# Critical Care Management of Acute Respiratory Distress Syndrome

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# The Obligatory First Slide…

- No conflicts of interest to disclose.
- Objectives:
  - Review definition, basic management, and advanced treatment considerations for ARDS patients
- Usual disclaimers:
  - All patient interactions are different. The content of this presentation should not supersede sound medical judgment. Know and follow local protocols.

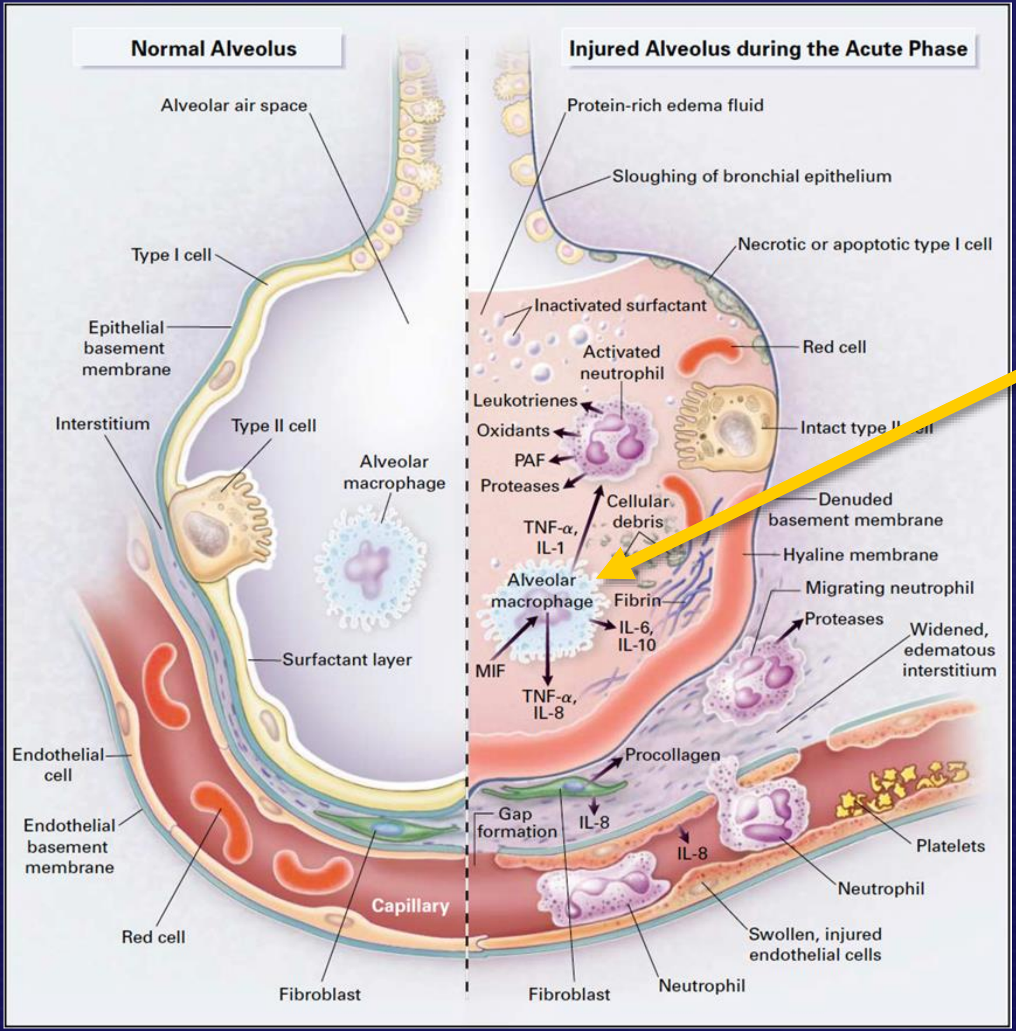
# Part I
## ARDS Overview

# Epidemiology

- Incidence 64/100,000
  - Approx 190,000 cases in US
- Mortality approaches 40%
  - Approx 75,000 deaths in US
- Risk factors for ARDS:
  - Sepsis (40%), Pneumonia, Trauma (~10%), TRALI (~10%), Burns (~40% if MV)

BMJ Best Practice 2016.

# Pathophysiology




Direct or indirect alveolar injury

↓

Alveolar macrophages release inflammatory mediators & pro-inflammatory cytokines

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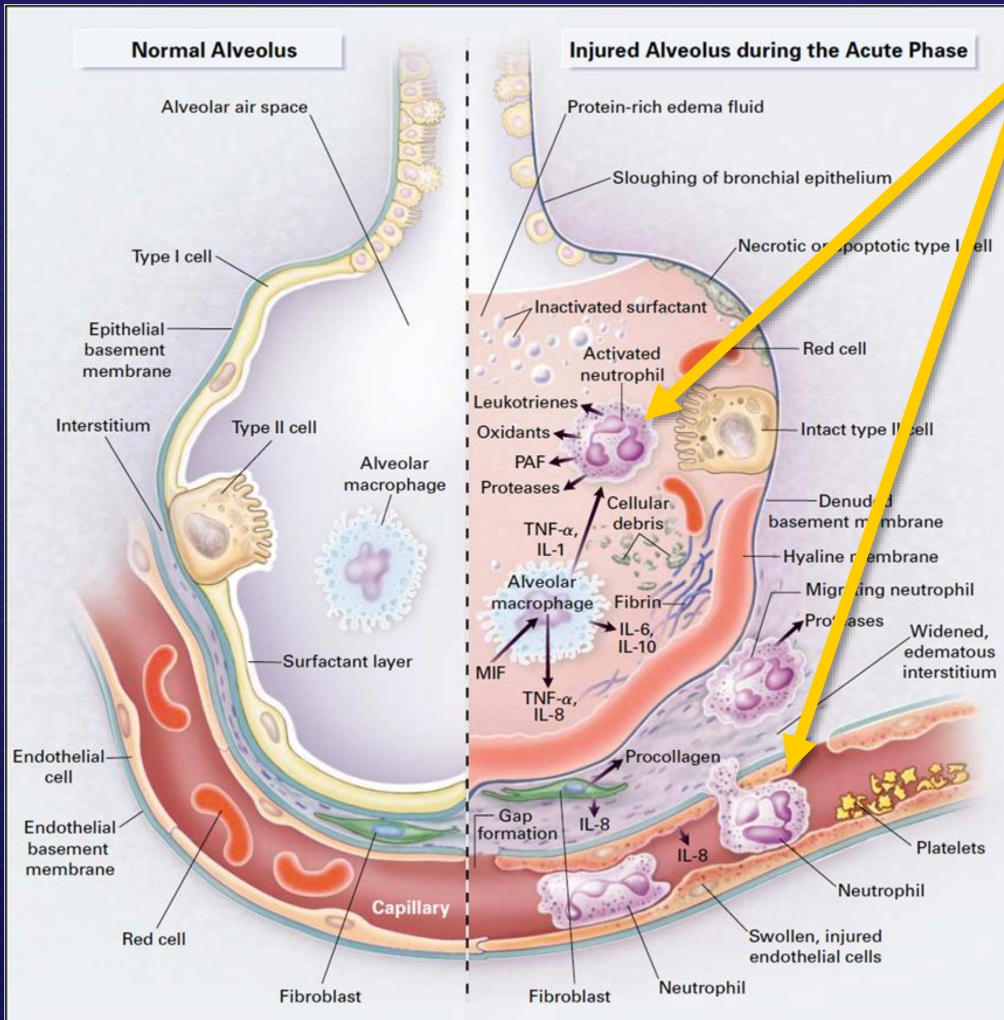
N Engl J Med 2000;342:1334-49.

