Acute Respiratory Distress Syndrome

Robert Kawa, OMS III
Predoctoral OMM Fellow
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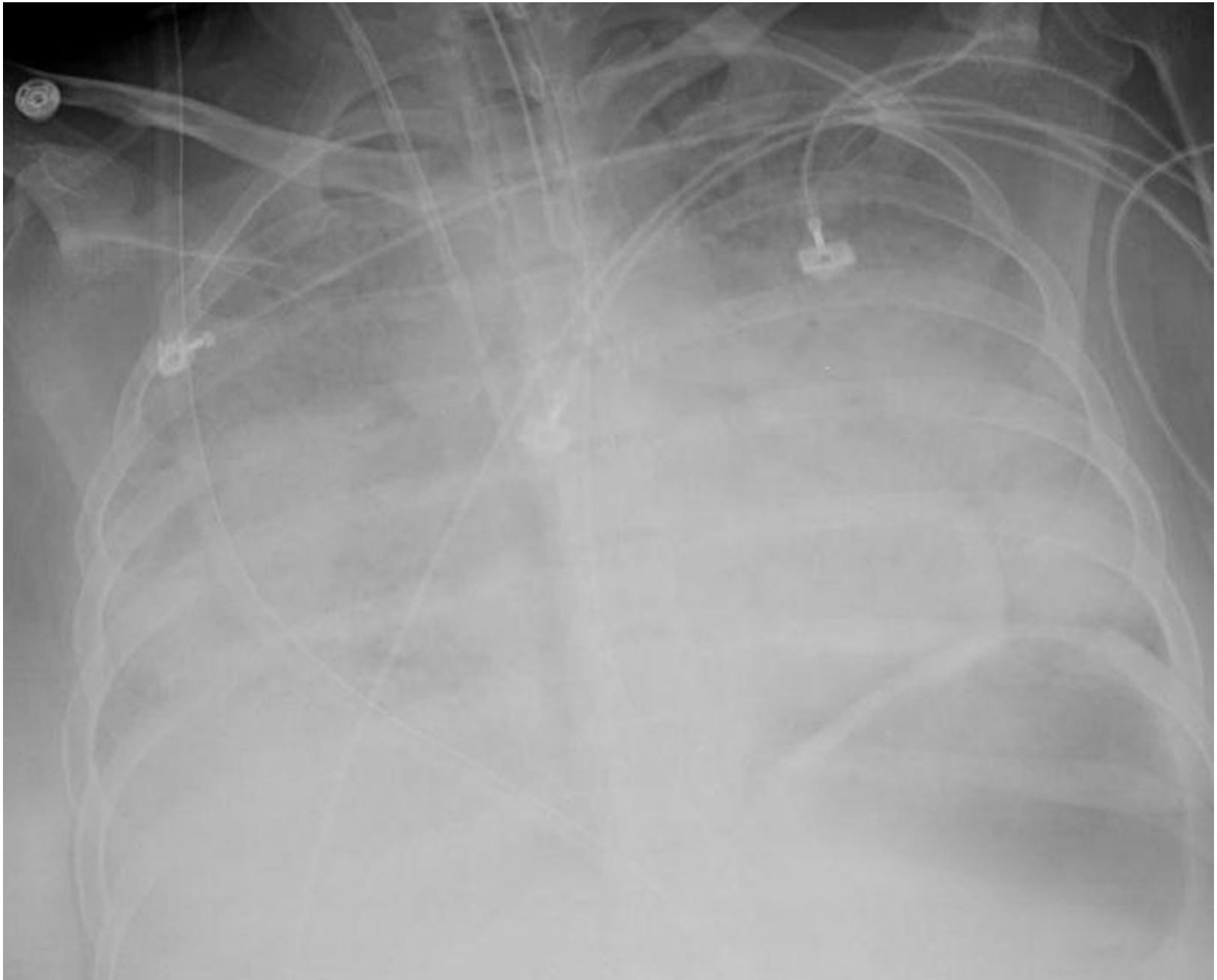
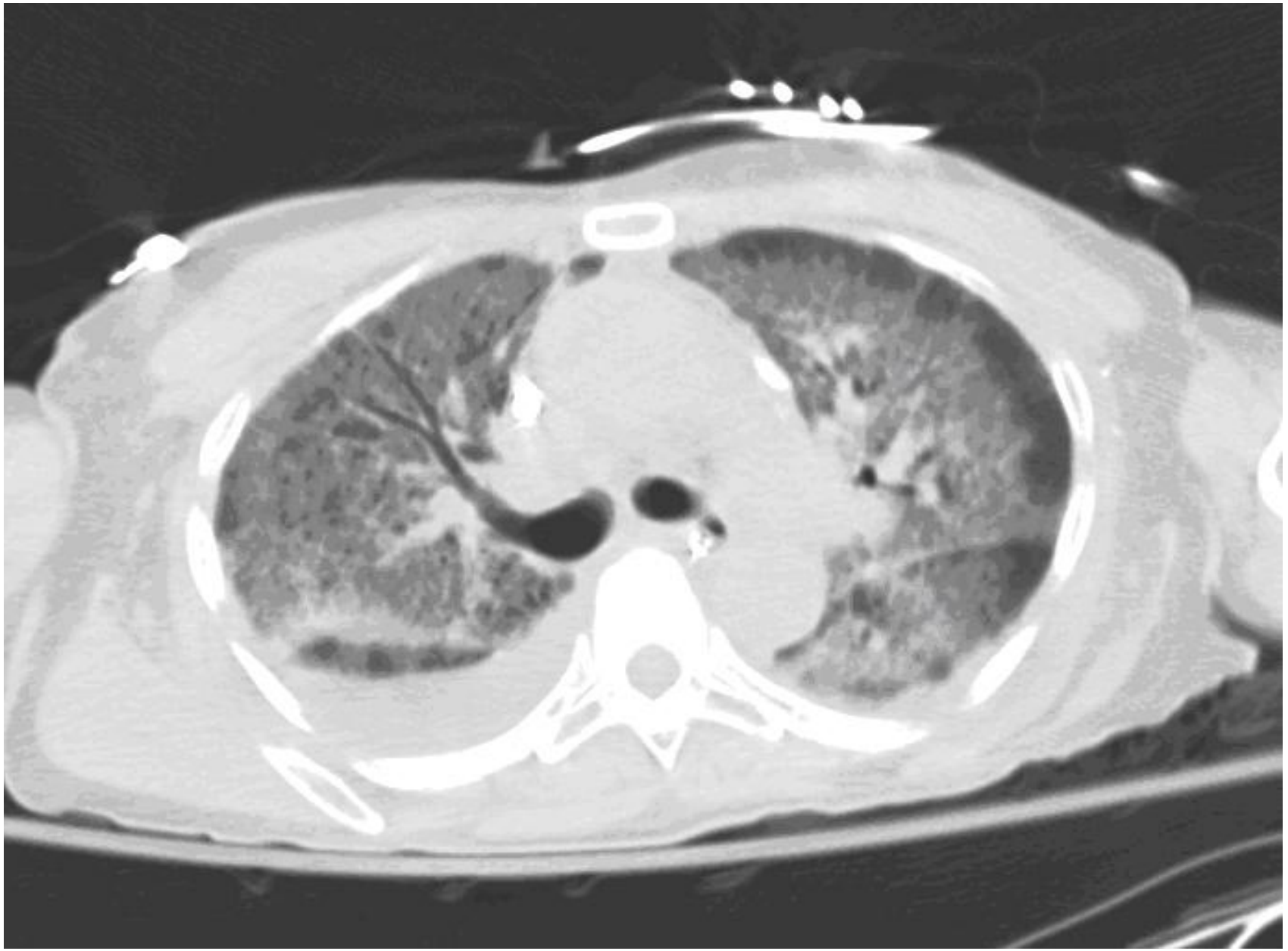
Objectives

