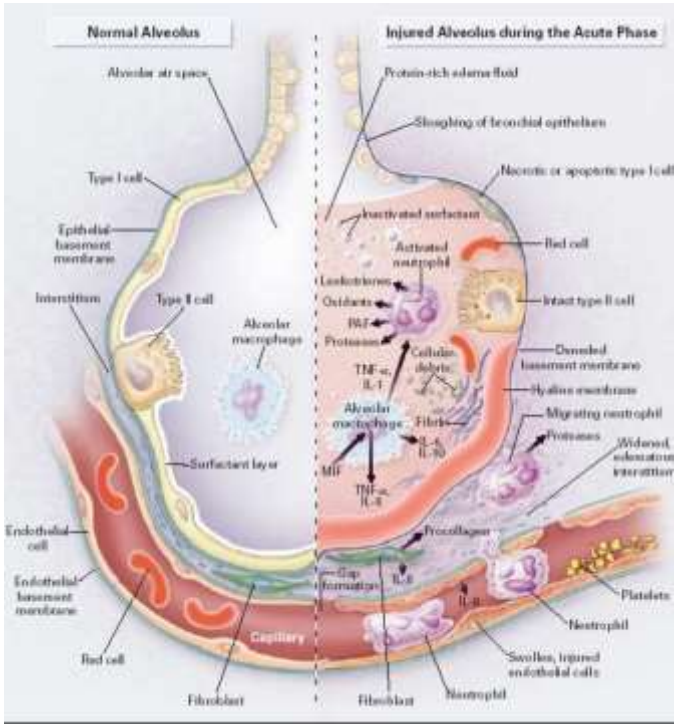
ARDS !!!



DR.R.ANAND
MD (RESP MED) EDRM (SWITZERLAND)
SENIOR RESIDENT
DEPARTMENT OF RESPIRATORY MEDICINE
VMCH&RI

OTHER NAMES

- Adult respiratory distress syndrome
- Adult hyaline membrane disease
- Capillary leak syndrome
- Congestion atelectasis
- Da Nang lung
- Hemorrhagic pulmonary edema
- Noncardiac pulmonary edema
- Oxygen pneumonitis
- Oxygen toxicity

AECC DEFINITION

- Acute in onset
- Po2/FiO2 ratio <200 (300 for ALI)
- Bilateral infiltrates on chest radiograph
- Absence of left atrial hypertension

AECC

Clinical Variable	Acute Lung Injury	Acute Respiratory Distress Syndrome
Onset	Acute	Acute
Hypoxemia	$Pa_{O_2}/F_{I_{O_2}} \leq 300$ mm Hg	$Pa_{O_2}/F_{I_{O_2}} \leq 200$ mm Hg
Chest radiograph	Bilateral infiltrates consistent with pulmonary edema	Bilateral infiltrates consistent with pulmonary edema
Noncardiac etiology	No clinical evidence of left atrial hypertension or, if measured, pulmonary artery wedge pressure ≤18 mm Hg	No clinical evidence of left atrial hypertension or, if measured, pulmonary artery wedge pressure ≤18 mm Hg