# Pathophysiology




Neutrophils enter alveolus & interstitum, damaging alveolar-capillary membrane and Type I & Type II cells

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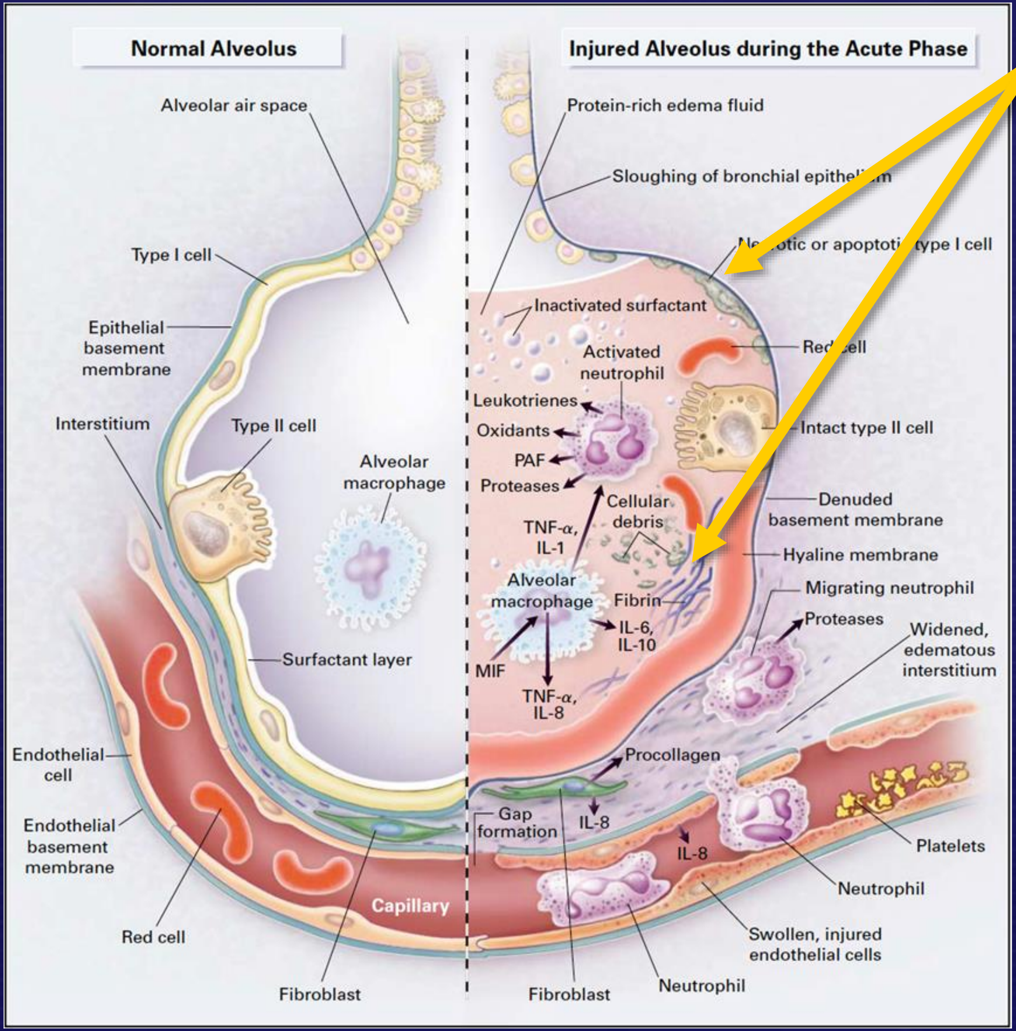
N Engl J Med 2000;342:1334-49.

# Pathophysiology




Damage to Type I cells leads to sloughing, exposed basement membrane, and fibrin deposition