- Understand the definition of Acute Lung Injury and Acute Respiratory Distress Syndrome
- Review the epidemiology, pathophysiology, and possible etiologies that exist for ALI/ARDS as well as the possible complications that can arise.
- Understand the supportive care measures necessary to facilitate the recovery of the patient with ALI/ARDS
- Evaluate ventilator settings and identify modes that may be most beneficial
- Explore and assess novel therapies in the treatment of ALI/ARDS, and identify which provide the pt with the most favorable outcome



History

- First described in the 1960's by military Physicians in Vietnam, termed "shock lung"
- Civilian physicians referred to the condition as "adult" respiratory distress syndrome
- Name was later changed to "acute" respiratory distress syndrome upon recognition that individuals of any age can be afflicted by this distinct type of respiratory failure



Acute Lung Injury
vs.
Acute Respiratory Distress Syndrome

ALI vs. ARDS

ALI

Requires all four:

- Acute onset
- Bilateral infiltrates
- No evidence of elevated left atrial pressure
- PaO_2/FiO_2 = 201-300 mmhg

ARDS

Requires all four:

- Acute onset
- Bilateral infiltrates
- No evidence of elevated left atrial pressure
- PaO_2/FiO_2 = <200 mmhg

Normal PaO_2/FiO_2 = 300-500 mmhg

Diagnosing ALI/ARDS

Diagnosis

- ALI/ARDS is a diagnosis of exclusion
- Other causes of acute B/L infiltrates and respiratory distress must be excluded
  - Cardiogenic pulmonary edema
  - Diffuse alveolar hemorrhage
  - Pneumonia
  - Idiopathic acute eosinophilic pneumonia
  - Cryptogenic organizing pneumonia
  - Miliary tuberculosis
  - Cancer

Diagnosis

- Cardiogenic Pulmonary Edema
  - Often difficult to distinguish from ALI/ARDS
  - Suspect ALI/ARDS if:
    - BNP < 100
    - Echo- no evidence of AV/MV dysfunction, or decreased LVEF
- Other causes can often be ruled out by clinical scenario and examination
  - Lung biopsy may be considered in cases that can not be defined