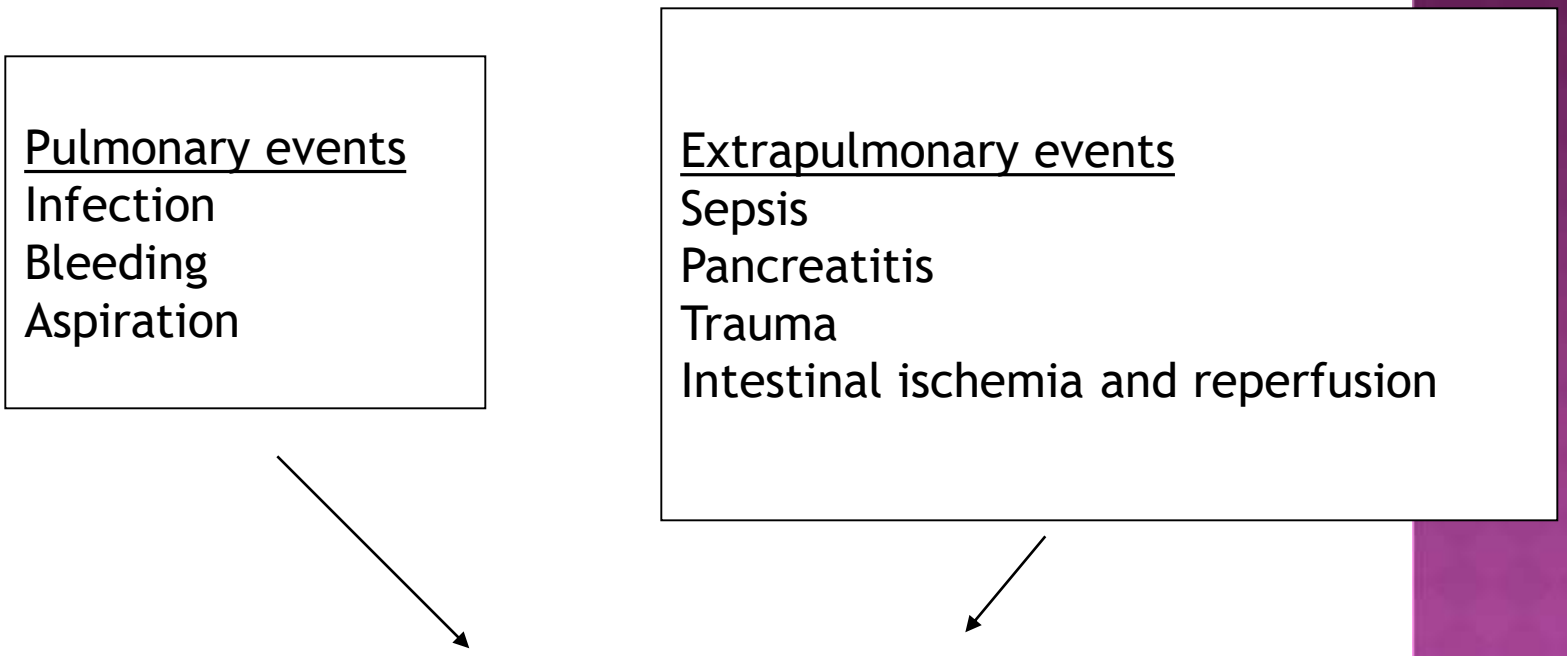
BERLIN

Clinical Variable	Mild ARDS	Moderate ARDS	Severe ARDS
Onset	Onset within 1 week of clinical insult known to result in ARDS		
Hypoxemia	$Pa_{O_2}/F_{I_{O_2}} \leq 300$ mm Hg PEEP or CPAP ≥ 5 cm H_2O	$Pa_{O_2}/F_{I_{O_2}} \leq 200$ mm Hg PEEP ≥ 5 cm H_2O	$Pa_{O_2}/F_{I_{O_2}} \leq 100$ mm Hg PEEP ≥ 5 cm H_2O
Chest radiograph	Bilateral opacities, not explained by effusions, atelectasis, or nodules		
Noncardiac etiology	Reparatory failure, not fully explained by cardiogenic pulmonary edema. Exclude hydrostatic edema if no clinical risk factor present.		

BERLIN CLASSIFICATION

- Mild ARDS(200-300)
- Moderate ARDS(100-200)
- Severe ARDS(<100)

THE NATURE OF ACUTE LUNG INJURY



Physiologic cascades may be different and responses to different therapies

MEDIATORS OF THE ACUTE INFLAMMATORY PROCESS

- Bacterial products
- Reactive oxygen intermediates
- Proinflammatory cytokines (high mobility group protein 1)
- Activated neutrophils, macrophages, epithelium, endothelium, and platelets
- Complements

MECHANISMS OF THE ACUTE INFLAMMATORY PROCESS

- Activation of transcriptional factors
- Initiation of proinflammatory cytokine cascades
- Activation of coagulation cascades
- Activation of pulmonary cell population