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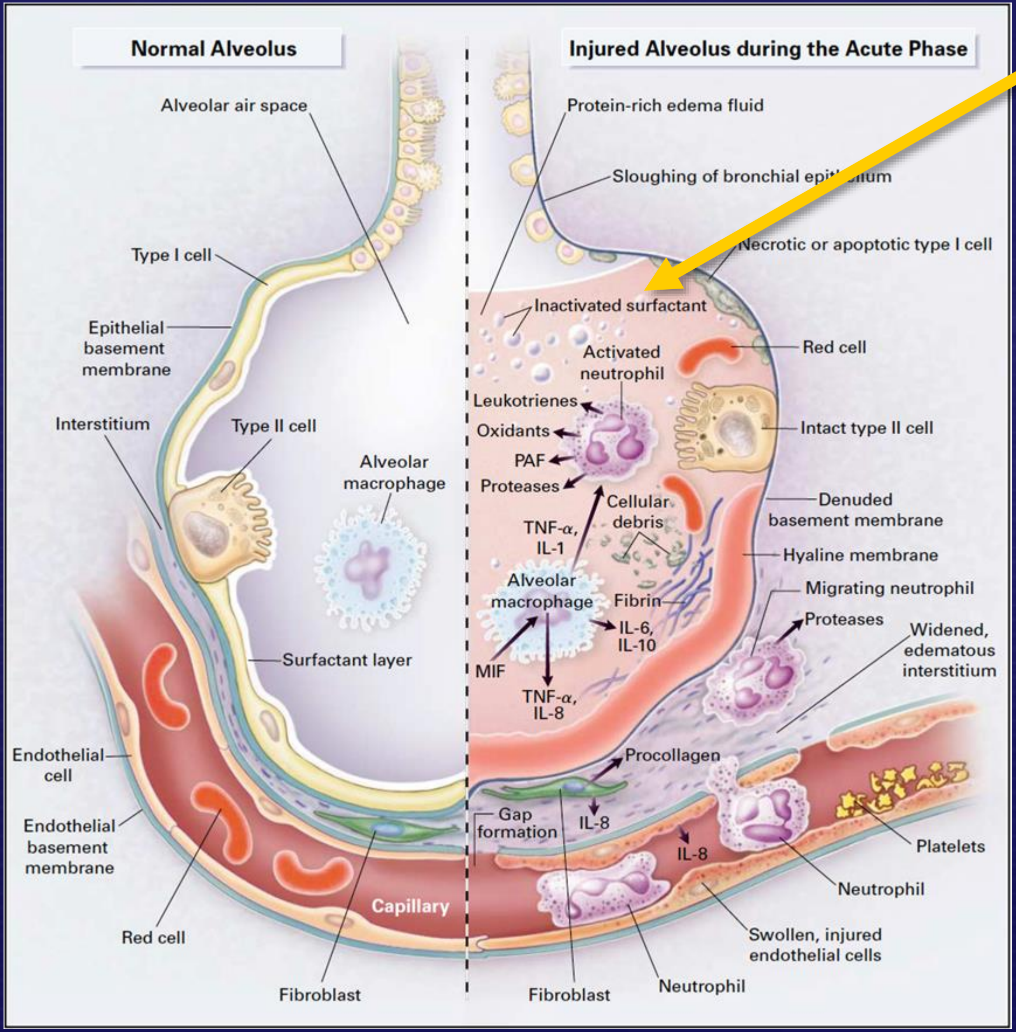
N Engl J Med 2000;342:1334-49.

# Pathophysiology




Damage to Type II cells and alveolar flooding contribute to surfactant dysfunction

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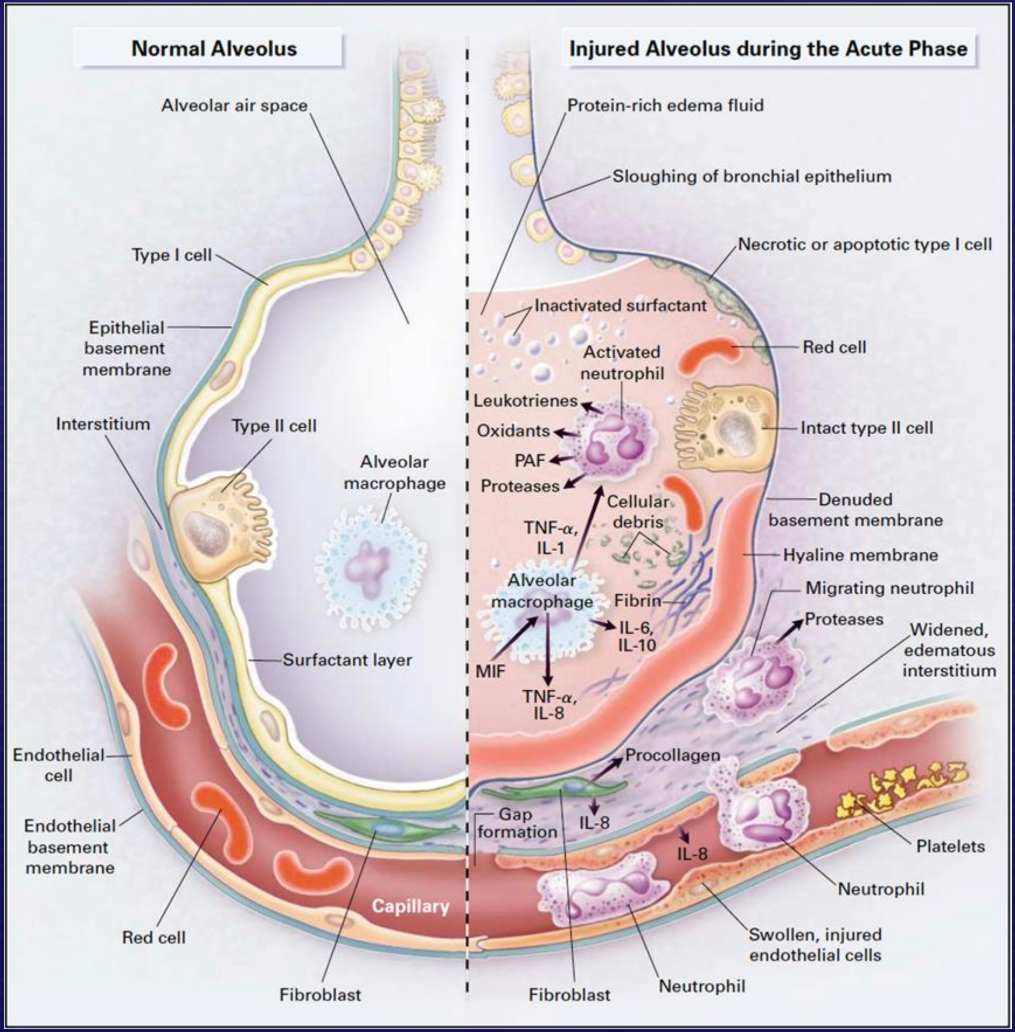
# Pathophysiology




Results of alveolar damage:

- Hypoxemic respiratory failure
- Increased A-a gradient
- Poor lung compliance

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N Engl J Med 2000;342:1334-49.

