Sepsis and Lung Injury

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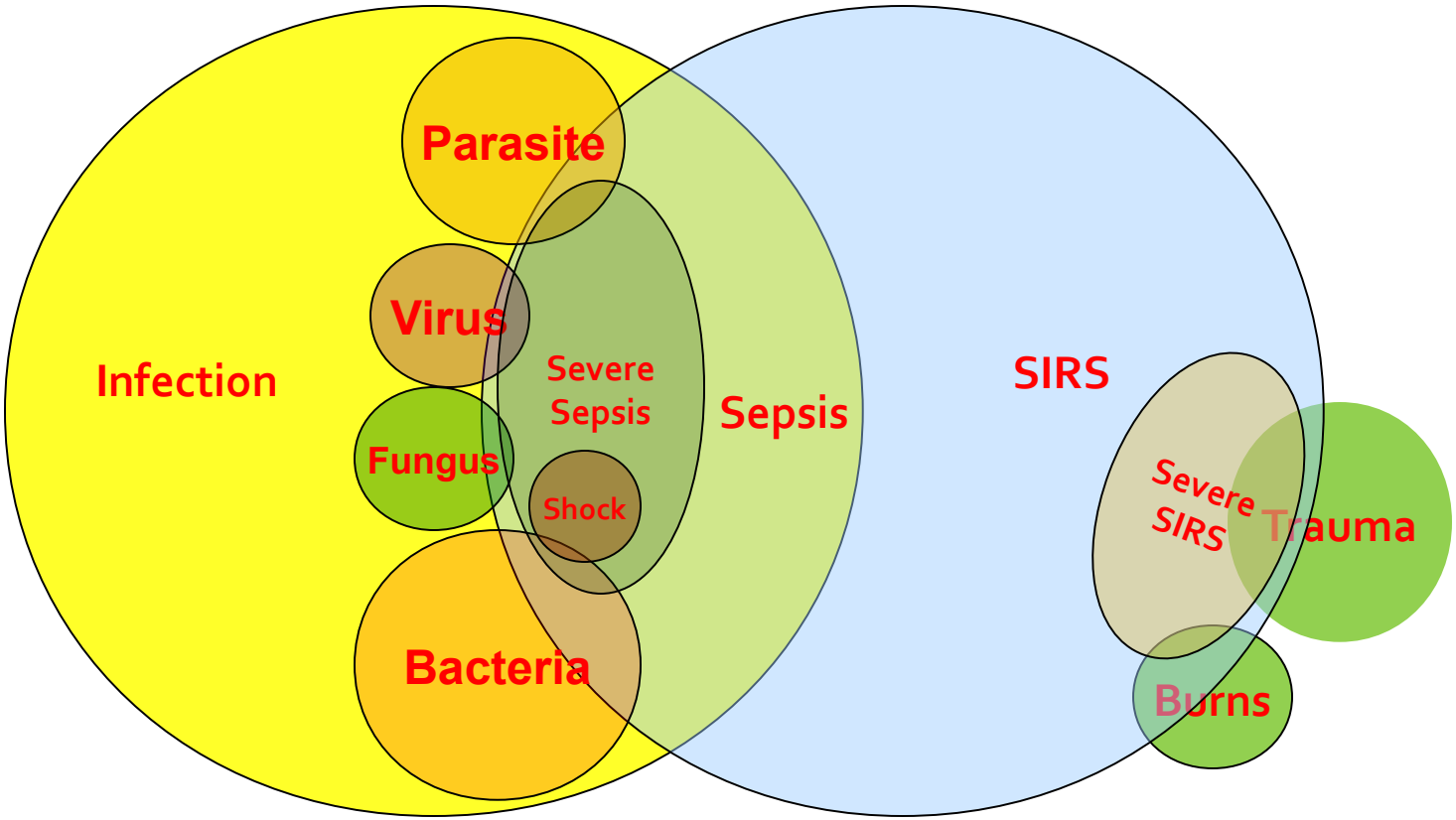
- Sepsis ***syndrome***
- Acute lung injury and adult respiratory distress ***syndrome***