ETIOLOGY

SHOCK
- Hemorrhagic
- Septic
- Cardiogenic
- Anaphylactic

TRAUMA
- Burns
- Fat emboli
- Lung contusion
- Nonthoracic trauma (especially head trauma)
- Near-drowning

INFECTION
- Viral pneumonia
- Bacterial pneumonia
- Fungal pneumonia
- Gram-negative sepsis
- Tuberculosis

INHALATION OF TOXIC GASES
- Oxygen
- Smoke
- NO_2, NH_3, Cl_2
- Cadmium
- Phosgene

ASPIRATION OF GASTRIC CONTENTS (ESPECIALLY WITH A pH < 2.5)

DRUG INGESTION
- Heroin
- Methadone
- Barbiturates
- Ethchlorvynol
- Thiazides
- Fluorescein
- Propoxyphene
- Salicylates
- Chlorodiazepoxide
- Colchicine
- Dextran 40

METABOLIC
- Uremia
- Diabetic ketoacidosis

MISCELLANEOUS
- Pancreatitis
- Postcardiopulmonary bypass
- Postcardioversion
- Multiple transfusions
- DIC
- Leukoagglutinin reaction
- Eclampsia
- Air or amniotic fluid emboli
- Bowel infarction
- Carcinomatosis

Direct Precipitating Causes	Indirect (Systemic) Precipitating Causes[a]
Aspiration of gastric fluids	Acute pancreatitis
Bacterial pneumonia (diffuse), e.g., Legionnaires' disease	Blood transfusions with transfusion-related acute lung injury (TRALI)
Chest trauma with lung contusion	Postcardiopulmonary bypass
Near drowning	Primary graft failure of lung transplantation
Pneumonia due to *Pneumocystis carinii*	Severe sepsis and septic shock
Toxic inhalations, e.g., smoke inhalation, inhaled crack cocaine	Toxic ingestions, e.g., aspirin, tricyclic antidepressants
Viral pneumonia, e.g., influenza, severe acute respiratory syndrome (SARS)	Trauma with multiple fractures and the fat-emboli syndrome

INFLUENCING MORTALITY

- advanced age,
- lower PaO2/FIO2,
- high plateau pressure (i.e., low respiratory system compliance),
- greater extent of pulmonary infiltrates,
- sepsis, chronic liver disease, nonpulmonary organ dysfunction,
- increased global severity of illness,
- hypoproteinemia, and greater length of hospitalization prior to onset of ARDS

1. Exudative Phase

Alveolar macrophages release pro-inflammatory cytokines (TNF-α, IL-1, IL-6, IL-8)