Epidemiology

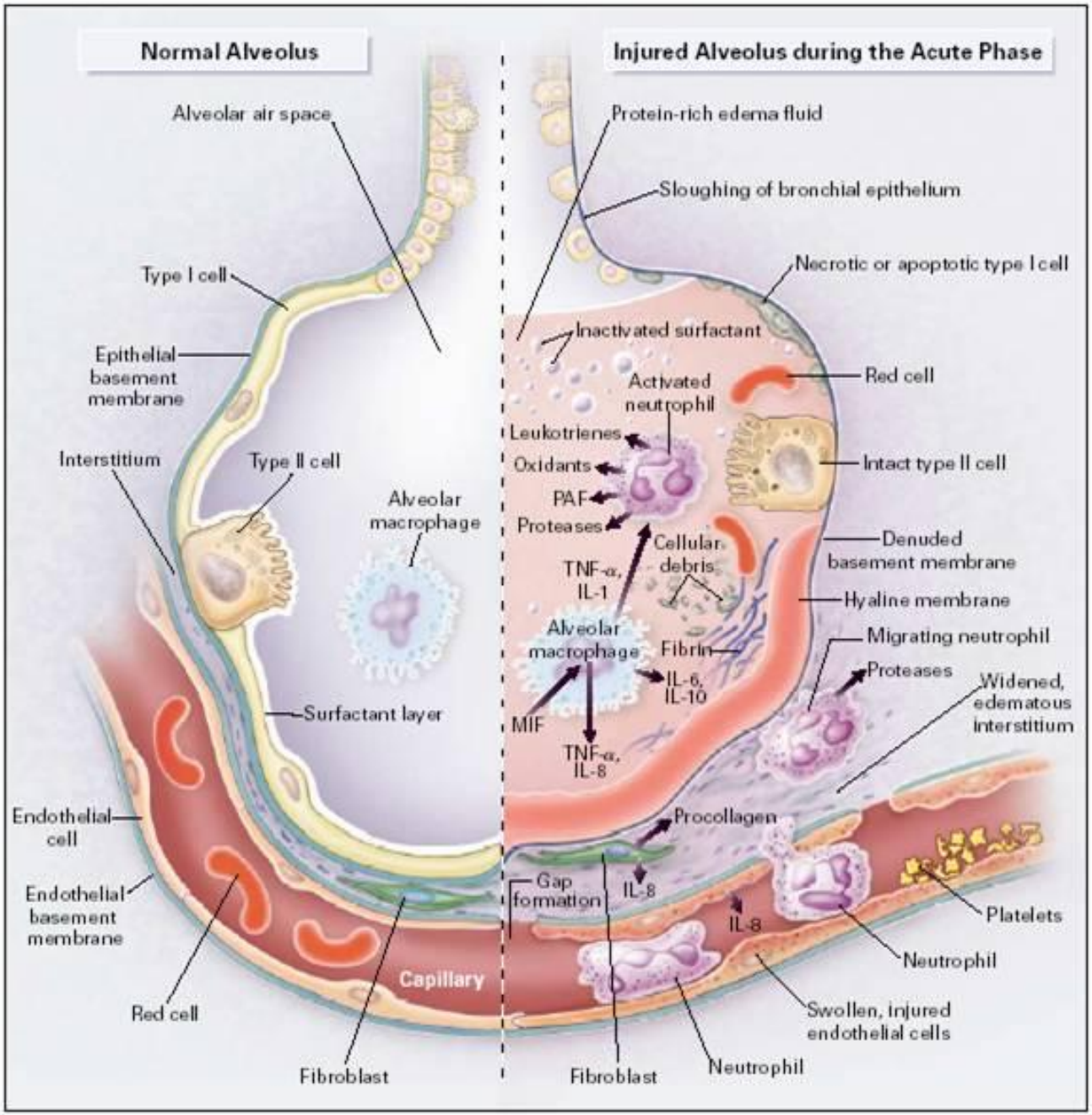
Epidemiology

- 10-15% of ICU pts will meet criteria for ALI/ARDS
- Incidence rises to 20% if pt is mechanically ventilated
- 190,000 cases of ALI/ARDS in the US each year
- Incidence increases with age:
  - Age 15-19: 16/100,000 person years
  - Age 75-84: 306/100,000 person years

Pathophysiology

Pathophysiology

- Strict regulation of fluid movement is needed to maintain both the small interstitial fluid and dry alveoli needed for normal gas exchange
- When lung injury occurs this regulation is compromised, causing excess interstitial fluid to accumulate and subsequent alveolar fluid filling.
- Fluid overload:
  - Impairs gas exchange
  - Decreases lung compliance
  - Increases pulmonary arterial pressure