# ARDS Definition

**Table 3.** The Berlin Definition of Acute Respiratory Distress Syndrome

| | Acute Respiratory Distress Syndrome |
|---|---|
| Timing | Within 1 week of a known clinical insult or new or worsening respiratory symptoms |
| Chest imaging[a] | Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules |
| Origin of edema | Respiratory failure not fully explained by cardiac failure or fluid overload<br>Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present |
| Oxygenation[b] | |
| Mild | 200 mm Hg $<$ $PaO_2/FIO_2 \leq$ 300 mm Hg with PEEP or CPAP $\geq$5 cm $H_2O$[c] |
| Moderate | 100 mm Hg $<$ $PaO_2/FIO_2 \leq$ 200 mm Hg with PEEP $\geq$5 cm $H_2O$ |
| Severe | $PaO_2/FIO_2 \leq$ 100 mm Hg with PEEP $\geq$5 cm $H_2O$ |

Abbreviations: CPAP, continuous positive airway pressure; $FIO_2$, fraction of inspired oxygen; $PaO_2$, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

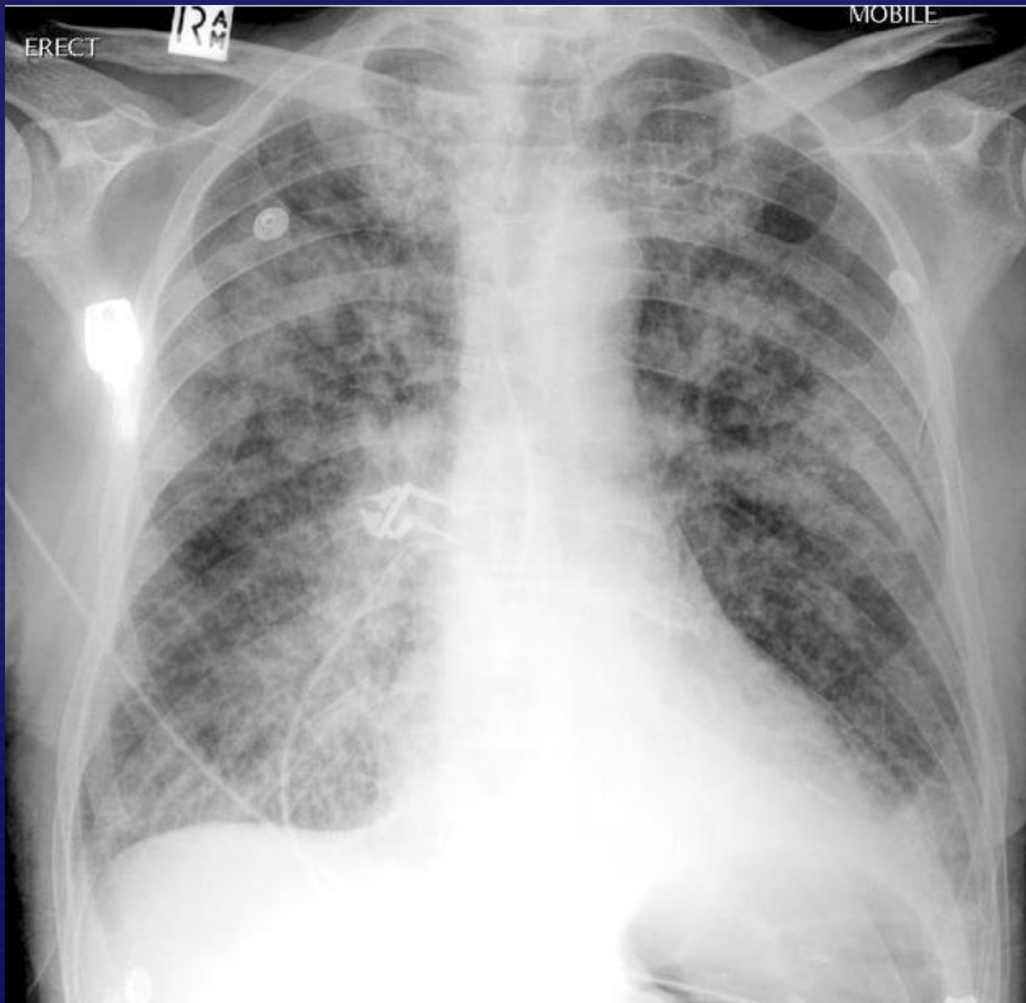
[a] Chest radiograph or computed tomography scan.

[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [$PaO_2/FIO_2 \times$ (barometric pressure/760)].

[c] This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

JAMA 2012;307:2526-33.