↓

Attract neutrophils to the lungs

↓

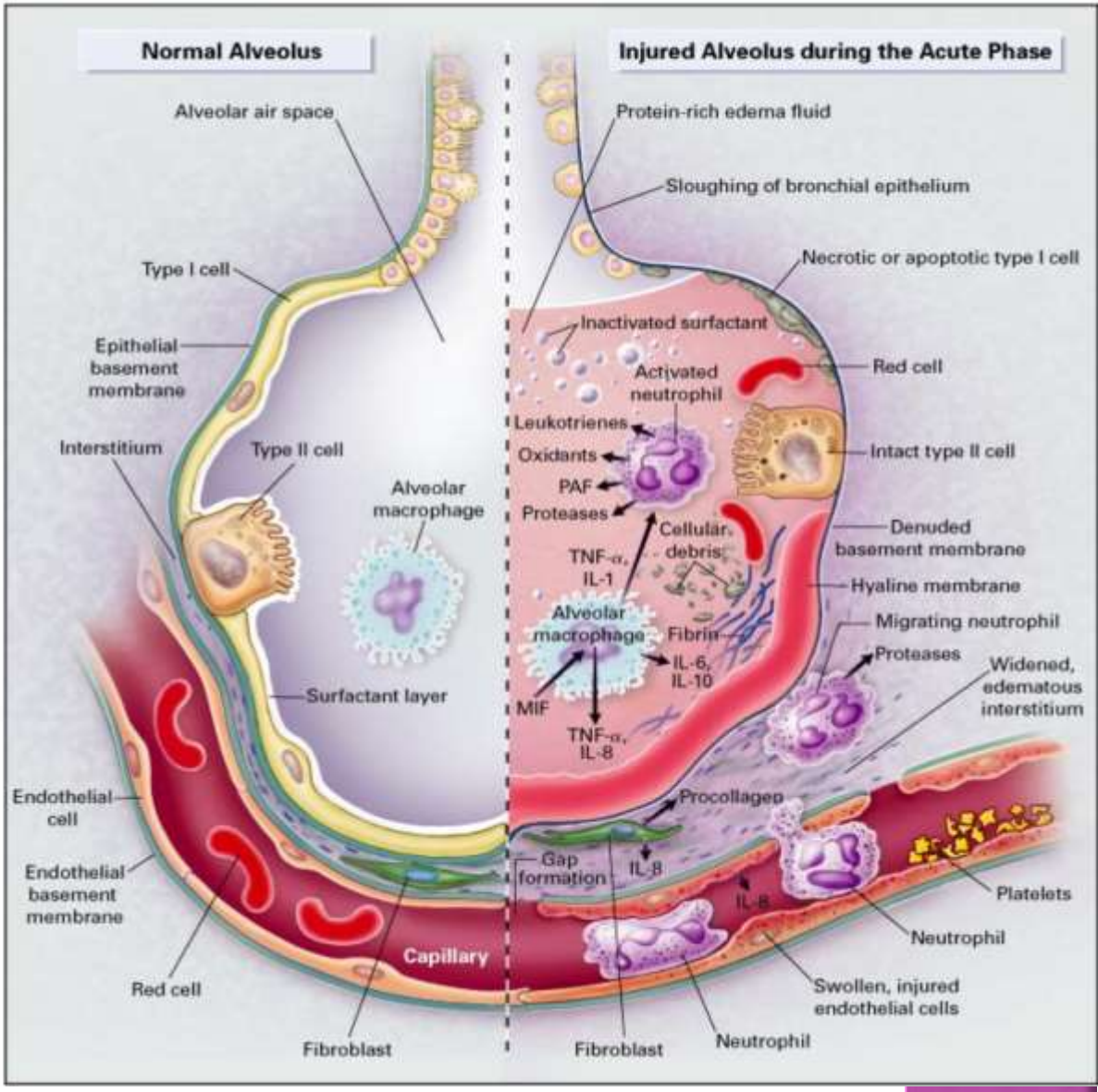
Release reactive oxygen species and proteolytic enzymes (*e.g.*, neutrophil elastase)

↓

Damage of the alveolar epithelium and the endothelium

↓

Proteinaceous edema fluid filling alveolar space



1.EXUDATIVE PHASE

- Commenses within 24 hours of injury
- Lasts 1-7 days
- Diffuse alveolar damage and microvascular injury
- Hyaline membrane formation
- Decreased surfactant production
- Basement membrane disruption
    - Type I pneumocytes destroyed
    - Type II pneumocytes preserved
- Surfactant deficiency
    - inhibited by fibrin
    - decreased type II production
- Atelectasis/alveolar collapse