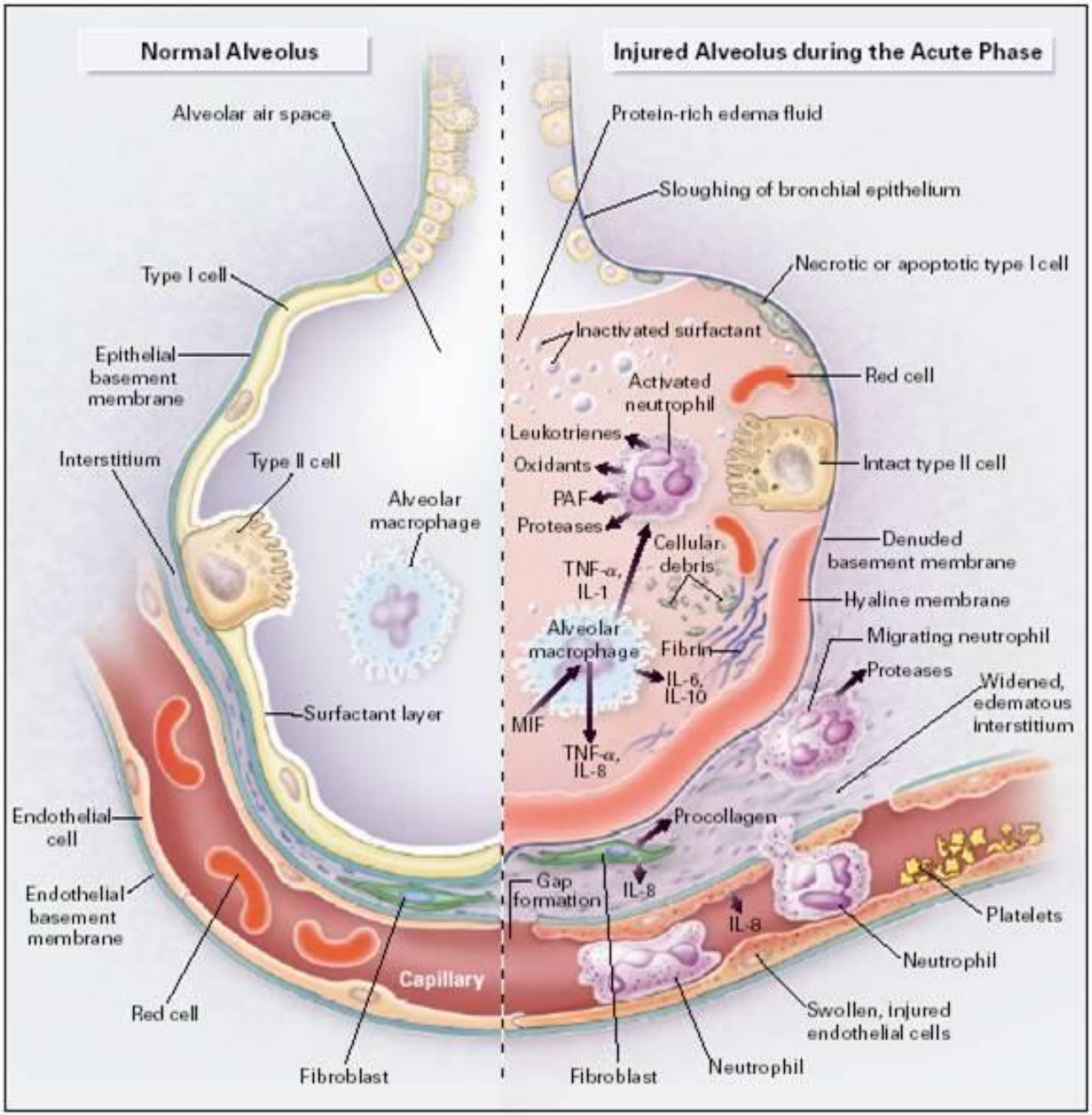

Normal Alveolus
Injured Alveolus during the Acute Phase
Alveolar air space
Type I cell
Epithelial basement membrane
Interstitium
Type II cell
Alveolar macrophage
Surfactant layer
Endothelial cell
Endothelial basement membrane
Red cell
Capillary
Fibroblast
Protein-rich edema fluid
Sloughing of bronchial epithelium
Necrotic or apoptotic type I cell
Inactivated surfactant
Activated neutrophil
Red cell
Leukotrienes
Oxidants
PAF
Proteases
Intact type II cell
Cellular debris
TNF-α, IL-1
Denuded basement membrane
Hyaline membrane
Alveolar macrophage
Fibrin
Migrating neutrophil
IL-6, IL-10
Proteases
Widened, edematous interstitium
MIF
TNF-α, IL-8
Procollagen
Gap formation
IL-8
IL-8
Platelets
Neutrophil
Swollen, injured endothelial cells
Fibroblast
Neutrophil

Pathophysiology

- Mechanism of Injury:
  - Many possibly etiologies, but all result in release of alveolar pro-inflammatory cytokines
  - Neutrophil recruitment/activation causing release of toxic mediators
  - Vascular endothelial and alveolar epithelial damage
    - Functional surfactant lost

