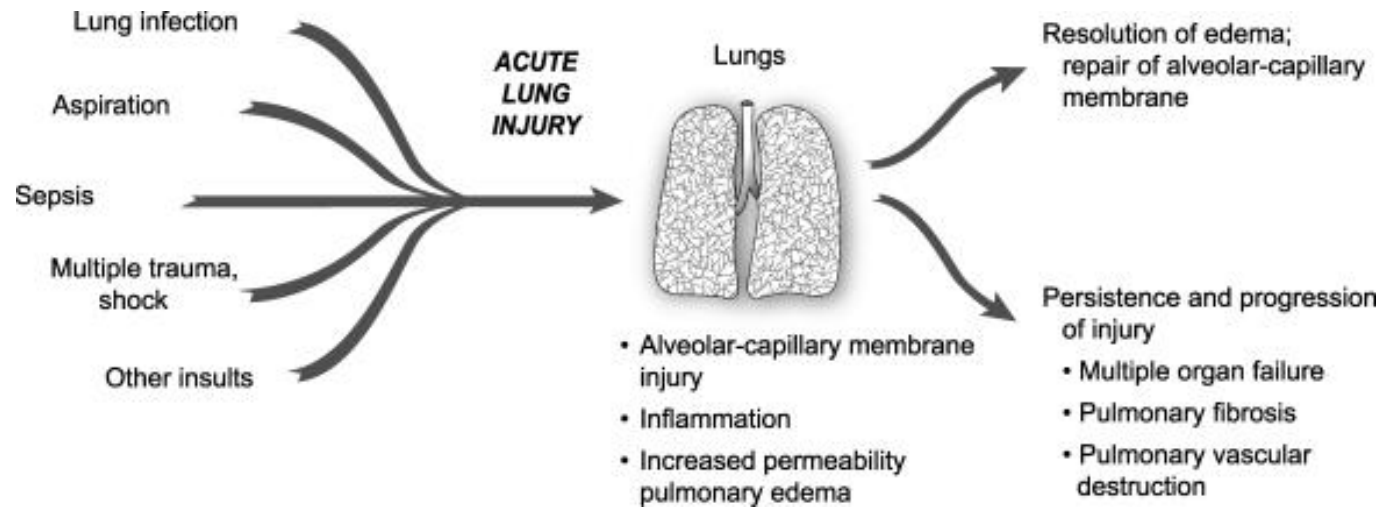


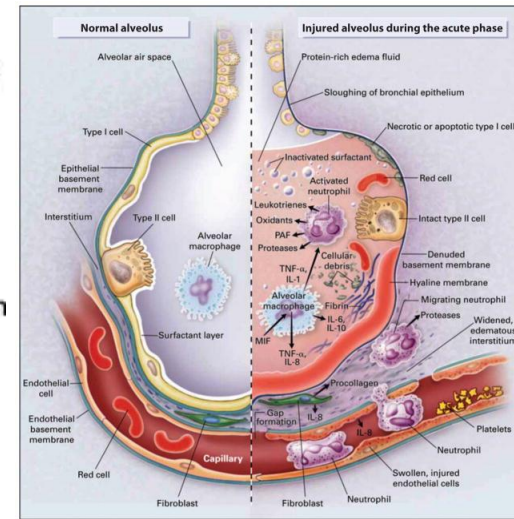
Said Audi, PhD
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<https://mcw.marquette.edu/biomedical-engineering/computational-lung-physiology-lab/index.php>

Pathogenesis of ALI/ARDS



Matthay and Zimmerman. *Am J Respir Cell Mol Biol.* 33:319, 2005



Ware & Matthay. *N Engl J Med* 342:1334, 2000

- **Oxidative stress, inflammation, and cell death** are common pathways in the pathogenesis of ALI/ARDS.
- Acute inflammation results in damage to the **alveolar-capillary barrier**, leading to alveolar edema and severe impairment of oxygenation.
- Injury to the **pulmonary capillary endothelium** is the **primary cause** of increased-permeability pulmonary edema in ALI/ARDS.

