Acute Respiratory Distress Syndrome

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Objectives

• Review the causes and differentials for ARDS
• Briefly discuss the pathophysiology
• Discuss the clinical manifestations of ARDS
• Understand evidence based treatment options
Case

51 y/o diabetic male is admitted with 3 day history of fever and increasing cough and SOB. He says he does not “believe in getting flu shots.” In the ER he is cyanotic and using accessory muscles with RR 44. O2 sat is 75%. He is placed on nonrebreather mask with O2 sat rising to 88%. 6 hours later he is in severe distress with O2 sat 80% and has become poorly responsive. He is then intubated and placed on mechanical ventilation. Nasal swab reveals influenza A.
Case Chest X-ray
Case

• He is placed on A/C FIO2 100%, PEEP 5, TV 10 cc per Kg and rate 12. He is agitated and O2 sat is 86%.
• Pulmonary fellow starts the ARDSnet protocol:
  
  TV 8cc/Kg ideal body weight then changed to 7cc/Kg and then 6cc/Kg.
  
  RR set to maintain patient comfort, safe pH – rate 30
  
  FIO2 titrated to maintain O2 sat 88% to 95% - FIO2 60%
  
  PEEP set based on ARDSnet table – PEEP 10

• Versed and fentanyl drips started
• Patient no longer agitated, O2 sat 93%
History of ARDS

• In 1821 Laennec described the gross pathology of the lungs in what he called idiopathic anasarca of the lungs

• Recognized by battlefield physicians for more than 100 years - called shock lung (following poison gas in WWI), traumatic wet lung (WWII), DaNang lung (Viet Nam War)

• In 1967, in a landmark article published in Lancet, Ashbaugh and colleagues provided the modern description of the clinical entity that they called “acute respiratory distress in adults.” They recognized it to be a syndrome following a wide variety of insults, some blood borne and some airway borne. They also described the use of PEEP to treat ARDS.

• Decades of debate followed on how to treat ARDS with focus on PEEP (and how to use it) and meds (corticosteroids, NSAIDs, etc) – lots of heat with little light - a new approach was needed – it took 33 years.
Statistics

• Epidemiology
  – Annual incidence: 60/100,000
  – 20% ICU patients meet criteria for ARDS

• Morbidity / Mortality
  – 26-44%, most (80%) deaths attributed to non-pulmonary organ failure or sepsis.

• Risk Factors for poor outcome
  – Advanced age, pre-existing organ dysfunction or chronic medical illness
  – Patient with ARDS from direct lung injury have higher incidence of death than those from non-pulmonary injury

Levy BD, & Choi AM, Harrison’s Principles of Internal Medicine, 2012
Definition

1) Acute onset
2) Bilateral infiltrates
3) No clinical evidence of left heart failure (or PCWP ≤ 18)

- PaO2:FiO2 ≤ 300
  - Or
  - SaO2:FiO2 ≤ 315
- PaO2:FiO2 ≤ 200
  - Or
  - SaO2:FiO2 ≤ 235

Acute Lung Injury

Acute Respiratory Distress Syndrome

Bernard et al. AJRCCM 1994; 149:818
- European Society of Intensive Care Medicine with endorsement from American Thoracic Society and Society of Critical Care Medicine
- Devised three mutually exclusive severity categories: Mild, Moderate and Severe
- Took into account: timing, chest imaging, origin of edema, oxygenation
<table>
<thead>
<tr>
<th>Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome</th>
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<tbody>
<tr>
<td><strong>Acute Respiratory Distress Syndrome</strong></td>
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<tr>
<td><strong>Timing</strong></td>
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<tr>
<td>Within 1 week of a known clinical insult or new or worsening respiratory symptoms</td>
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<td><strong>Chest imaging</strong></td>
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<td>Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules</td>
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<td><strong>Origin of edema</strong></td>
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<td>Respiratory failure not fully explained by cardiac failure or fluid overload</td>
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<td><strong>Oxygenation</strong></td>
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<tr>
<td><strong>Mild</strong></td>
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<td>$200 \text{ mm Hg} &lt; \frac{\text{PaO}_2}{\text{FiO}_2} \leq 300 \text{ mm Hg}$ with PEEP or CPAP $\geq 5 \text{ cm H}_2\text{O}$</td>
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<tr>
<td><strong>Moderate</strong></td>
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<td>$100 \text{ mm Hg} &lt; \frac{\text{PaO}_2}{\text{FiO}_2} \leq 200 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$</td>
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<tr>
<td><strong>Severe</strong></td>
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<tr>
<td>$\frac{\text{PaO}_2}{\text{FiO}_2} \leq 100 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$</td>
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Abbreviations: CPAP, continuous positive airway pressure; FiO₂, fraction of inspired oxygen; PaO₂, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

a Chest radiograph or computed tomography scan.

b If altitude is higher than 1000 m, the correction factor should be calculated as follows: \[ \frac{\text{PaO}_2/\text{FiO}_2 \times \text{(barometric pressure/760)}} \]

c This may be delivered noninvasively in the mild acute respiratory distress syndrome group.
Mild ARDS
Severe ARDS
Causes of ARDS

- Pneumonia: 35%
- Severe Sepsis: 26%
- Other: 13%
- Trauma: 11%
- Aspiration: 15%
- Other: drowning, pancreatitis, reperfusion, salicylate and narcotic OD, fat/amniotic embolism, smoke/chemical inhalation.