# Imaging Findings

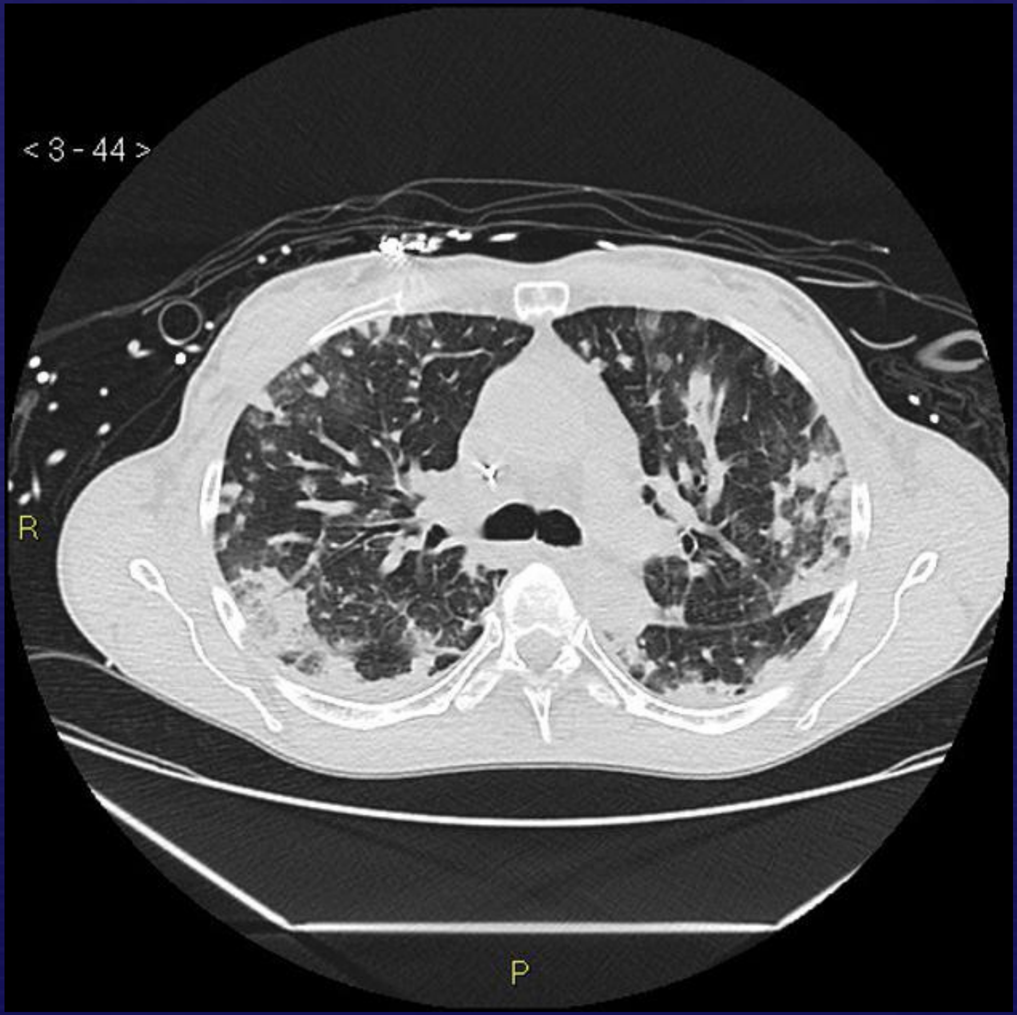



Plain CXR:

- Nonspecific
- Similar to acute pulmonary edema
- *Bilateral* diffuse opacification

Radiopaedia.org.

# Imaging Findings




CT Chest:

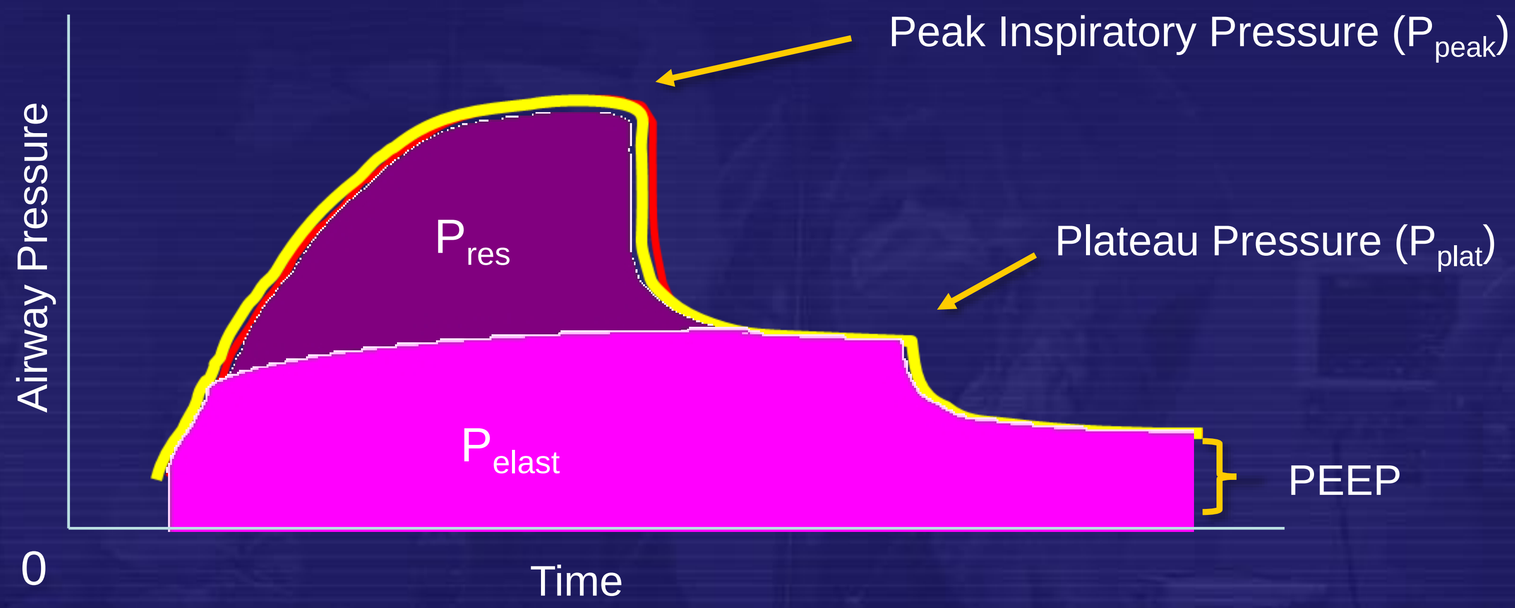
- GGO
- Usually AP density gradient, more consolidated in dependent regions
- *Bilateral* diffuse opacification, may be symmetric (extra-pulm) or asymmetric

Radiopaedia.org.

# Part II

# Basic ARDS Vent Management

# Airway Pressure Review




Compliance ($P_{elast}$):

- ARDS
- PTX
- PNA

Resistance ($P_{res}$):

- Mucous plug
- Kinked tubing
- Asthma

# Ventilator Management 101: Basic Settings

**Table 1. Summary of Ventilator Procedures in the Lower- and Higher-PEEP Groups.***

| Procedure | Value |
|---|---|
| Ventilator mode | Volume assist/control |
| Tidal-volume goal | 6 ml/kg of predicted body weight |
| Plateau-pressure goal | ≤30 cm of water |
| Ventilator rate and pH goal | 6–35, adjusted to achieve arterial pH ≥7.30 if possible |
| Inspiration:expiration time | 1:1–1:3 |
| Oxygenation goal | |
| $PaO_2$ | 55–80 mm Hg |
| $SpO_2$ | 88–95% |

MD CALC

## FORMULA

The Dr. Devine formula:

- Ideal Body Weight (men) = 50kg + 2.3kg*( Height(in) - 60 )
- Ideal Body Weight (women) = 45.5kg + 2.3kg *( Height(in) - 60 )

N Engl J Med 2004;351:327-36.