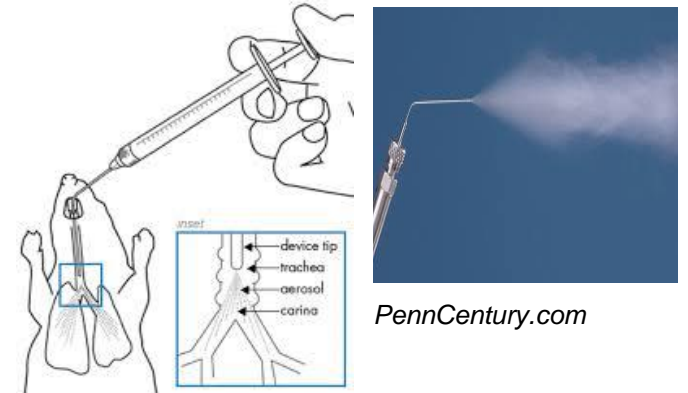
Animal Models of Human ALI/ARDS

- Animal models have been developed to evaluate the time course, severity and pathophysiological mechanisms of ALI/ARDS.
- Two well-established rat models (direct insult):
 - Exposure to 100% O₂ (hyperoxia).
 - Treatment with intratracheal endotoxin (lipopolysaccharide, **LPS**).
- Both models reproduce the cardinal features of clinical ALI/ARDS:
 - Bilateral infiltration
 - Increased microvascular permeability
 - Low-pressure edema
 - Hypoxemia
 - Endothelial cell death

