CRC 428 Cardiorespiratory Pathophysiology

Acute Respiratory Distress Syndrome

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University of South Alabama
OUTLINE

• Definition of ARDS
• Pathophysiologic Considerations of ARDS
• Signs & symptoms
• Common Causes
• Guidelines for Mechanical Ventilation of ARDS Patients
• Case Study
DEFINITION OF ARDS
DEFINITION OF ARDS

Hypoxemic respiratory failure resulting from acute injury to the lungs, characterized by an influx of protein-rich fluid into the pulmonary interstitium and alveolar spaces resulting from either:

- damage imposed directly to the alveolar epithelium, or
- damage indirectly incurred to the lungs via the capillary endothelium

All causes of ARDS evoke disruption of pulmonary capillary endothelial and alveolar epithelial membranes, i.e., the alveolar-capillary membrane.
PATHOPHYSIOLOGY
ARDS
Normal Alveolar-Capillary Membrane Components

- Alveolar epithelium
- Alveolar basement membrane
- Alveolar lining layer with pulmonary surfactant
- Capillary basement membrane
- Capillary endothelium
- Interstitial space
- Blood
- Alveolus
- Capillary
PATHOPHYSIOLOGY ARDS

Diffuse alveolar damage  Capillary endothelial injury

ARDS

Exudative Phase  Fibroproliferative Phase

ARDS
Primary site of injury focused on either:

- **Alveolar epithelium:**
  - Type I cells
  - Type II cells

  e.g., smoke inhalation and aspiration of gastric contents

- **Capillary endothelium**

  e.g., acute pancreatitis and sepsis
PATHOPHYSIOLOGY ARDS

Alveolar Epithelial Damage
- Pulmonary edema formation
- Damaged Type I alveolar cells
  - Increased permeability
  - Decreased fluid clearance
- Damaged Type II alveolar cells
  - Decreased surfactant
  - Decreased compliance
  - Alveolar collapse (atelectasis)
  - Pulmonary surfactant deficiency
  - Fibrosis

Capillary Endothelial Damage
- Increased capillary permeability
- Protein-rich fluid into alveoli

Interstitial and alveolar edema are also present.
Exudative stage:
- interstitial and alveolar edema
- appearance of hyaline membranes
- destruction of Type I alveolar epithelial cells
- microvascular endothelium is characterized by intracellular gaps

Proliferative stage:
- fibrin deposition and inflammatory cells and fibroblasts
- alveolar-capillary membrane thickened
- altered pulmonary vascular bed

Fibrotic stage:
- occurs about 2 weeks after initial insult
- fibrotic changes in the alveolar ducts, alveoli, and interstitium
Normal Lung Mechanics

**Alveolar Wall**

**Alveolar Fluid**

**Pulmonary Surfactant Molecules**

**Increased Surfactant-to-Alveolar Surface Area**

**Decreased Surfactant-to-Alveolar Surface Area**

**Hydrophobic End**

**Hydrophilic End**

**END-EXPIRATION (Low Surface Tension)**

**END-INSPIRATION (High Surface Tension)**
Use of Surfactant for RDS: Surfactant Structure and Function

- Surfactant lines alveoli on top of the water layer, lowering the surface tension and allowing alveoli to expand

Hydrophilic heads of phospholipid molecules in alveolar-lining fluid

Hydrophobic tails of phospholipid molecules away from alveolar-lining fluid

- Insufficient surfactant
  - Collapsed alveolus
  - Inadequate oxygen exchange

- Sufficient surfactant
  - Expanded alveolus
  - Adequate oxygen exchange
Pulmonary surfactant composition

80% phospholipids
- Dipalmitoylphosphatidylcholine DPPC (60%)
- Phosphatidyl glycerol / ethanolamine / inositol (20%)

10% neutral lipids
- Mostly cholesterol

10% Surfactant proteins
- SP-A, SP-D: hydrophilic
- SP-B, SP-C: hydrophobic
Surfactant precursors

Type II cell

Endocytosis and recycling or destruction of surfactant components

Type I cell

Exocytosing lamellar body

Tubular myelin

Fluid

Surfactant

Air space

Macrophage
1 Injury reduces normal blood flow to the lungs, allowing platelets to aggregate. These platelets release substances, such as serotonin (S), bradykinin (B), and histamine (H), that inflame and damage the alveolar membrane and later increase capillary permeability.