Pathophysiology

- Endothelium losses selective permeability
- Protein free to move into extravascular space
  - oncotic gradient lost
- Fluid accumulation in interstitium and alveoli as the lymphatics quickly become overwhelmed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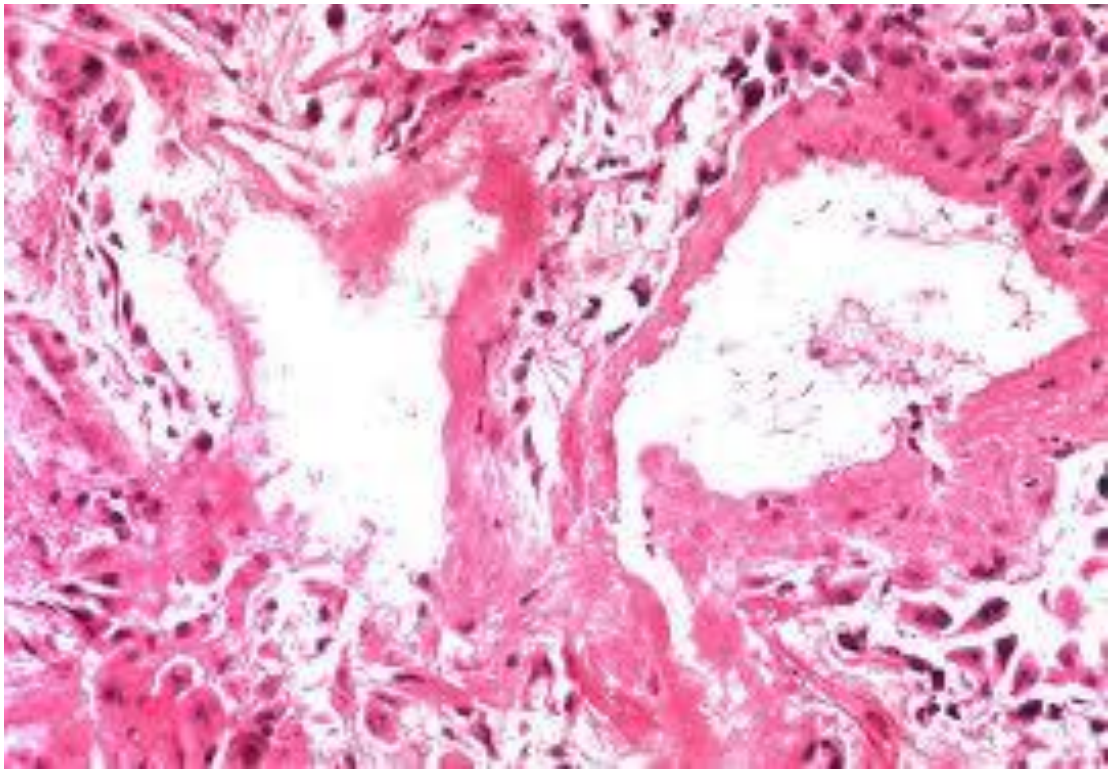
Pathological Staging

Pathology

- Stage I- Exudative
  - Day 1-7
    - Diffuse damage to alveoli
- Stage II- Proliferative
  - Day 7-20
    - Endothelial and alveolar repair, pulmonary edema resolution, deposition of interstitial collagen
- Stage III- Fibrotic
  - If occurs, day >20
    - Diffuse fibrosis, cyst formation