Sepsis Syndrome



Causes of ARDS

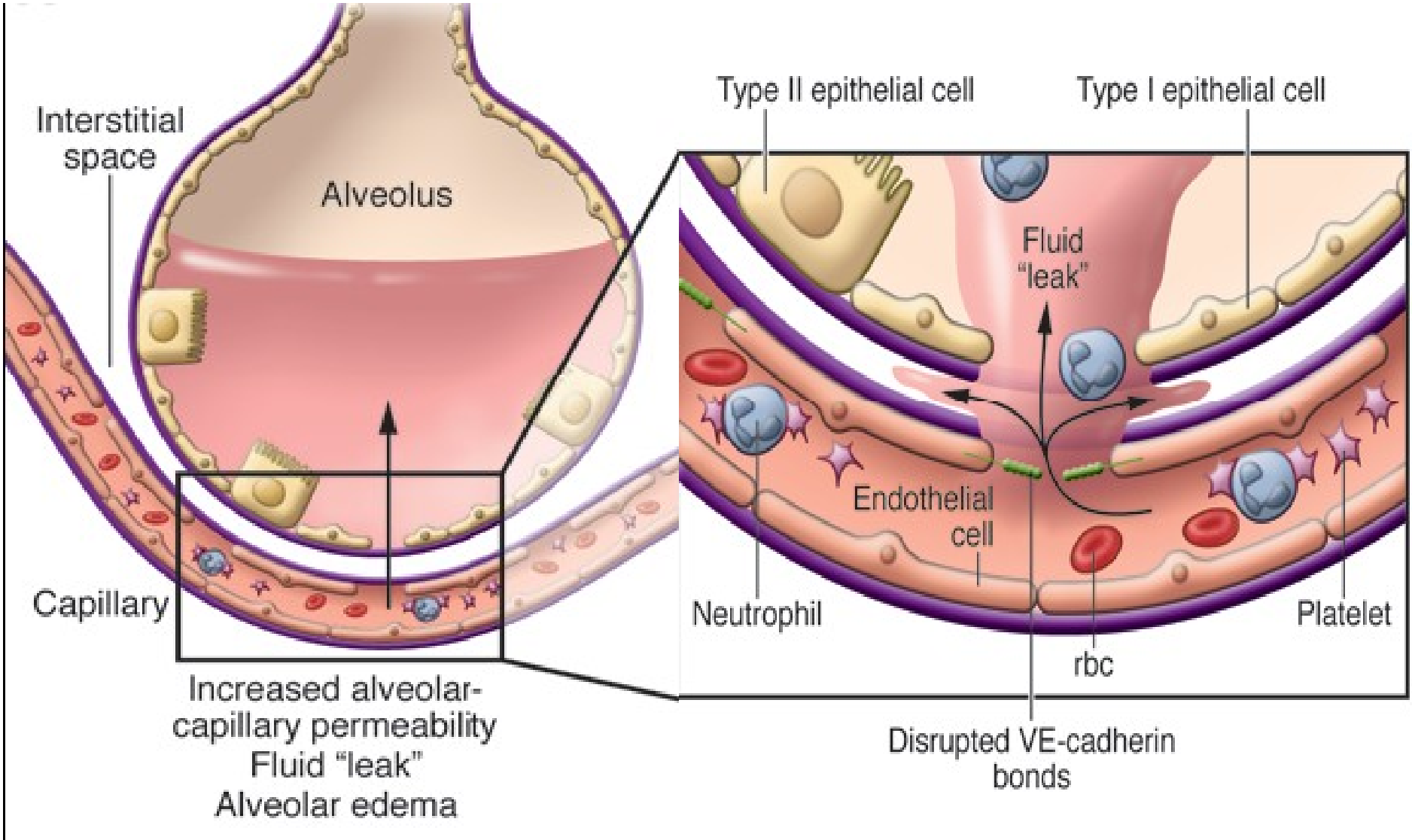
- ***Direct Injury***
- Aspiration of Gastric Juice
- Pneumonia
- Near Drowning
- Toxic Inhalation
- Lung Contusion
- Smoke Inhalation
- Radiation Pneumonitis
- Oxygen Toxicity