# Ventilator Management 101: High *v* Low PEEP

| Characteristic | Trial: ALVEOLI,[8] 2004 | Trial: LOVS,[9] 2008 | Trial: EXPRESS,[10] 2008 |
|---|---|---|---|
| Inclusion criteria | Acute lung injury with $PaO_2:FIO_2 \leq 300$[a] | Acute lung injury with $PaO_2:FIO_2 \leq 250$[a] | Acute lung injury with $PaO_2:FIO_2 \leq 300$[a] |
| Recruitment period | 1999-2002 | 2000-2006 | 2002-2005 |
| Recruiting hospitals (country) | 23 (United States) | 30 (Canada, Australia, Saudi Arabia) | 37 (France) |
| Patients randomized to higher vs lower PEEP | 276 vs 273 | 476 vs 509[b] | 385 vs 383[c] |
| Validity | | | |
| Concealed allocation | Yes | Yes | Yes |
| Follow-up for primary outcome, % | 100 | 100 | 100 |
| Blinded data analysis | Yes | Yes | Yes |
| Stopped early | Stopped for perceived futility | No | Stopped for perceived futility |
| Experimental intervention | Higher PEEP according to $FIO_2$ chart, recruitment maneuvers for first 80 patients | Higher PEEP according to $FIO_2$ chart, required plateau pressures $\leq 40$ cm $H_2O$, recruitment maneuvers | PEEP as high as possible without increasing the maximum inspiratory plateau pressure >28-30 cm $H_2O$ |
| Control intervention | Conventional PEEP according to $FIO_2$ chart, required plateau pressures $\leq 30$ cm $H_2O$, no recruitment maneuvers | Conventional PEEP according to $FIO_2$ chart, required plateau pressures $\leq 30$ cm $H_2O$, no recruitment maneuvers | Conventional PEEP (5-9 cm $H_2O$) to meet oxygenation goals |
| Ventilator procedures | Target tidal volumes of 6 mL/kg of predicted body weight; plateau pressures $\leq 30$ cm $H_2O$ (with exception as above); respiratory rate $\leq 35$/min, adjusted to achieve arterial pH 7.30-7.45; ventilator mode: volume-assist control (except higher PEEP group in LOVS required pressure control); oxygenation goals: $PaO_2$ 55-80 mm Hg and $SPO_2$ 88%-95%; standardized weaning) | | |

- Higher PEEP improved mortality in ARDS patients
- No significant benefit in non-ARDS dx

JAMA 2010;303:865-73.

# Ventilator Management 101: $FiO_2$ & PEEP

**Table 1. Summary of Ventilator Procedures in the Lower- and Higher-PEEP Groups.***

| Procedure | Value | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ventilator mode | Volume assist/control | | | | | | | | | | | | | |
| Tidal-volume goal | 6 ml/kg of predicted body weight | | | | | | | | | | | | | |
| Plateau-pressure goal | ≤30 cm of water | | | | | | | | | | | | | |
| Ventilator rate and pH goal | 6–35, adjusted to achieve arterial pH ≥7.30 if possible | | | | | | | | | | | | | |
| Inspiration:expiration time | 1:1–1:3 | | | | | | | | | | | | | |
| Oxygenation goal | | | | | | | | | | | | | | |
| $PaO_2$ | 55–80 mm Hg | | | | | | | | | | | | | |
| $SpO_2$ | 88–95% | | | | | | | | | | | | | |
| Weaning | Weaning attempted by means of pressure support when level of arterial oxygenation acceptable with PEEP ≤8 cm of water and $FiO_2$ ≤0.40 | | | | | | | | | | | | | |
| Allowable combinations of PEEP and $FiO_2$† | | | | | | | | | | | | | | |
| Lower-PEEP group | | | | | | | | | | | | | | |
| $FiO_2$ | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.6 | 0.7 | 0.7 | 0.7 | 0.8 | 0.9 | 0.9 | 0.9 | 1.0 |
| PEEP | 5 | 5 | 8 | 8 | 10 | 10 | 10 | 12 | 14 | 14 | 14 | 16 | 18 | 18–24 |
| Higher-PEEP group (before protocol changed to use higher levels of PEEP) | | | | | | | | | | | | | | |
| $FiO_2$ | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.5–0.8 | 0.8 | 0.9 | 1.0 | |
| PEEP | 5 | 8 | 10 | 12 | 14 | 14 | 16 | 16 | 18 | 20 | 22 | 22 | 22–24 | |
| Higher-PEEP group (after protocol changed to use higher levels of PEEP) | | | | | | | | | | | | | | |
| $FiO_2$ | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.5–0.8 | 0.8 | 0.9 | 1.0 | | | | |
| PEEP | 12 | 14 | 14 | 16 | 16 | 18 | 20 | 22 | 22 | 22–24 | | | | |

N Engl J Med 2004;351:327-36.

# Ventilator Management 102: VCV vs PCV?

**Cochrane Library**

**Cochrane** Database of Systematic Reviews

**Pressure-controlled versus volume-controlled ventilation for acute respiratory failure due to acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) (Review)**

Chacko B, Peter JV, Tharyan P, John G, Jeyaseelan L

- "Currently available **data from RCTs are insufficient** to confirm or refute whether pressure-controlled or volume-controlled ventilation offers any advantage for people with acute respiratory failure due to acute lung injury or acute respiratory distress syndrome…"

Cochrane Database 2015;1:CD008807.

# Ventilator Management 201: Weaning

- Assess daily for ability to wean
  - PEEP $\leq 8$
  - $FiO_2 \leq 0.4$
  - SBP $\geq 90$ mmHg (without vasopressors)
  - Off NMBA
  - Acceptable spontaneous breathing efforts
- Sedation vacation / SBT

N Engl J Med 2004;351:327-36.