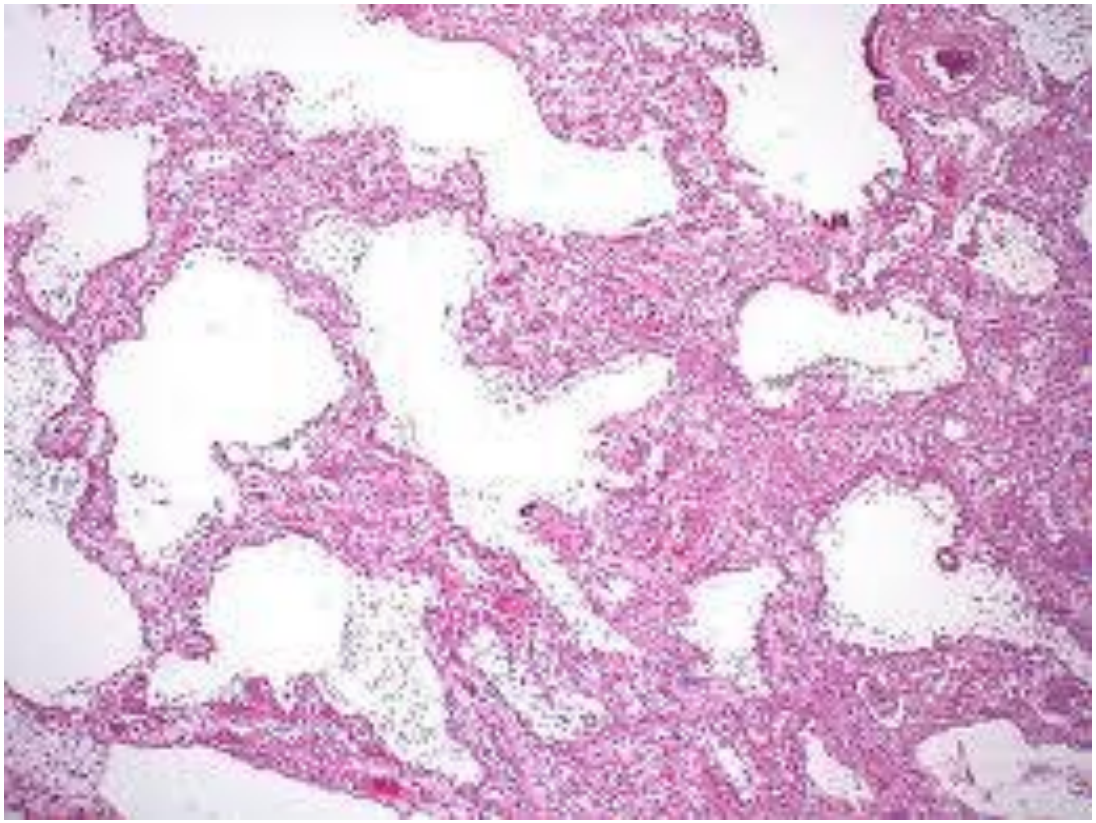
Pathology

- Stage I- Exudative



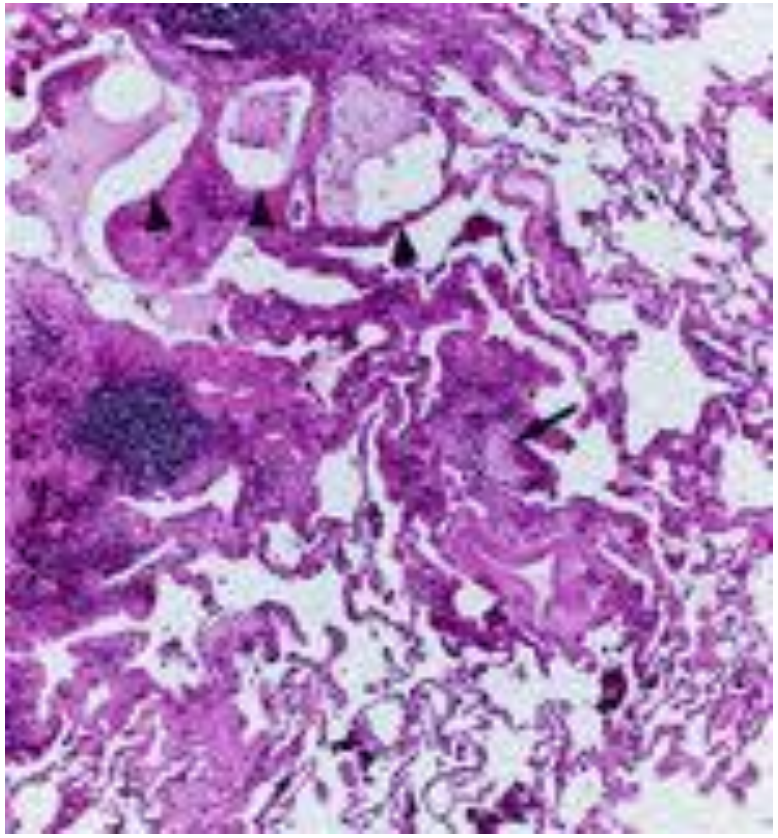
Pathology

- Stage II- Proliferative



Pathology

- Stage III- Fibrotic

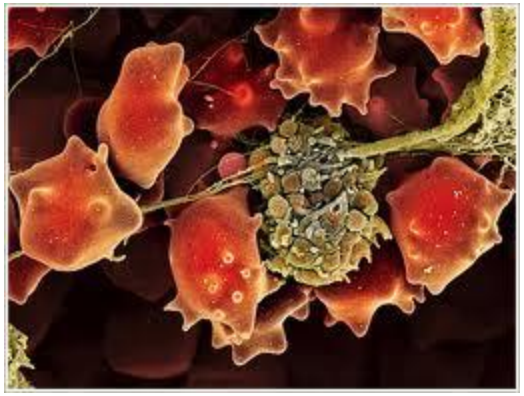


Etiologies of Lung Injury

Etiology

- Sepsis
- Aspiration
- Pneumonia
- Severe Trauma
- Burns
- Multiple Blood Transfusions
- TRALI
- Pancreatitis
- Drug Overdose
- Near Drowning
- Smoke Inhalation
- Cardiopulmonary Bypass
- Pulmonary Contusions
- Multiple Fractures
- Upper Airway Obstruction
- Bone Marrow Transplant
- Venous Air Embolism
- Amniotic Fluid Embolism
- Neurogenic Pulmonary Edema
- Acute Eosinophilic Pneumonia
- Miliary TB

Etiology



- Sepsis
  - MCC of ALI/ARDS
    - Should be the first etiology evaluated
- Aspiration
  - 1/3 or hospitalized pts with diagnosed aspiration will develop ALI/ARDS
  - Even if pH>2.5, gastric contents can cause widespread severe lung injury
    - Gastric enzymes?

Etiology

- Trauma
  - Lung contusions
    - Blunt trauma
  - Fat embolism
    - Long bone fractures
  - Burns

  - *ALI/ARDS from trauma poses a significantly lower risk of mortality than from different origins.