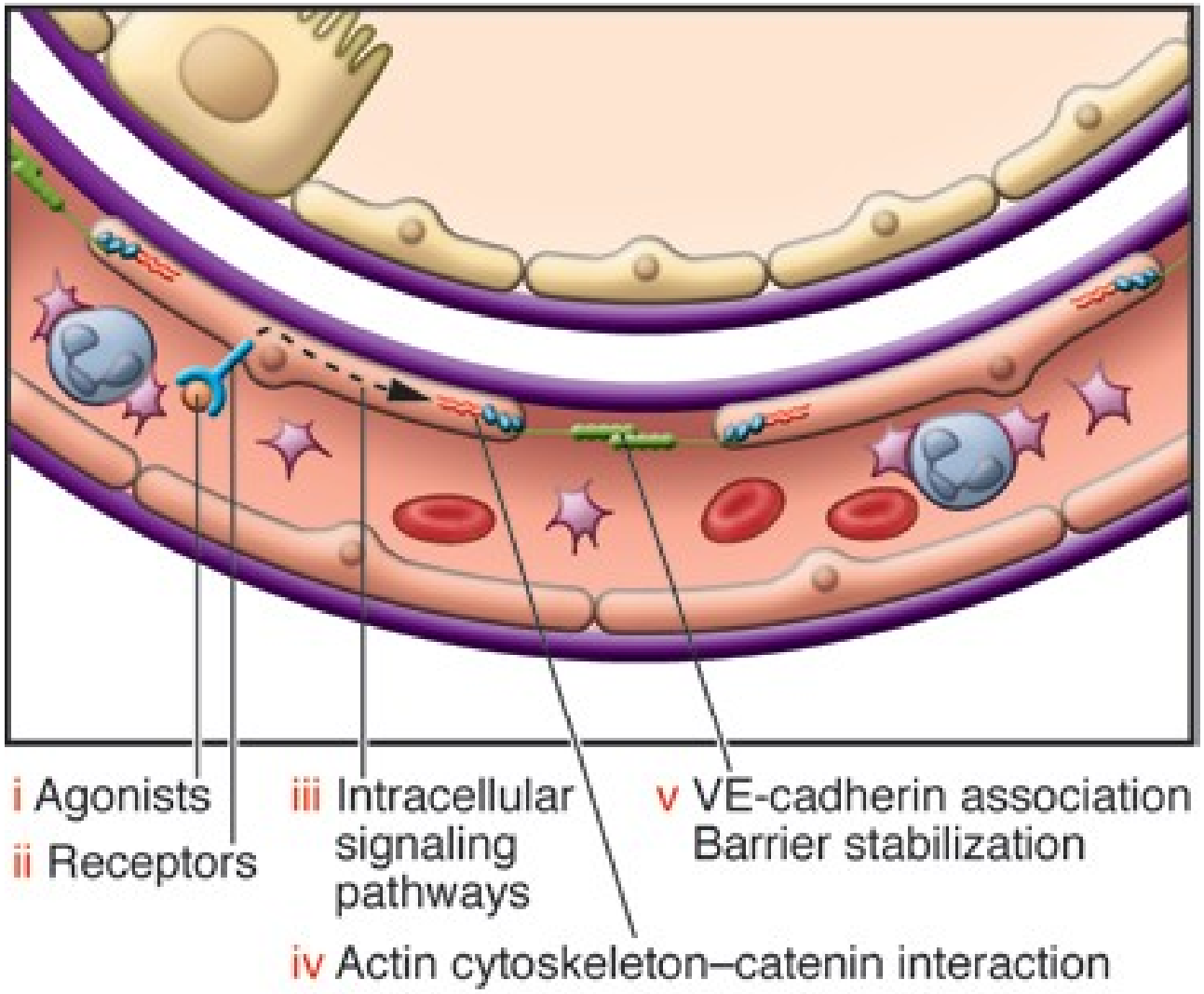
- ***Indirect Injury***
- Sepsis, SIRS
- Trauma (multiple fractures)
- Multiple Transfusions
- Cardio-pulm Bypass (rare)
- Fat Embolism
- CNS Injury
- Drugs

- Unfortunately, progression to ALI occurs in a third of patients with sepsis.

