

# Acute Respiratory Distress Syndrome (ARDS)

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## General Information

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### Berlin Criteria <sup>1</sup> **MN**

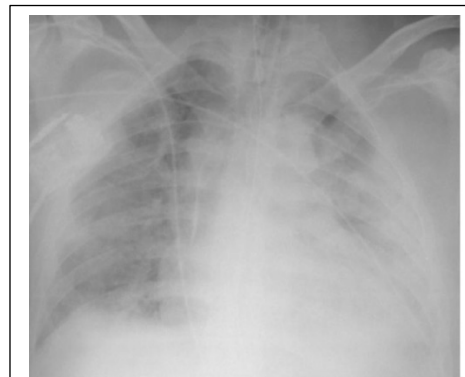
- *Timing*: Onset Must Be Within One Week of a Known Clinical Insult or New/Worsening Respiratory Symptoms
- *Chest Imaging*: Bilateral Opacities (Not Fully Explained by Effusions, Lobar Collapse, or Nodules)
- *Origin*: Respiratory Failure Cannot Be Fully Explained by Cardiac Failure or Fluid Overload
- *Oxygenation*:  $PaO_2:FiO_2 < 300$

### Severity <sup>1</sup>

- \*Based on  $PaO_2/FiO_2$  (P:F Ratio)
- *Mild*:  $P:F \leq 300$
- *Moderate*:  $P:F \leq 200$
- *Severe*:  $P:F \leq 100$

### Prevalence <sup>3</sup>

- Mild: 30.0%
- Moderate: 46.6%
- Severe: 23.4%



ARDS on Chest X-Ray <sup>2</sup>

## Mortality

- Overall High Mortality (37-43%)<sup>4,5</sup>
- Increases with Disease Severity<sup>3,6</sup>
  - Mild: 27-35%
  - Moderate: 32-40%
  - Severe: 45-46%

## Causes<sup>7-10</sup>

- Sepsis (31-43%) – Most Common Cause
- Pneumonia (40-42.3%)
- Aspiration (8-30%)
- Trauma (9-17%)
- Massive Transfusion/Transfusion-Related Acute Lung Injury (TRALI)
- Pancreatitis
- Inhalation Injury
- Cardiothoracic Surgery
- Medications
- Drugs
- Alcohol
- \*Risk Increased by Simultaneous Factors<sup>7</sup>

## Clinical Features<sup>11,12</sup>

- Dyspnea
- Tachypnea
- Tachycardia
- Altered Mental Status
- Respiratory Distress

# Phases and Pathophysiology

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## Starling Equation<sup>13</sup>

- Describes Fluid Movement Between the Vasculature & Interstitium
- $Q = K \times [(P_c - P_i) - \sigma (\pi_c - \pi_i)]$ 
  - Q: Net Transvascular Flow
  - K: Filtration Coefficient of Endothelial Membrane Permeability
  - P<sub>c</sub>: Capillary Hydrostatic Pressure
  - P<sub>i</sub>: Interstitial Hydrostatic Pressure
  - $\sigma$ : Reflection Coefficient of the Capillary Barrier
  - $\pi_c$ : Capillary Oncotic Pressure
  - $\pi_i$ : Interstitial Oncotic Pressure

- Normal Lung Function Prevents Alveolar Edema <sup>14</sup>
  - Retained Intravascular Proteins Increase Oncotic Pressure
  - Interstitial Lymphatic Reabsorb Large Volumes of Fluid
  - Tight Junctions Between Alveolar Epithelium Prevent Leakage

### Stage 1 (Exudative Phase)

- Characterized by Diffuse Alveolar Damage (DAD) <sup>15</sup>
- Occurs Over the First 7-10 Days
- Effects:
  - Lung Injury Causes Release of Proinflammatory Cytokines (TNF, IL-1, IL-6, and IL-8) <sup>16-19</sup>
    - Causes Inflammation and Edema
    - Cytokines Recruit Neutrophils Causing Release of Toxic Mediators that Further Damage Capillary/Alveolar Epithelium <sup>20,21</sup>
  - Necrosis and Sloughing of Type I Pneumocytes and Capillary Endothelium <sup>22</sup>
    - Loss of Tight Junctions that Normally Prevent Fluid Movement <sup>22</sup>
  - Increased Vascular Permeability Causes an Inflammatory Exudate (Protein Rich Fluid) to Flood the Alveoli <sup>23</sup>
  - Surfactant Inhibition Causes Collapse and Shunting <sup>24</sup>
  - Hyaline Membranes Form within the Alveoli <sup>25</sup>

### Stage 2 (Fibroproliferative Phase)

- Characterized by Proliferation of Type II Pneumocytes <sup>23</sup>
- Occurs After 7-10 Days
- Generally Lasts About 14-21 Days
- Effects:
  - Early Collagen Formation <sup>26,27</sup>
  - Interstitial Infiltration of Myofibroblasts with Myointimal Thickening
  - Squamous Metaplasia <sup>28</sup>
  - Decreased Compliance <sup>29</sup>
- Effects are Still Reversible