2 Histamines (H) and other inflammatory substances increase capillary permeability. Fluids shift into the interstitial space.

3 As capillary permeability increases, proteins and more fluid leak out, causing pulmonary edema.

4 Fluid in the alveoli and decreased blood flow damage surfactant in the alveoli. This reduces the alveolar cells’ ability to produce more surfactant. Without surfactant, alveoli collapse, impairing gas exchange.

5 The patient breathes faster, but sufficient oxygen (O₂) can’t cross the alveolar capillary membrane. Carbon dioxide (CO₂), however, crosses more easily and is lost with every exhalation. Both O₂ and CO₂ levels in the blood decrease.

6 Pulmonary edema worsens. Meanwhile, inflammation leads to fibrosis, which further impedes gas exchange. The resulting hypoxemia leads to respiratory acidosis.
SCHEMATIC REPRESENTATION OF PATHOPHYSIOLOGY OF ARDS

Lung injury
  ▸ Damaged alveolar cell
    ▼ Surfactant production
    ▼ Alveolar Compliance
      ▼ Atelectasis
        ▼ Hyaline membrane formation
          ▼ Lung compliance
            ▼ Impairment in gas exchange
              ▼ ARDS
  ▸ Release of Vasoactive substances (serotonin, histamine, bradykinin)
    ▼ Alveolocapillary membrane permeability
      ▸ Outward migration of blood cells & fluids from capillaries
        ▶ Pulmonary Edema
          ▼ Vascular narrowing & obstruction
            ▼ Pulmonary hypertension
Increased Capillary Permeability

Alveolar Instability

Surfactant Deactivation

Alveolar Edema
• https://www.youtube.com/watch?v=749reIhymq8
• https://www.youtube.com/watch?v=cVCvYxVxSt4
PREVIOUS NAMES FOR ARDS

• Adult respiratory distress syndrome
• Capillary leak syndrome
• Da Nang lung
• Post-perfusion lung
• Pump lung
• Shock lung
• Stiff lung syndrome
• Wet lung
• White lung
EPIDEMIOLOGY OF ARDS
EPIDEMIOLOGY OF ARDS

- 43K to 100K per year
- 40% to 45% mortality rate
- 20K to 45K deaths per year
- Majority of death caused by multisystem organ failure (MSOF)
- Most survivors will have normal pulmonary function in about one year after ARDS resolution
- Sepsis most common cause
- Sepsis highest mortality
SIGNS & SYMPTOMS OF ARDS
SIGNS & SYMPTOMS OF ARDS

- Severe shortness of breath
- Labored breathing
- Hypoxemia (intrapulmonary shunting); cyanosis possible
- Increased respiratory rate (tachypnea)
- Diaphoresis (sweating)
- Low blood pressure (hypotension)
- Tachycardia
- Bilateral crackles
- Confusion (decreased mentation)
- Anxiety/agitation

Latent period of onset of 6 to 72 hours following inciting event.
COMMON CAUSES OF ARDS
COMMON CAUSES OF ARDS

**Direct Lung Injury**
- Pneumonia
- Aspiration (food, beverage, vomitus)
- Near-drowning
- Smoke/chemical inhalation
- Pulmonary contusion (trauma)
- O₂ toxicity (prolonged FIO₂ > 0.60)

**Indirect Lung Injury**
- Sepsis
- Acute pancreatitis
- Fat embolism
- Severe trauma (massive blood loss)
- Prolonged cardiopulmonary bypass
- Drug overdose (heroin, barbiturates, methadone)
DIFFERENTIATING CHF (LVF) FROM ARDS