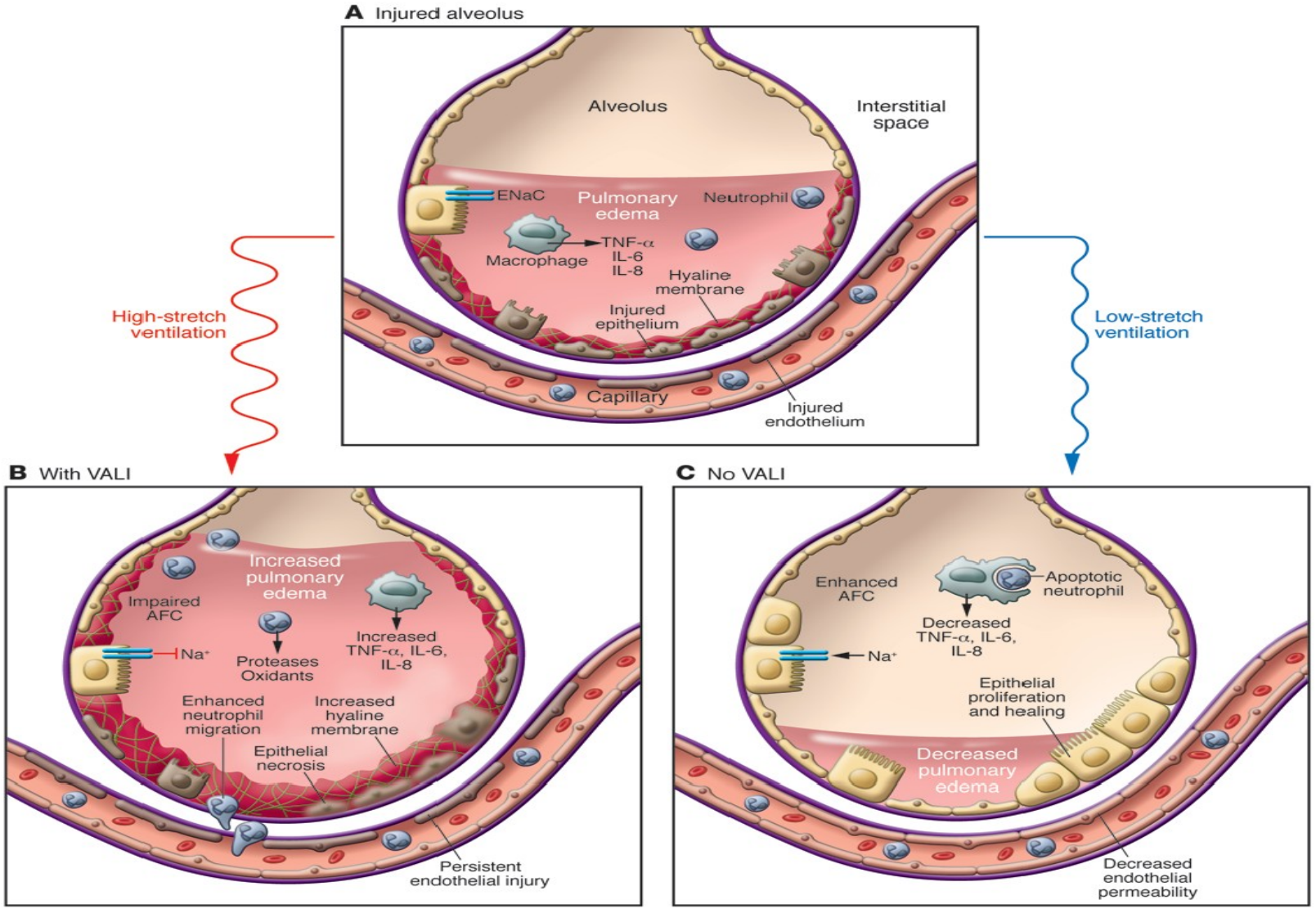
- ALI is an extraordinarily complex lung-associated disorder characterized by a neutrophilic inflammatory response and associated with increased pulmonary vascular permeability.