### Stage 3 (Fibrotic Phase)

- Characterized by Interstitial Fibrosis <sup>30-32</sup>
- Not a Universal Outcome Seen in All Patients
- Associated with Prolonged Mechanical Ventilation and Increased Mortality <sup>30,31</sup>

### Complications

- Impaired Gas Exchange & Hypoxemia <sup>33</sup>
  - Primarily Due to a Ventilation-Perfusion Mismatch Due to Physiologic Shunting and Increased Dead Space <sup>33</sup>
  - The Most Common Long-Term Defect in Recovered Patients is Decreased Diffusion Capacity <sup>34</sup>

- Decreased Lung Compliance <sup>29</sup>
- Barotrauma <sup>35</sup>
- Pulmonary Hypertension Due to Hypoxic Vasoconstriction, Vascular Compression Due to Positive Airway Pressure Ventilation, Airway Collapse, Parenchymal Destruction, and Hypercarbia <sup>36</sup>

## Diagnosis

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### Diagnosis <sup>37</sup>

- Clinical Diagnosis Based on the Berlin Criteria <sup>1</sup>
- Evaluation Should Focus on Identifying ARDS and the Underlying Cause
- Laboratory Testing is Nonspecific
- Imaging Includes CXR or CT
- Exclude Acute Cardiogenic Pulmonary Edema by Clinical Evaluation, BNP, and/or Echocardiogram <sup>38,39</sup>

### Berlin Criteria <sup>1</sup> **MN**

- *Timing*: Onset Must Be Within One Week of a Known Clinical Insult or New/Worsening Respiratory Symptoms
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- *Origin*: Respiratory Failure Cannot Be Fully Explained by Cardiac Failure or Fluid Overload
- *Oxygenation*: PaO<sub>2</sub>:FiO<sub>2</sub> < 300

### Severity <sup>1</sup>

- \*Based on PaO<sub>2</sub>/FiO<sub>2</sub> (P:F Ratio)
- *Mild*: P:F ≤ 300
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- *Severe*: P:F ≤ 100

### Lung Injury Prediction Score (LIPS) <sup>40</sup>

- Scoring System to Evaluate the Risk for Developing ARDS
- Features: <sup>40</sup>
  - Predisposing Conditions:
    - Shock (+2 Points)
    - Aspiration (+2 Points)
    - Sepsis (+1 Points)
    - Pneumonia (+1.5 Points)

- High-Risk Surgery:
  - Orthopedic Spine (+1 Points)
  - Acute Abdomen (+2 Points)
  - Cardiac (+2.5 Points)
  - Aortic Vascular (+3.5 Points)
  - Emergency Surgery (+1.5 Points)
- High-Risk Trauma:
  - Traumatic Brain Injury (+2 Points)
  - Smoke Inhalation (+2 Points)
  - Near Drowning (+2 Points)
  - Lung Contusion (+1.5 Points)
  - Multiple Fractures (+1.5 Points)
- Risk Modifiers:
  - Alcohol Abuse (+1 Points)
  - Obesity (BMI > 30) (+1 Points)
  - Hypoalbuminemia (+1 Points)
  - Chemotherapy (+1 Points)
  - FiO<sub>2</sub> > 0.35 (> 4 L/min) (+2 Points)
  - Tachypnea (RR > 30) (+1.5 Points)
  - SpO<sub>2</sub> < 95% (+1 Points)
  - Acidosis (pH < 7.35) (+1.5 Points)
  - Diabetes (Only if Sepsis) (-1 Points)
- Interpretation: <sup>41</sup>
  - Score ≤ 4: Low Risk of Developing ARDS
    - Negative Predictive Value 97% – Better at Defining Patients at Low Risk than Defining Patients at High Risk <sup>41</sup>
  - Score > 4: High Risk of Developing ARDS
    - Sensitivity 69%, Specificity 78% <sup>41</sup>

## Treatment

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### Primary Treatment

- Primarily Supportive Care <sup>42</sup>
  - Treat Underlying Pathology
  - Nutritional Support <sup>43</sup>
  - General Critical Care Managements (VTE Prophylaxis, Hemodynamic Monitoring, Stress Ulcer Prophylaxis)
  - Manage Patient-Ventilator Dyssynchrony
- Lung Protective Ventilation <sup>44</sup>

- Conservative Fluid Management <sup>45-47</sup>
  - Goal CVP < 4 mmHg or PAOP < 8 mmHg <sup>45</sup>
  - May Require Diuretics as Long as the Patient is Hemodynamically Stable
  - Liberal Fluid Management Has a Higher Risk for Pulmonary Edema
  - Improves Ventilator-Free Days and ICU-Free Days <sup>45</sup>
  - No Clear Mortality Benefit <sup>45</sup>
  - Possibly an Increased Risk for Cognitive Impairment (Not Clear) <sup>48</sup>