CHF (LVF) = High Pressure (Cardiogenic) Pulmonary Edema
ARDS = Permeability (Non-Cardiogenic) Pulmonary Edema
DIFFERENTIATING CHF (LVF) FROM ARDS

Common Features of CHF (LVF) & ARDS

- Anxiety, diaphoresis, dyspnea, tachypnea
- Decreased lung volumes
- Decreased pulmonary compliance
- ABGs (early): uncompensated respiratory alkalosis with mild to moderate hypoxemia (hypoxemic or type I respiratory failure)
- CXR: diffuse alveolar and interstitial infiltrates
DIFFERENTIATING CHF (LVF) FROM ARDS

<table>
<thead>
<tr>
<th>Features Indicating ARDS</th>
<th>Features Indicating CHF</th>
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<tbody>
<tr>
<td>ARDS risk factors present</td>
<td>History: LVF, mitral/aortic valve disease, systemic HTN, volume overload</td>
</tr>
<tr>
<td>CXR: peripheral infiltrates</td>
<td></td>
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<tr>
<td>PCWP: &lt; 18 mm Hg</td>
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<td>PAP: Normal</td>
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<td>BALF: proteinaceous &amp; inflammatory</td>
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<td>P/F ratio: &lt; 200</td>
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RADIOGRAPHIC PRESENTATION OF ARDS
Cardiogenic Pulmonary Edema

This patient has fulminant pulmonary edema from CHF.
The pattern shown is the 'bat wing'.

Bat-wing Pattern

severe and sudden onset
Chest X-ray of ARDS patient

Normal

ARDS
Cardiogenic vs. Non-Cardiogenic Edema via CXR

Cardiogenic

Bilateral infiltrates predominately in lung bases.

Non-Cardiogenic

Diffuse Bilateral patchy infiltrates homogenously distributed throughout the lungs.
Classic Pulmonary Edema

- Batwing or butterfly appearance
- Smoke inhalation
RESPIRATORY CARE
MANAGEMENT OF ARDS
RESPIRATORY CARE
MANAGEMENT OF ARDS

- Oxygen therapy protocol
- Bronchodilator therapy protocol (when wheezing is present)
- Lung expansion therapy protocol
- Mechanical ventilation protocol
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS
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- $V_T$ 4 to 8 ml/kg (ARDSnet Protocol)
- PC- or VC-CMV
- RR 15 to 25 breaths/minute
- Adequate $T_E$ to avoid auto-PEEP
- $\text{SaO}_2 > 88\%$, or $\text{PaO}_2 > 60$ mm Hg; $\text{FiO}_2$ generally begun at 1.00
- PEEP to prevent alveolar collapse & reduce need for high $\text{FiO}_2$
- Sedate, paralyze, reposition when oxygenation is problematic
- Maintain $P_{\text{plateau}} < 30$ cm H$_2$O
- Permissive hypercapnia may be necessary
PC-CMV or VC-CMV? Which is superior?

- VC-CMV: descending waveform with $\dot{V}_I > 60$ L/min
  - Ensures early $V_T$ delivery
  - Higher mean airway pressure ($P_{aw}$)
  - Minimizes PIP – $P_{plateau}$ difference

- PC-CMV:
  - $T_I$ long enough to enhance oxygenation
  - $T_I$ short enough ($< 1.0$ sec) to avoid auto-PEEP (longer $T_E$)
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

VC-CMV
- Constant $V_T$ as:
  - $C_L$ changes
  - $R_{aw}$ changes
  - PIP increases as:
    - $C_L$ decreases
    - $R_{aw}$ increases

PC-CMV
- Constant PIP as:
  - $C_L$ decreases
  - $R_{aw}$ increases
  - $V_T$ changes as:
    - $C_L$ changes
    - $R_{aw}$ changes
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

Acute Phase of ARDS

- High levels of ventilatory support
- Often full ventilatory support (FVS)
- PC-CMV or VC-CMV or SIMV + PSV
- $V_T$ 4 to 8 ml/kg with $P_{\text{plateau}} < 30 \text{ cm H}_2\text{O}$, and RR 15 to 25 bpm
- Frictional forces/shear stress can cause lung injury
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

• PEEP* responsible for:
  • recruiting additional alveoli
  • increasing FRC
  • improving lung compliance
  • improving gas distribution
  • reducing shunt
  • improving oxygenation
• Improving PaO₂ enables FIO₂ reduction, lowering risk of O₂ toxicity, and lowering risk of multiple organ system failure.
• PEEP prevents repeated opening/closing of alveoli, thereby reducing risk of barotrauma.