Hyperoxia chamber



Penn-Century LPS sprayer

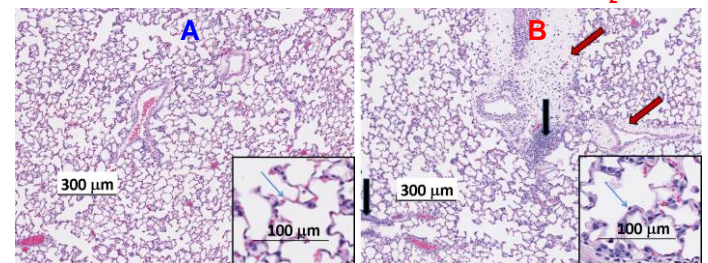


PennCentury.com

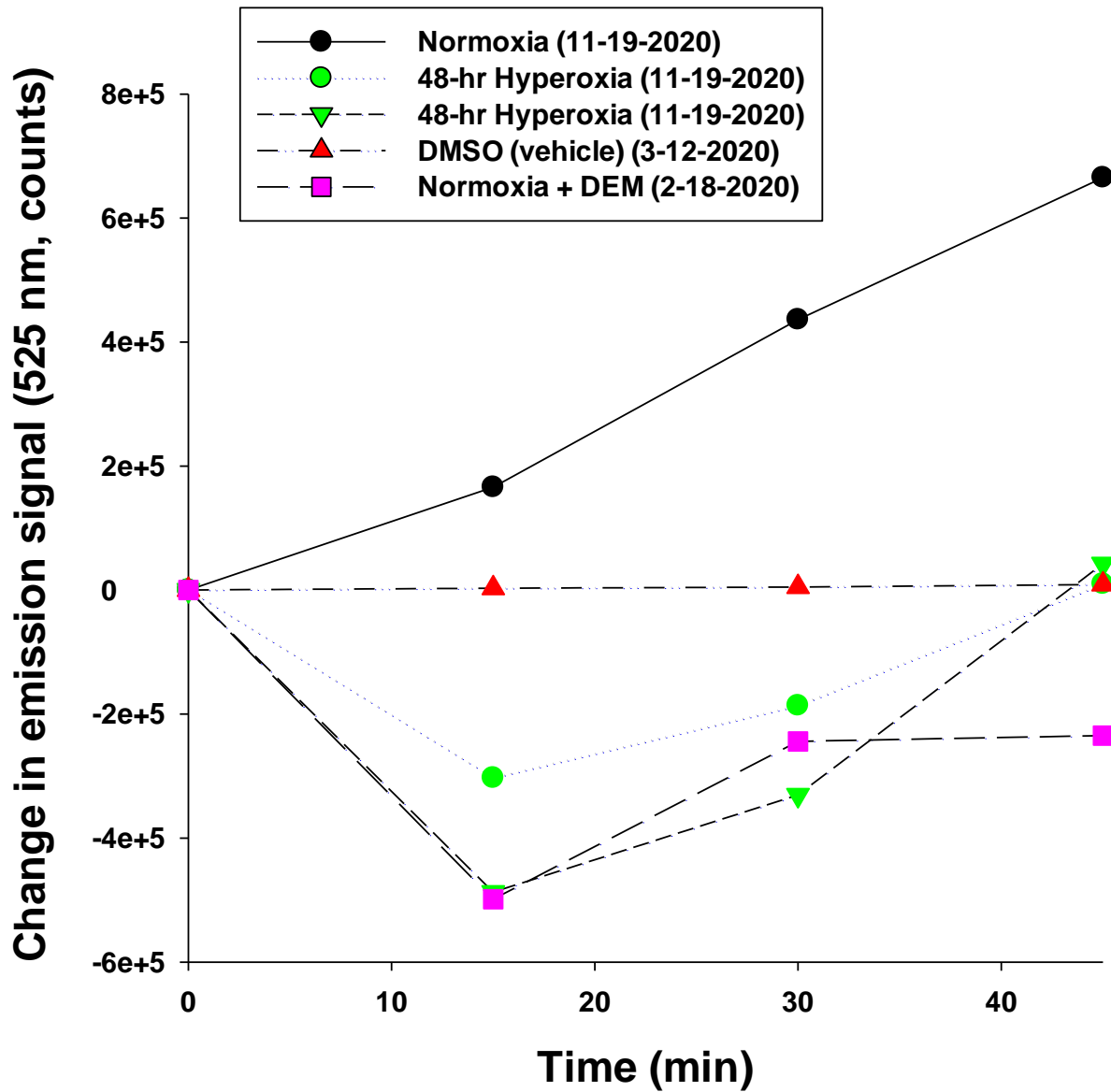
Normoxic

Figure 2

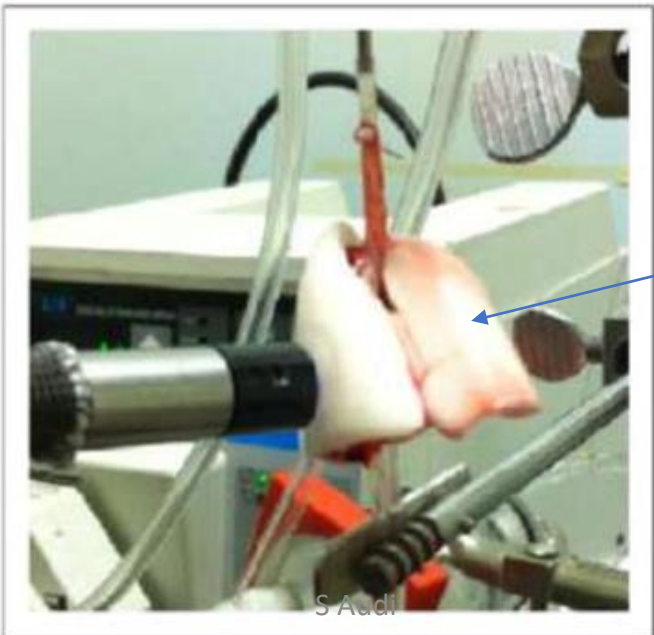
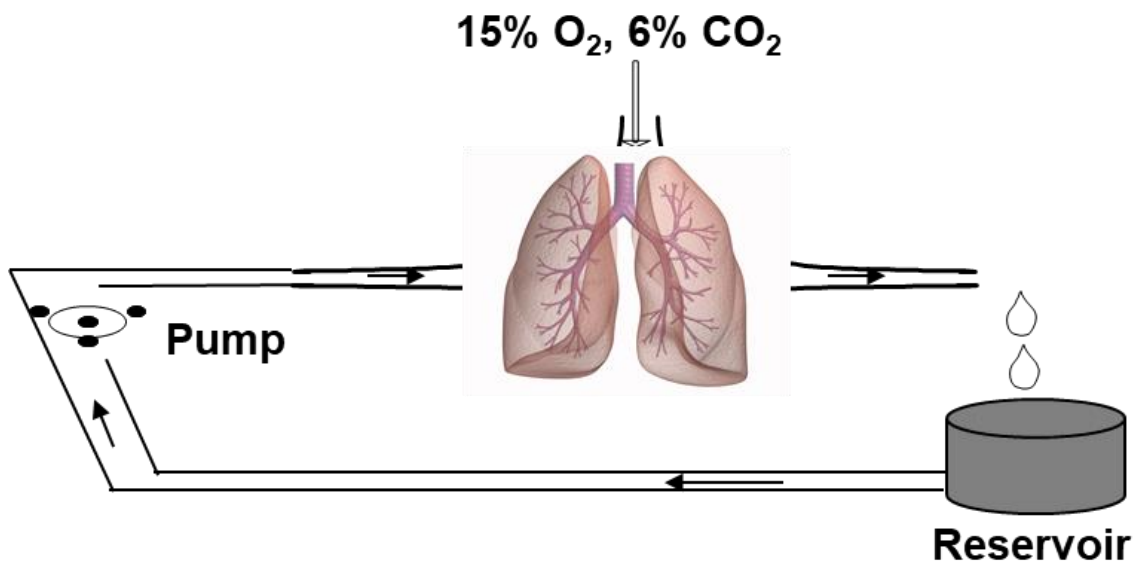
60-hr 100% O₂



Preliminary results using DSSQ in lungs from rats exposed to room air (normoxia) or high oxygen (hyperoxia) as a model of human ARDS



Isolated Perfused Rat Lung Preparation



Rat lung

Preliminary results (DSSQ reduction) in plasma from rats exposed to room air (normoxia) or high oxygen (hyperoxia) as a model of human ARDS

DSSQ (50 mM) in plasma from normoxic and hyperoxic rats
(Nrf2 WT, Nrf2 homo, NOX4 homo)
EX 485 nm, EM 525 nm