## Lung Protective Ventilation

- Definition: Ventilation with Low Tidal Volumes to Reduce Alveolar Overdistention & Barotrauma
  - Based Largely on ARDSnet Protocols <sup>44</sup>
- Improves Mortality for ARDS of All Severities <sup>49-53</sup>
- Ventilation (Tidal Volume/Respiratory Rate)
  - Initial Tidal Volume: 8 ml/kg x Ideal Body Weight (General Standard) <sup>44</sup>
  - Decrease Tidal Volume 1 ml/kg Every 1-2 Hours <sup>44</sup>
  - **Goal Tidal Volume: 4-6 ml/kg x Ideal Body Weight** <sup>44</sup>
  - Initial Respiratory Rate Should Approximate Baseline Minute Ventilation (Not > 35 bpm) <sup>44</sup>
  - Adjust Tidal Volume & Respiratory Rate for Goal Plateau Pressure ≤ 30 cm H<sub>2</sub>O <sup>44</sup>
- Oxygenation (PEEP/FiO<sub>2</sub>)
  - Oxygenation Goals: PaO<sub>2</sub> 55-80 mmHg or SpO<sub>2</sub> 88-95% <sup>44</sup>
  - Adjust PEEP to Required FiO<sub>2</sub>
  - Initially Recommended to Start with Lower-PEEP Strategy <sup>44</sup>

<b>FiO<sub>2</sub></b>	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
<b>PEEP</b>	5	5-8	8-10	10	10-14	14	14-18	18-24

- Consider High-PEEP Strategy if Refractory <sup>44</sup>

<b>FiO<sub>2</sub></b>	0.3	0.4	0.5	0.6-0.7	0.8-0.9	1.0
<b>PEEP</b>	5-14	14-16	16-18	20	22	22-24

- Complications:
  - *Permissive Hypercapnia*
    - **Respiratory Acidosis Allowed to Maintain Low Tidal Volumes**
    - Anticipated and Generally Well Tolerated <sup>54,55</sup>
    - pH Goal: 7.30-7.45 <sup>44</sup>
      - If pH < 7.30: Increase Rate (Maximum 35 bpm) <sup>44</sup>
      - If pH Remains < 7.15: Can Increase Tidal Volume in 1 ml/kg Increments Until pH > 7.15 <sup>44</sup>
    - PaCO<sub>2</sub> Goal Not Well Defined
  - *Patient-Ventilator Dyssynchrony*
    - May Require Increased Sedation
    - **\*See Patient-Ventilator Dyssynchrony**

## Adjuncts

- *Systemic Glucocorticoids (Steroids)*
  - Indicated for Moderate-Severe ARDS Refractory to Standard Treatments
    - Generally Only Used if Early in the Disease Course (< 13-14 Days)
    - May Also Use Steroids if Otherwise Indicated for Other Underlying Conditions
  - Associated with Improved Mortality and Ventilator-Free Days <sup>56-58</sup>
  - Initiation 13-14 Days After Onset was Associated with Increased Mortality <sup>59-61</sup>
- *Inhaled Pulmonary Vasodilators (Nitric Oxide/Prostacyclin)*
  - Improves Oxygenation for Severe ARDS with Refractory Hypoxemia <sup>62-65</sup>
  - No Proven Morbidity or Mortality Benefit <sup>66</sup>
  - **\*See Ventilator Management**
- *Paralysis/Neuromuscular Blockade*
  - Generally Reserved Only for Severe ARDS with Refractory Hypoxemia
  - Early Short-Term (48 Hour) Paralytics May Improve Mortality in Severe ARDS (Debated with Conflicting Results) <sup>67,68</sup>
- *Prone Positioning*
  - Indicated for Severe ARDS with Refractory Hypoxemia <sup>69</sup>
    - May Also Consider as a Bridge to ECMO
  - Associated with Improved Mortality for Severe ARDS <sup>69,70</sup>
  - **\*See Ventilator Management**
- *Extracorporeal Membrane Oxygenation (ECMO)*
  - Considered for Acute Severe Pulmonary Failure that is Potentially Reversible & Unresponsive to Conventional Measures
  - Associated with Improved Mortality for Severe ARDS <sup>71</sup>
  - **\*See Mechanical Circulatory Support**
- Alternative Modes of Ventilation:
  - *Airway Pressure Release Ventilation (APRV)*
  - *High-Frequency Oscillatory Ventilation (HFOV)*
  - **\*See Mechanical Ventilation: Settings & Modes**

## Mnemonics

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### Berlin Criteria for ARDS

- “ABC-3”
- Acute Onset (< 7 Days)
- Bilateral Opacities
- CHF Not Fully Explained
- P:F < 300

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