*PEEP increases mean airway pressure.
ARDS Meets All the Indications for PEEP

- Recurrent atelectasis with low FRC
- \( \text{PaO}_2 < 60 \text{ mm Hg with } \text{FiO}_2 > 0.60 \)
- CXR revealing bilateral (diffuse) infiltrates (sometimes “bat wing”)
- Reduced pulmonary compliance
- Refractory hypoxemia
- P/F ratio < 200
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

Optimum PEEP

- Increase in increments of 3 to 5 cm H₂O
- Generally, optimum PEEP ranges between 8 to 15 cm H₂O
- For PEEP > 15 cm H₂O, Vₜ may need to decreased
- O₂ delivery-titrated PEEP
- Compliance-titrated PEEP
- P-V curve used for titrating PEEP
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

Optimum PEEP Based on $O_2$ Delivery

$DO_2 = C.O. \times CaO_2$

- After increasing PEEP by 3 to 5 cm H$_2$O & waiting 20 minutes, measure:
  - BP
  - $P\overline{V}O_2$
  - $S\overline{V}O_2$
  - C.O.
- When $DO_2$ declines, drop PEEP to the next preceding level.
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

<table>
<thead>
<tr>
<th>PEEP</th>
<th>0 cm H₂O</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20 cm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>F₁O₂</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
<td>0.80</td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td>30</td>
<td>32</td>
<td>35</td>
<td>42</td>
<td>50</td>
</tr>
<tr>
<td>Pₚₚₚₚₚₚ</td>
<td>25</td>
<td>27</td>
<td>29</td>
<td>36</td>
<td>43</td>
</tr>
<tr>
<td>PᵥO₂ (torr)</td>
<td>32</td>
<td>35</td>
<td>37</td>
<td>37</td>
<td>36</td>
</tr>
<tr>
<td>SᵥO₂</td>
<td>61%</td>
<td>66%</td>
<td>71%</td>
<td>69%</td>
<td>64%</td>
</tr>
<tr>
<td>BP</td>
<td>131/78</td>
<td>133/82</td>
<td>130/79</td>
<td>125/74</td>
<td>110/69</td>
</tr>
<tr>
<td>C.O. (L/min)</td>
<td>5.9</td>
<td>5.7</td>
<td>5.9</td>
<td>5.4</td>
<td>4.8</td>
</tr>
<tr>
<td>DO₂ (ml/min)</td>
<td>989</td>
<td>1,022</td>
<td>1,105</td>
<td>1,021</td>
<td>917</td>
</tr>
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</table>

Optimum PEEP for this patient is 10 cm H₂O.
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

Compliance-Titrated PEEP

$$Cs = \frac{V_T - V_{\text{lost}}}{P_{\text{plateau}} - \text{PEEP}}$$

- Best PEEP exceeded when $C_s$ begins to fall.
- CAUTION: Problems with compliance-titrated PEEP:
  - Regional overdistension of the lungs
  - Drop in C.O. can occur below best PEEP with this method
### GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

#### Compliance-Titrated PEEP

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<td>42</td>
<td>50</td>
</tr>
<tr>
<td>P_plateau (cm H₂O)</td>
<td>25</td>
<td>27</td>
<td>29</td>
<td>36</td>
<td>43</td>
</tr>
<tr>
<td>Cₛ (ml/cm H₂O)</td>
<td>24</td>
<td>27</td>
<td>32</td>
<td>29</td>
<td>26</td>
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Optimum PEEP for this patient is 10 cm H₂O.
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