Injury


Interstitial space
Alveolus
Capillary
Increased alveolar-capillary permeability
Fluid "leak"
Alveolar edema
Type II epithelial cell
Type I epithelial cell
Fluid "leak"
Endothelial cell
Neutrophil
rbc
Platelet
Disrupted VE-cadherin bonds


i Agonists
ii Receptors
iii Intracellular signaling pathways
iv Actin cytoskeleton–catenin interaction
v VE-cadherin association Barrier stabilization

Resolving


A Injured alveolus
Alveolus
Interstitial space
ENaC
Pulmonary edema
Neutrophil
Macrophage
TNF-α
IL-6
IL-8
Hyaline membrane
Injured epithelium
Capillary
Injured endothelium
High-stretch ventilation
Low-stretch ventilation
B With VALI
Increased pulmonary edema
Impaired AFC
Na+
Proteases
Oxidants
Increased TNF-α, IL-6, IL-8
Enhanced neutrophil migration
Increased hyaline membrane
Epithelial necrosis
Persistent endothelial injury
C No VALI
Enhanced AFC
Apoptotic neutrophil
Decreased TNF-α, IL-6, IL-8
Na+
Epithelial proliferation and healing
Decreased pulmonary edema
Decreased endothelial permeability

Is there any difference in the prognosis of ARDS in terms of it's etiology?

Mortality in sepsis versus non-sepsis induced acute lung injury

Jonathan E Sevransky et al

- In this study those with sepsis vs. non-sepsis-induced ALI had a significantly higher crude mortality rate.

- However, after adjustment for patient demographics, severity of illness and clinical factors, sepsis was not independently associated with more mortality.

Is there any way to recognize the progression of a sepsis to ARDS?

Biomarkers of lung epithelial injury and inflammation distinguish severe sepsis patients with acute respiratory distress syndrome

Lorraine B Ware et al

- *Although several plasma biomarkers have been studied in ARDS, the majority of studies have focused on prognosis, rather than diagnosis.*

- *Given the complex pathophysiology of ARDS , it is unlikely that a single biomarker will have adequate specificity for ARDS.*

- RAGE(receptor for advanced glycation end products)
- Interleukin-8 (IL-8)
- Surfactant protein D (SPD)
- Club cell secretory protein (CC16, formerly known as Clara cell secretory protein)
- Interleukin-6 (IL-6)

Table 3 Comparison of models for diagnosis of ARDS using single biomarkers to a combined model utilizing the top five performing biomarkers

Model	All data (100 pairs) AUC (95% CI)[1]	Enrollment day cases (91 pairs) AUC (95% CI) [1]	Severe cases only (66 pairs) AUC (95% CI) [1]
Single marker models			
SPD	0.69 (0.6, 0.76)	0.71 (0.63, 0.79)	0.72 (0.62, 0.81)
RAGE	0.64 (0.56, 0.72)	0.68 (0.6, 0.75)	0.67 (0.57, 0.76)
IL8	0.61 (0.54, 0.69)	0.63 (0.55, 0.7)	0.64 (0.55, 0.73)
CC16	0.60 (0.52, 0.68)	0.60 (0.52, 0.68)	0.64 (0.55, 0.74)
IL6	0.59 (0.52, 0.67)	0.61 (0.53, 0.69)	0.63 (0.53, 0.72)
Multivariable model (includes SPD, RAGE, IL-8, CC16, IL6)	**0.75 (0.7, 0.84)**	**0.78 (0.74, 0.87)**	**0.82 (0.77, 0.9)**

[1]All AUCs are bootstrap bias-corrected. All 95% CI are bootstrap CIs.

Treatment

There is no specific treatment for ALI.

Treatment is entirely supportive and aims to maintain adequate oxygenation and ventilation while minimizing secondary lung injury.

Non pharmacologic treatments

- *The Lung Protective Strategy*
- *Alveolar Recruitment*
- *Fluid Management Strategies*
- *Extracorporeal Membranous Oxygenation*

Pharmacologic treatments

- *Corticosteroids*
- *β2-Agonists*
- *Furosemide*
- *Neuromuscular Blockade*
- *Surfactant Replacement Therapy*
- *Inhaled Nitric Oxide*
- *Ω-3 Fatty Acids*
- *Liquid Ventilation*
- *Activated Protein C*

Metabolic consequences of sepsis-induced acute lung injury revealed by plasma 1H-nuclear magnetic resonance quantitative metabolomics and computational analysis.

Stringer KA et al

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