# Part III
# Perfusion Management

# Fluids: NS vs Albumin

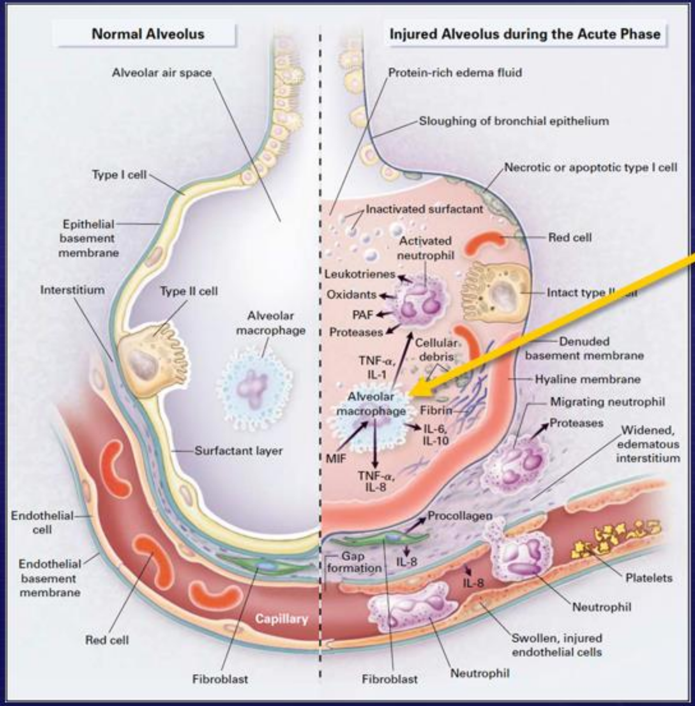
- SAFE Trial
  - No difference in saline vs albumin in critically ill patients
  - Not ARDS-specific
- FACTT Trial
  - Conservative fluid management associated with:
    - Improved oxygenation index
    - Improved lung injury score
    - Reduced ICU and ventilator days
    - No mortality benefit
  - No benefit to PAC over CVC
    - PAC had more non-fatal complications

N Engl J Med 2004;350:2247-56.
N Engl J Med 2006;354:2564-75.

# Part IV
# Severe ARDS Management Strategies

# ARDS Treatment: Steroids?

## Pathophysiology




Direct or indirect alveolar injury

↓

Alveolar macrophages release inflammatory mediators & pro-inflammatory cytokines

BMJ Best Practice 2016.
N Engl J Med 2000;342:1334-49.

# ARDS Treatment: Steroids?

the NNT

## Corticosteroids for Acute Respiratory Distress Syndrome (ARDS)

No benefit found

**In Summary, for patients that received early high-dose corticosteroids:**

### Benefits in NNT

- None were helped (life saved)

### Harms in NNT

- 1 in 3 were harmed (infection)

*Cochrane Database* 2004;4:CD004477.

# ARDS Treatment: HFOV?

- OSCAR Trial
  - No difference in mortality outcomes (41.7% vs 41.1%)
- OSCILLATE Trial
  - Planned enrollment of 1200
  - Ended early (n=548) due to increased mortality: 47% vs 35%

N Engl J Med 2013;368:863-5.

# ARDS Treatment: Paralytics?

**Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome**

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*

- Most beneficial in **severe** ARDS (P/F <120)
  - 48-hour infusion of cisatracurium used
- Reduced adjusted 90-day mortality (NNT 7)
- Increased vent-free and out-of-ICU days

N Engl J Med 2010;363:1107-16.

# ARDS Treatment: Paralytics?

ORIGINAL

CrossMark

## Effects of neuromuscular blockers on transpulmonary pressures in moderate to severe acute respiratory distress syndrome

Christophe Guervilly[1*], Magali Bisbal[2,3], Jean Marie Forel[1], Malika Mechati[3], Samuel Lehingue[1], Jeremy Bourenne[3], Gilles Perrin[3], Romain Rambaud[1], Melanie Adda[1], Sami Hraiech[1], Elisa Marchi[1], Antoine Roch[1,4], Marc Gainnier[3] and Laurent Papazian[1]



- Followed ARMA & ACURASYS protocols
  - Randomized "moderate" ARDS (100<PF<150)
- Improved recruitment / reduced de-recruitment
- Lower $P_{plat}$ in NMBA group

Intensive Care Med 2016.

# ARDS Treatment: iNO?

**Inhaled Nitric Oxide for Acute Hypoxic Respiratory Failure in Children and Adults: A Meta-analysis**

Jennifer Sokol, FRACP, FJFICM*†, Susan Elizabeth Jacobs, FRACP‡, and Desmond Bohn, FRCPC*

**Effect of nitric oxide on oxygenation and mortality in acute lung injury: systematic review and meta-analysis**

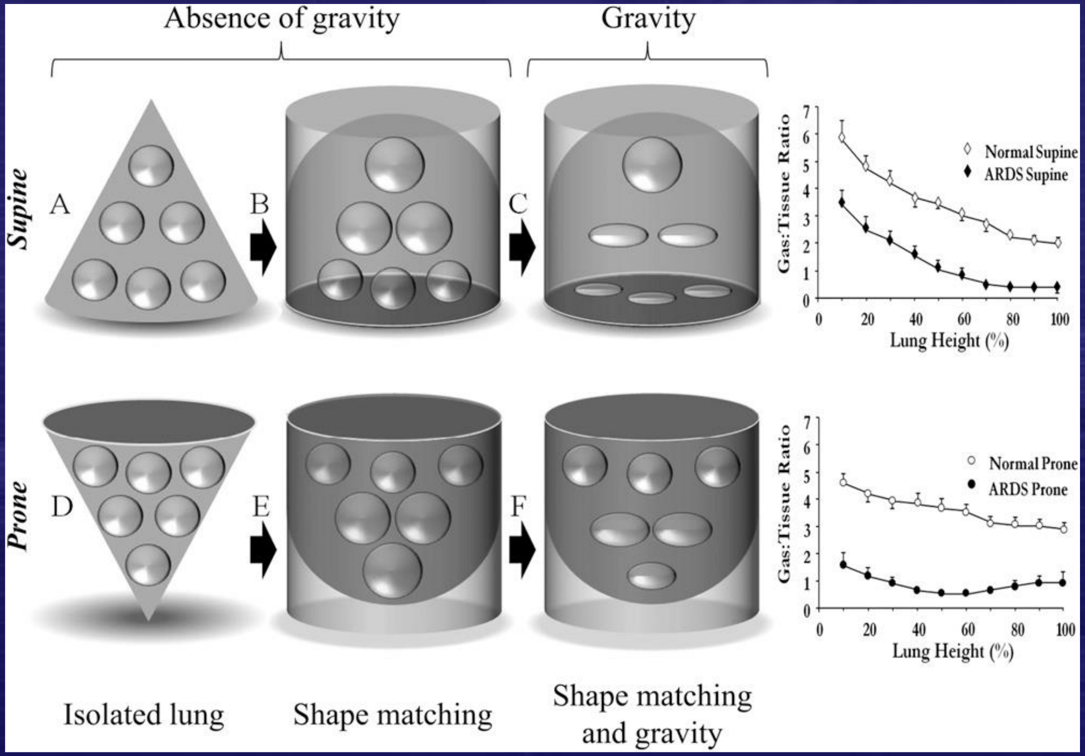
Neill K J Adhikari, lecturer,[1] Karen E A Burns, assistant professor,[1] Jan O Friedrich, assistant professor,[1] John T Granton, associate professor,[1] Deborah J Cook, professor,[2] Maureen O Meade, associate professor[2]

- Insufficient data to evaluate iNO use for acute hypoxemic respiratory failure, including ARDS
- ?Transient improved oxygenation, without significant mortality benefit

BMJ 2007;334:779-86.
Anesth Analg 2003;97:989-98.