P-V Curve for Titrating PEEP

Pressure (cm H₂O)

Volume (ml)

1400
1200
1000
800
600
400
200

LIP

UIP

A

B

C

5 15 25 35 45
GUIDELINES FOR MECHANICAL VENTILATION OF ARDS PATIENTS

- Static P-V curve for ARDS patient
- Volume increased in 100 ml increments
- $P_{\text{plateau}}$ measured and plotted
- Tangents A, B, & C drawn to curve
- LIP intersection of tangents A & B
- UIP intersection of tangents B & C
- PEEP (short white arrow) set above LIP to prevent derecruitment and alveolar damage
Increasing Mean Airway Pressure

1. Increase flow
2. Increase peak pressure
3. Lengthen inspiratory time
4. Increase PEEP
5. Increase Rate
CASE STUDY
CASE STUDY

- 60-year-old Caucasian male; car accident victim
- Entered ER with
  - Fractured left femur
  - Deep right arm laceration
  - Right-sided open pneumothorax
  - Abdominal bruising
  - Evident injury to head or neck
- Surgical repair of internal injuries
- Thoracostomy tube inserted to drain pleural space
Case Study

4 Days Status Post-op

- 39°C body temperature
- Severe refractory hypoxemia
  - CXR: pneumothorax resolved
  - Bilateral fluffy infiltrates
- ABGs using nonrebreathing mask at FiO₂ 0.70
  - pH 7.29
  - PaCO₂ 51 mm Hg
  - PaO₂ 76 mm Hg
  - HCO₃ 24.8 mEq/L
CASE STUDY

4 Days Status Post-op

- BP 148/90 mm Hg
- Pulse 152 beats/min
- RR 42 breaths/min
- Breathing: labored & dyspneic
- Patient anxious, restless, & diaphoretic
- CPAP via face mask initiated at F₁O₂ 1.00 at 10 cm H₂O
- Face mask not tolerated
4 Days Status Post-op

Mechanical ventilation initiated: Pt 6’2” & 268 lbs (122 kg)

- VC-SIMV + PSV with descending ramp \( \dot{V} \)-T waveform
- \( V_T \) 600 ml (4.9 ml/kg)
- mandatory RR 16 breaths/min
- \( \dot{V}_I \) 100 L/min
- PEEP 5 cm H\(_2\)O
- FiO\(_2\) 1.00
CASE STUDY

ABGs after 30 Minutes ($\text{FiO}_2$ 1.00)
- pH 7.43
- $\text{PaCO}_2$ 38 mm Hg
- $\text{PaO}_2$ 189 mm Hg
- $\text{HCO}_3$ 22 mEq/L

Mechanical Ventilator Pressures
- PIP 24 cm H$_2$O
- $P_{\text{plateau}}$ 18 cm H$_2$O
- PEEP 5 cm H$_2$O
- PSV 10 cm H$_2$O
CASE STUDY

- 15 cm H₂O PEEP based on LIP from P-V curve
- Mode changed to PC-CMV
  - Pressure control 15 cm H₂O
  - Mandatory rate 15 breaths/min
  - PEEP 15 cm H₂O (PIP 30 cm H₂O)
  - I:E 1:2
  - FİO₂ 0.80
- Measured Vₜ 525 ml
## CASE STUDY

### ABGs 30 Minutes After PC-CMV
- pH 7.36
- PaCO\(_2\) 48 mm Hg
- PaO\(_2\) 224 mm Hg
- HCO\(_3\) 29 mEq/L

### Mechanical Ventilator Changes/Considerations
- FiO\(_2\) decreased to 0.50
- Maintain PaO\(_2\) > 60 mm Hg
- Keep acid-base status acceptable

Patient successfully managed over next 2 weeks. Mechanical ventilation weaned & discontinued. Patient extubated.
CASE STUDY

- UNNECESSARY: 15 cm H$_2$O PEEP based on LIP from P-V curve

- UNNECESSARY: Mode changed to PC-CMV