Etiology

- Genetics
  - Insults listed do not cause ALI/ARDS in all pts
  - It seems almost certain that genetics play a role
  - Possible mutations:
    - Surfactant protein B
    - Angiotensin converting enzyme
      - Potential treatment options????

Etiology

- Lung Injury Prediction Score:
  - 3.5 pts-
    - Aortic vascular surgery
  - 2.5 pts-
    - Cardiac surgery
  - 2 pts-
    - Shock, aspiration, acute abdominal surgery, TBI, smoke inhalation, near-drowning, FiO2>3.5
  - 1.5 pts-
    - Spine surgery, pneumonia, lung contusion, multiple fractures, acidosis
  - 1 pt-
    - Sepsis, ETOH abuse, obesity, chemotherapy, hypoalbuminemia
- LIPS<4 =Pt unlikely to develop ARDS

ALI/ARDS Complications

Complications

- Pts at high risk for complications both as a direct result of ALI/ARDS and from ICU setting
  - Pulmonary barotrauma
  - Sedation/paralysis
  - Multisystem organ failure
  - Nosocomial pneumonia
  - DVT
  - Catheter-related infections
  - Poor nutrition
  - Stress ulcers

Supportive Care of the Patient with ALI/ARDS

Supportive Care

- The majority of pts with ALI/ARDS do not die from the condition itself, but from the associated complications and multisystem organ failure that accompany the process

- Meticulous supportive care is needed to provide the best possible outcome in all ALI/ARDS patients.

Supportive Care

- Sedation/Analgesia
  - Improves tolerance of mechanical ventilation and decreases the body's O2 consumption
  - Propofol/Lorazepam are great choices for sedation, but provide little/no analgesia
    - Opioids should be used in addition
    - Morphine decrease O2 demand by 6-8%
  - Intermittent sedation has been suggested to be beneficial to continuous infusion
  - Recently, studies have suggested that pts receiving "verbal comforting and reassurance" instead of standard sedation therapies had fewer ICU and ventilator-dependant days

Supportive Care

- Paralysis
  - Neuromuscular blockade is both strongly supported and opposed
  - In trials involving ARDS, most show a benefit with paralytic agents use with a decrease in ventilator-dependent days and incidence of barotrauma
  - With changes in ventilator technology the need for paralysis has decreased and is generally not used because of the feared complications of ICU related neuromuscular weakness

Supportive Care

- Hemodynamic Monitoring
  - PAC has shown no advantage over CVC
    - PAC had 2x risk of infection than CVC
  - CVC has proven to be useful in assessing fluid status in ALI/ARDS patients
    - Patients treated with strict fluid intake to keep a CVC pressure <4mmHg decreases ventilator-dependant and ICU days
    - Hypotension and organ hypoperfusion need to be monitored and avoided

Supportive Care

- Hemodynamic Monitoring
  - Transfusions in ALI/ARDS
    - Drops in hemoglobin are generally more tolerated because of the risk of acute lung injury following transfusions
    - Primed pulmonary neutrophils may lead to a heightened inflammatory response

Supportive Care

- Nutrition
  - ALI/ARDS induces an intensively catabolic state
    - However, overfeeding provides no additional benefit
  - Enteral feedings are preferred
    - Benefits
      - Fewer vascular infections
      - Less GI bleeding
      - Intestinal mucosa preserved
  - Semirecumbent position essential

Supportive Care

- Pneumonia
  - 60% of ARDS patients develop nosocomial pneumonia
    - Difficult to diagnose due to most pneumonia-associated symptoms already being present
  - No difference in the treatment of the nosocomial pneumonia, but prompt diagnosis and antibiotic initiation is even more crucial

Supportive Care

- Prophylaxis
  - DVT/GI prophylaxis should be employed as in any ICU patient
    - DVT prevention may be of additional importance for patients with ALI/ARDS may have multiple other risk factors
      - Immobility/paralysis
      - Trauma
      - Fractures
      - Hypercoaguability
      - Obesity

Ventilator Management

Ventilator Management

- Invasive vs. Non-invasive ventilation
  - Invasive ventilation is clearly the best option
  - Noninvasive positive pressure ventilation may be considered in hemodynamically stable patients who are oxygenating well
    - However, even in these patients, there is no evidence of benefit in any outcome

Ventilator Management

- Low Tidal Volume Ventilation
  - TV < 7 mL/Kg
  - "Lung Protective" because less likely to cause alveolar overdistension
  - Overwhelming majority of trials have shown benefit in mortality and ventilator free days
  - An increase in hypercapnic respiratory acidosis is expected and generally clinically non-significant
    - May be prevented by increasing respiratory rates to highest level without inducing auto-PEEP
    - Possible role in prevention of ventilator associated lung injury

Ventilator Management

- Open Lung Ventilation
  - Combines LTVV with PEEP to maximize alveolar recruitment
  - Suggested to maximize oxygenation and minimize cyclic atelectasis
  - Results vary widely on the use of OLV, and recommendations can not be made for or against its use in ALI/ARDS