# ARDS Treatment: Prone Positioning?

Primarily depends on generation of more recruitment in dorsal zones than derecruitment in ventral zones




Am J Respir Crit Care Med 2013;188:1286-93.

# ARDS Treatment: Prone Positioning?

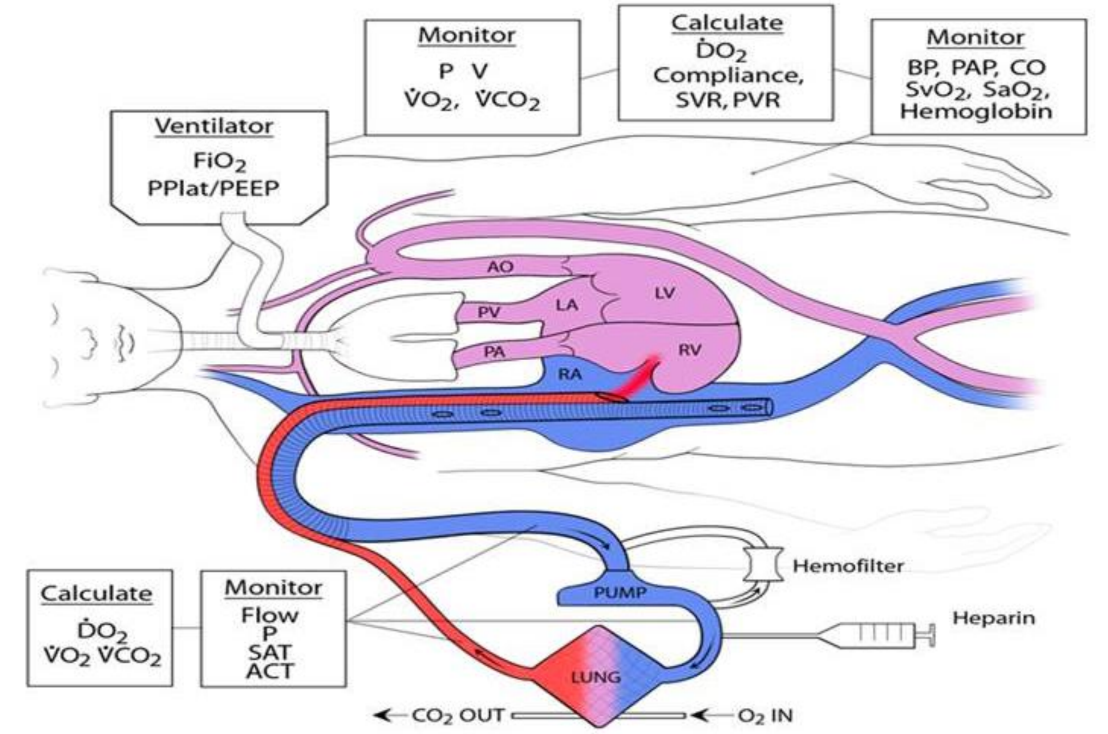
**The Efficacy and Safety of Prone Positional Ventilation in Acute Respiratory Distress Syndrome: Updated Study-Level Meta-Analysis of 11 Randomized Controlled Trials***

Joo Myung Lee, MD, MPH[1]; Won Bae, MD[2]; Yeon Joo Lee, MD[2]; Young-Jae Cho, MD, MPH[2]

- Most benefit in **severe** ARDS (P/F <150): NNT 16
  - Prone >10 hrs / session (OR 0.62)
- **Risks** of prone positioning:
  - Pressure ulcers
  - Major airway complications (none fatal)
    - ET tube obstruction (OR 2.16)
    - Unplanned extubation *not* significantly > prone

Am J Respir Crit Care Med 2013;188:1286-93.

# ARDS Treatment: ECMO?




**Veno-venous ECLS with a double lumen cannula**

RHB

ELSO.org

# ARDS Treatment: ECMO?

Extracorporeal membrane oxygenation for severe respiratory failure in adult patients: A systematic review and meta-analysis of current evidence☆,☆☆

Fernando Godinho Zampieri, MD [a,b,*], Pedro Vitale Mendes, MD [a,c], Otavio T. Ranzani, MD [a], Leandro Utino Taniguchi [a,c], Luciano Cesar Pontes Azevedo, MD, PhD [a,c], Eduardo Leite Vieira Costa, MD, PhD [a,c], Marcelo Park, MD, PhD [a,c]

- “Extracorporeal membrane oxygenation benefit on hospital mortality is unclear…”
- Results varied depending on method of analysis
- Tended to weakly favor ECMO for **severe** ARDS

J Crit Care 2013;28:998-1005.

# ARDS Treatment: ECMO?

- ELSO Guidelines:
  - ECMO indications:
    - PF < 100 on $FiO_2$ > 0.9
      - *Consider* for PF < 150 on $FiO_2$ > 0.9
    - $CO_2$ retention despite $P_{plat}$ >30
- VV – ECMO unless cardiac involvement
- Goal vent settings while *on* ECMO:
  - » $FiO_2$ < 0.4
  - » $P_{plat}$ < 25

ELSO Guidelines for Adult Respiratory Failure, Dec 2013.

# Part V
# Summary

- Lower tidal volumes ✓
- Higher PEEP / Lower $FiO_2$ ✓
- Keep $P_{plat}$ < 30 $cmH_2O$ ✓
- Volume control mode (vs pressure control) ?
- Assess for readiness to wean ✓
- Conservative fluid management ✓
- ~~PA catheter-guided therapy~~ ✗
- ~~High-dose steroids~~ ✗
- ~~HFOV ventilation~~ ✗
- iNO ?
- NMBA ? *Severe ARDS* ?/✓
- Prone positioning ? *Severe ARDS* ✓
- ECMO ?

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