INCLUSION CRITERIA: Acute onset of
1. PaO₂/FiO₂ ≤ 300 (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: 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
3. Set ventilator settings to achieve initial VT = 8 ml/kg PBW
4. Reduce VT by 1 ml/kg at intervals ≤ 2 hours until VT = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust VT and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95%
Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/ higher FiO2

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
</tr>
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<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
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<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
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<table>
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<tr>
<th>FiO₂</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
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<tbody>
<tr>
<td>PEEP</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
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</table>

<table>
<thead>
<tr>
<th>PEEP</th>
<th>18-24</th>
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</table>

Higher PEEP/ lower FiO2

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>16</td>
</tr>
</tbody>
</table>

| PEEP | 18  | 20  | 22  | 22  | 22  | 24  |

PLATEAU PRESSURE GOAL: ≤ 30 cm H₂O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or VT.
If Pplat > 30 cm H₂O: decrease VT by 1ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H₂O and VT < 6 ml/kg, increase VT by 1 ml/kg until Pplat > 25 cm H₂O or VT = 6 ml/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase VT in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H₂O.
pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)
If pH 7.15-7.30: Increase RR until pH > 7.30 or PaCO$_2$ < 25
(Maximum set RR = 35).
If pH < 7.15: Increase RR to 35.
If pH remains < 7.15, V$_T$ may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).
May give NaHCO$_3$

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

I:E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING
A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:
1. FiO$_2$ ≤ 0.40 and PEEP ≤ 8 OR FiO$_2$ ≤ 0.50 and PEEP ≤ 5.
2. PEEP and FiO$_2$ ≤ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

B. SPONTANEOUS BREATHING TRIAL (SBT):
If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with FiO2 ≤ 0.5 and PEEP ≤ 5:
1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H$_2$O with PS ≤ 5
2. Assess for tolerance as below for up to two hours.
   a. SpO$_2$ ≥ 90: and/or PaO$_2$ ≥ 60 mmHg
   b. Spontaneous V$_T$ ≥ 4 ml/kg PBW
   c. RR ≤ 35/min
   d. pH ≥ 7.3
   e. No respiratory distress (distress= 2 or more)
      - HR > 120% of baseline
      - Marked accessory muscle use
      - Abdominal paradox
      - Diaphoresis
      - Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING
(Different from the spontaneous breathing criteria as PS is not allowed)
1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H$_2$O without pressure support or IMV assistance.