
danno dell’epitelio

ridotta rigidità strutturale

ridotta compliance

dilatazione delle ultime vie aeree

danno dell’epitelio

fluidi e proteine

atelectasia
Maria

EG: 26 settimane
Nata da TC

Peso alla nascita:
650 gr
La Prevenzione della Patologia Polmonare Cronica

- Prevenzione della prematurità
- Steroidi prenatali
- Trattamento delle infezioni pre e post-natali
- Surfactant
- Gentle Ventilation
- Uso precoce dalla CPAP
- Gestione del dotto arteriosso
- Apporto nutrizionale
- Steroidi
Ventilator Induced Lung Injury

- Barotrauma
- Volutrauma
- Stretch Injury
- Biochemical Injury
Ventilator Induced Lung Injury

- Barotrauma
  - Air leaking into pleural space
  - Air leaking into interstitial space (PIE)
  - Tearing at Bronchio-Alveolar junction as lung is recruited and allowed to collapse
- Most occurs in dependent lung zones (transition zone)
Ventilator Induced Lung Injury

- Stretch Injury
- Alters capillary transmural pressures
- Changes in transmural pressure causes breaks in capillary endothelium and epithelium
- Increases leak of proteinacious material
- Promotes Atelectasis
“Open up the lung up and keep it open!”

Burkhard Lachmann, 1992
La Prevenzione della Patologia Polmonare Cronica

✓ Prevenzione della prematurità
✓ Steroidi prenatali
✓ Trattamento delle infezioni pre e post-natali
✓ Surfactant
✓ Gentle Ventilation
✓ Uso precoce dalla CPAP
✓ Gestione del dotto arterioso
✓ Apporto nutrizionale
✓ Steroidi