Airway borne insult examples:
Toxic gas inhalation: phosgene, chlorine
Aspiration
Near drowning
Smoke inhalation
Pneumonia

Blood borne insult examples:
Sepsis
Drug over dose: opiates, aspirin
Fat or amniotic fluid embolism (not PE)
Pancreatitis
Transfusion-related acute lung injury
Burns
Multiple trauma
Differentials - mimics

- Left ventricular failure/volume overload
- Mitral stenosis
- Pulmonary veno-occlusive disease
- Lymphangitic spread of malignancy
- Interstitial and/or airway disease
  - Hypersensitivity pneumonia
  - Acute eosinophilic pneumonia
  - Acute interstitial pneumonitis
1. Direct injury (airway borne) or indirect injury (blood borne) to the alveolus causes alveolar macrophages to release pro-inflammatory cytokines.

2. Neutrophiles are attracted to the alveolus and interstitium, where they damage the alveolar-capillary membrane (ACM).

3. ACM integrity is lost, interstitium and alveolus fill with proteinaceous fluid, surfactant can no longer support alveolus.

Ware et al. NEJM 2000; 342:1334
Pathophysiology

• Consequences of lung injury include:
  – Impaired gas exchange
  – Decreased compliance
  – Increased pulmonary arterial pressure
Impaired Gas Exchange

• V/Q mismatch
  – Related to filling of alveoli
  – Shunting causes hypoxemia

• Increased dead space
  – Related to capillary dead space and V/Q mismatch
  – Impairs carbon dioxide elimination
  – Results in high minute ventilation
Decreased Compliance

• Hallmark of ARDS
• Consequence of the stiffness of poorly or nonaerated lung – loss of surfactant
• Fluid filled lung becomes stiff/boggy
• Requires increased pressure to deliver Vt
Increased Pulmonary Arterial Pressure

- Occurs in up to 25% of ARDS patients
- Results from hypoxic vasoconstriction
- Positive airway pressure causing vascular compression
- Can result in right ventricular failure
Hypothesis:

- In patients with ALI, ventilation with smaller tidal volumes (6 mL/kg) will result in better clinical outcomes than traditional tidal volume (12 mL/kg) ventilation.
- Large multicenter randomized trial.
- Based on extensive animal research.
Low Tidal Volume Ventilation

- When compared to larger tidal volumes, Vt of 6ml/kg of ideal body weight:
  - Decreased mortality
  - Increased number of ventilator free days
  - Decreased extrapulmonary organ failure
  - Showed that larger tidal volumes damaged lungs and increased mortality

ARDSnet. *NEJM* 2000; 342: 1301
Low Tidal Volume Ventilation

ARDS affects the lung in a heterogeneous fashion

- **Normal alveoli**
- **Injured alveoli** can potentially participate in gas exchange, susceptible to damage from opening and closing (recruitment/derecruitment)
- **Damaged alveoli** filled with fluid, do not participate in gas exchange
- “Baby Lung”
Low Tidal Volume Ventilation or Lung Protective Ventilation

• Protective measure to avoid over distention of normal alveoli and repeated opening and closing of damaged alveoli.
• Uses low tidal volumes – baby lung
• Minimizes airway pressures
• Uses Positive end-expiratory pressure (PEEP)
• Note volutrauma vs barotrauma
PEEP
• Positive End Expiratory Pressure
• Every ARDS patient needs it
• Goal is to maximize alveolar recruitment and prevent cycles of recruitment/derecruitment
• Strategy is to minimize oxygen toxicity while preventing ventilator induced lung injury
ARDSnet Protocol: **INCLUSION CRITERIA**

**Acute onset of**

1. $\text{PaO}_2/\text{FiO}_2 \leq 300$
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension
ARDSnet Protocol: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   
   **Males** = 50 + 2.3 [height (inches) - 60]
   
   **Females** = 45.5 + 2.3 [height (inches) - 60]

2. Select any ventilator mode – usually A/C or IMV

3. Set ventilator settings to achieve initial $V^T = 8 \text{ ml/kg PBW}$

4. Reduce $V^T$ by 1 ml/kg at intervals ≤ 2 hours until $V^T = 6\text{ml/kg PBW}$.

5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).