Ventilator Management

- Recruitment Maneuvers
  - Brief application of a high level of positive airway pressure (35-40 mmHg) for 40 seconds- mimics yawning
  - Proposed to open collapsed alveoli and increase the PaO2 while doing so infrequently enough to avoid lung injury from overdistension
    - May be most beneficial when the patient has been disconnected from the ventilator for even a short period of time
  - Mixed clinical trial results
  - Recommendations can not be made for against the use of recruitment maneuvers in ALI/ARDS

Novel Therapies

Novel Therapies

- Beta-Agonists
  - IV Albuterol is the only B-agonist to suggest clinical benefit in ALI/ARDS
  - Theory is it decreases endothelial/alveolar permeability by stimulating alveolar wound repair
  - Small trials demonstrate less lung water and lower plateau airway pressure, but possible higher incidence of supraventricular arrhythmias
  - Additional studies are need before routine use is recommended

Novel Therapies

- Surfactant
  - Replaces endogenous surfactant lost from the destruction of type II alveolar cells
  - Lowers surface tension, prevents atelectasis, scavenges free radicals, and suppresses inflammation
  - Numerous large trials and meta-analysis studies have shown little to no overall benefit
  - Intratracheal Calfactant has shown promise in infant/pediatric trials
  - Different combinations of surfactant, dosages, and routes of administration are all currently being explored

Novel Therapies

- Inhaled Vasodilators
  - Nitric Oxide and Prostacyclin
  - Theorized to address the issue of V/Q mismatching and the resultant hypoxemia in ARDS by preferentially vasodilating non-congested alveoli vessels for maximum recruitment of functional gas exchange surface area
  - Improved oxygenation was clearly observed, but was not sustained over placebo
  - Potential harm of free radical formation, renal dysfunction, immunosuppression, and mutagenic properties clearly outweigh the short-lived benefits

Novel Therapies

- Ventilator Strategies
  - High Frequency Ventilation
  - Uses high frequencies of respiration to deliver adequate oxygenation in small volumes. TV are less than the anatomical dead space, thereby reducing barotrauma and improving V/Q mismatching
  - Airway damage and shear forces from high air velocities can cause complications, although 74% of patients tolerate HFV well
  - Trials have shown modest benefit in oxygenation with no improvement in overall mortality
  - Current recommendations call for the consideration of HFV only as salvage therapy in patients who have failed conventional ventilation

Novel Therapies

- Anti-inflammatory Agents
  - Steroids- methylprednisolone
  - Originally had widespread use in 1970's that fell out of favor after several studies clearly showed no benefit and potential harm
  - Steroids have been revisited in the past decade as possible means for decreasing the Fibrotic stage of ARDS
  - Ironically, a large study showed:
    - A decrease in mortality if Tx started 7-13 days after onset of ARDS
    - An increase in mortality if Tx started >14 days after onset of ARDS
    - Methylprednisolone increased ventilator-free days, oxygenation, lung compliance, and blood pressure, but also increased neuromuscular weakness.
  - This has prompted a reanalysis of steroids as a possible treatment option, and numerous trials have been since been conducted
  - Results vary widely, and steroids continue to be the most highly debated topic in ARDS treatment. Whether to begin steroids at all, when to start, how long to give them, and whether they should be tapered are all questions that clearly need more research to be answered

Novel Therapies

- Anti-inflammatory Agents
  - Statins
  - Well known for the lipid-lower properties, they also decrease the concentration of proinflammatory mediators, TNF, and IL-1 in plasma
  - One human trial conducted which showed non-statistically significant improvement in oxygenation and airway positive pressure
  - More studies underway to explore these potential benefits

Novel Therapies

- Anti-oxidants
  - Glutathione
  - Proposed as a way to decrease oxidative damage in the lungs, as it was observed that glutathione plasma levels rapidly deplete in early ALI/ARDS
  - Human trials have not replicated the exciting success that was seen during animal studies, no improvement in oxygenation or survival has been shown
  - No further studies are underway, as little interest remains in this treatment potential

Novel Therapies

- Anti-oxidants
  - Eicosapentaenoic acid and Gamma-linolenic acid
  - As a dietary supplement to modulate arachidonic acid metabolism and the inflammatory process in ALI/ARDS
  - 2 trials have shown improved oxygenation, fewer ICU and ventilator-dependant days
  - Current trial by the ARDS Network is underway, which will hopefully shed light on this treatment modality
  - While results are promising, further trials are needed before routine use is encouraged

Novel Therapies

- Proning
  - Used as rescue therapy in ARDS for over 30 yrs.
  - MOA increased chest wall elastance, decreased compression of dependant tissue regions, homogeneous ventilation due to decreased V/Q inequalities
  - PROSEVA trial published May 20, 2013 at NEJM.org

Prognosis

Prognosis

- When first described, ARDS had a mortality of >50%
- In 1990's great advances were made that decreased mortality rates to 30-38%
- Since year 2000, survival has improved slightly, with most studies showing ARDS mortality at 20-30%
  - No clear change in treatment regimen can be linked to the decrease in mortality
  - Improved results are certainly multifactorial in origin
  - A reflection of improved supportive care and prophylactic measures is likely

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