6. Adjust $V^T$ and RR to achieve pH and plateau pressure goals of protocol
FIO2 Goal: Adjust FIO2 to maintain 
\[ \text{PaO}_2 \text{ 55-80 mmHg or SpO}_2 \text{ 88-95\%} \]
Use a minimum PEEP of 5 cm H\textsuperscript{2}O.
Set PEEP based on FIO2 as shown below

<table>
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<tr>
<th>Lower PEEP/higher FiO2</th>
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<tr>
<td>FiO\textsubscript{2}</td>
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<tr>
<td>PEEP</td>
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| FiO\textsubscript{2} | 0.7 | 0.8 | 0.9 | 0.9 | 0.9 | 1.0 |
| PEEP                  | 14  | 14  | 14  | 16  | 18  | 18-24 |

PLATEAU PRESSURE GOAL: ≤ 30 cm H\textsubscript{2}O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or VT.
If Pplat > 30 cm H\textsubscript{2}O: decrease VT by 1ml/kg steps (minimum = 4 ml/kg). Plateau pressure is surrogate for volume of “baby lung”
pH GOAL: 7.30-7.45

Acidosis Management:

• If pH 7.15-7.30: Increase RR until pH > 7.30 or PaCO2 < 25 (Maximum set RR = 35).

• If pH < 7.15: Increase RR to 35. If pH remains < 7.15, VT may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

• May give NaHCO3

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.
Airway Pressures

- Peak Inspiratory Pressure
- Plateau Pressure
- PEEP

Airway Pressures vs. Time
Hypothesis:
In patients with ALI ventilated with 6 mL/kg, higher levels of PEEP will result in better clinical outcomes than lower levels of PEEP.

PEEP

• Randomized trial of higher vs lower PEEP
• Higher levels of PEEP/FiO2 did not improve outcomes
  – may negatively impact outcomes:
    • Causing increased airway pressure
    • Increase dead space
    • Decreased venous return
    • Barotrauma
Airway Pressures in ARDS

- Plateau pressure is most predictive of lung injury
- Goal plateau pressure < 30, the lower the better
  - Decreases alveolar over-distention and reduces risk of lung strain
- Adjust tidal volume to ensure plateau pressure at goal
- It may be permissible to have plateau pressure > 30 in some cases
  - Obesity
  - Pregnancy
  - Ascites

Hypothesis: Diuresis or fluid restriction may improve lung function but could jeopardize extrapulmonary organ perfusion
Randomized to conservative fluids vs liberal fluids.
Conclusion: Conservative fluid management improved lung function and shortened mechanical ventilation times and ICU days without increasing nonpulmonary organ failures
Hypothesis: Early application of prone positioning will improve survival in patients with severe ARDS.

Multicenter, prospective, randomized, controlled trial assigned 466 patients with severe ARDS to undergo prone-positioning sessions of at least 16 hours or to be left in the supine position.

Conclusion: Early application of prolonged prone positioning significantly decreased 28 day and 90 mortality in patients with severe ARDS.

Requires trained team and protocol to avoid complications

Guerin et al. NEJM. 2013; 368:2159
Benefits of Prone Positioning
Benefits of Prone Positioning

**Supine position**
- Ventral lung (overdistended)
- Dorsal lung (collapsed)
- Blood flow: - - - -
- PTP: ++++

**Prone position**
- Ventral lung (decreased overdistention)
- Dorsal lung (decreased collapse)
- Blood flow: -
- PTP: +
“Rescue Therapies” for Refractory Hypoxia – most patients do not need. ARDS deaths are usually not due to ARDS or hypoxia but due to underlying disease and complications of prolonged critical illness

- Inverse ratio ventilation
- Airway pressure release ventilation
- Recruitment maneuvers
- High PEEP
- High-frequency oscillatory ventilation (HFOV)
- Inhaled epoprostenol and nitric oxide
- Extracorporeal membrane oxygenation (ECMO).

Above therapies often improve oxygenation, but are not conclusively shown to improve mortality. Some of above are complex, expensive and require special equipment and expertise.
No benefit of corticosteroids on survival

When initiated 2 weeks after onset of ARDS, associated with significant increase in mortality rate compared to placebo group
Evidence based management of ARDS

- Treat the underlying cause
- Low tidal volume ventilation – ARDSnet Protocol
- Use PEEP
- Monitor Airway pressures
- Conservative fluid management
- Prone positioning if manpower and expertise are available
Questions

What is ARDS?
What are keys points in managing ARDS?
  What is goal tidal volume?
How is FIO2 set?
How is PEEP set?
How is plateau pressure managed?