2. PROLIFERATIVE PHASE

- 7-14 days
- Proliferation of inflammatory cells and fibroblasts

Obliteration of airspaces, atelectatic alveoli & poorly compliant lung leads to

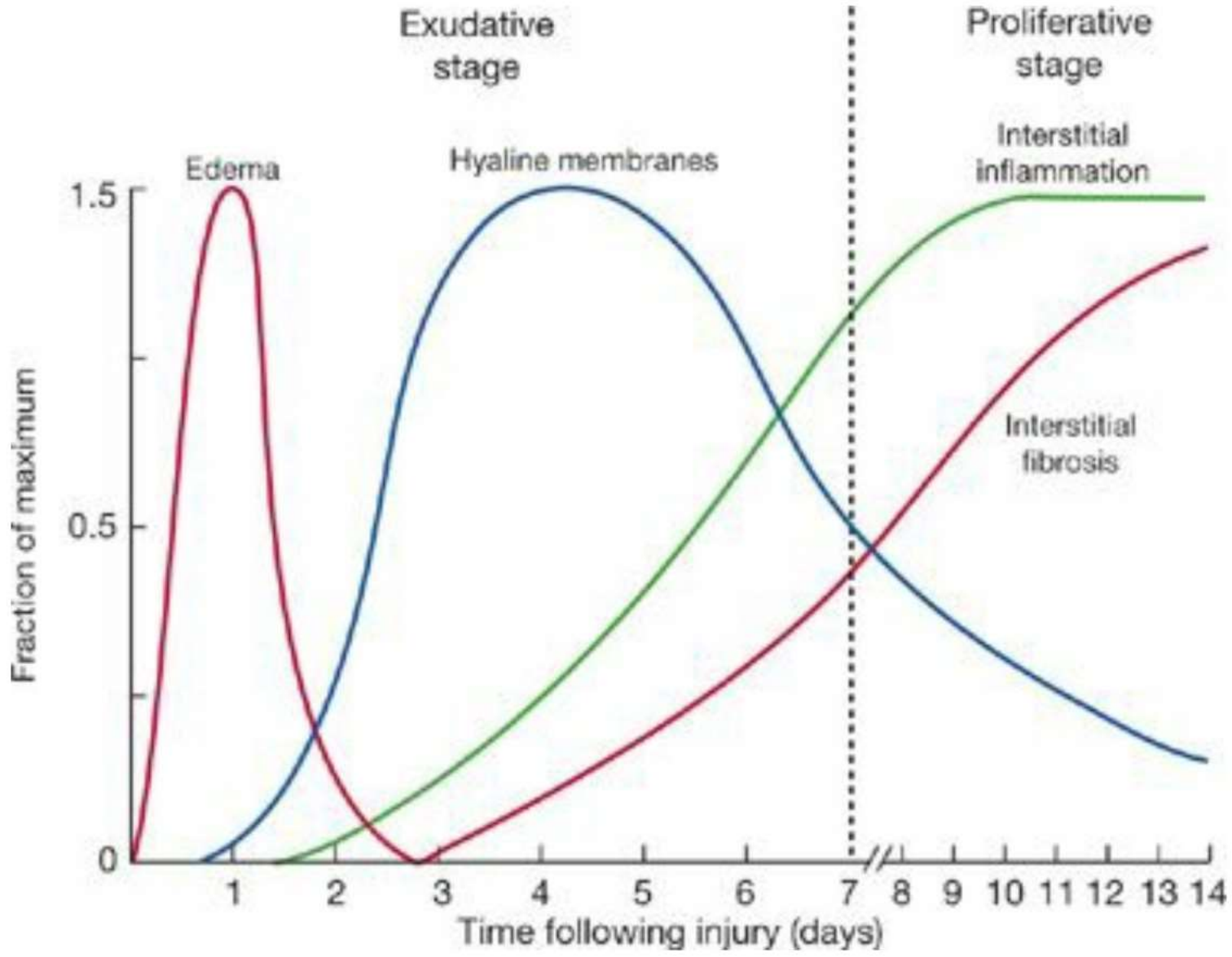
  - persistent hypoxemia
  - development of hypercarbia
  - fibrosing alveolitis
  - pulmonary hypertension

3. FIBROTIC PHASE

- >14 days
- Extensive fibroblast proliferation
- Deposition of collagen and proteoglycans
- Involvement of the pulmonary vasculature from edema -
intractable pulmonary hypertension

RESOLUTION

- Reabsorption of alveolar edema
- Repair of epithelial and endothelial barrier
- Removal of inflammatory cells and exudates from distal airspaces


Exudative stage
Proliferative stage
Edema
Hyaline membranes
Interstitial inflammation
Interstitial fibrosis
1.5
0.5
0
Fraction of maximum
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Time following injury (days)

CLINICAL FINDINGS

- Progression of clinical findings
- Tachypnea, tachycardia, and respiratory alkalosis usually develop within the first 12 to 24 hours.
- The inflammatory process and alveolar flooding lead to severe ventilation-perfusion mismatch.
- Generally, a marked reduction in lung compliance

- *Most patients with ARDS develop diffuse alveolar infiltrates and progress to respiratory failure within 48 hours of the onset of symptoms.*

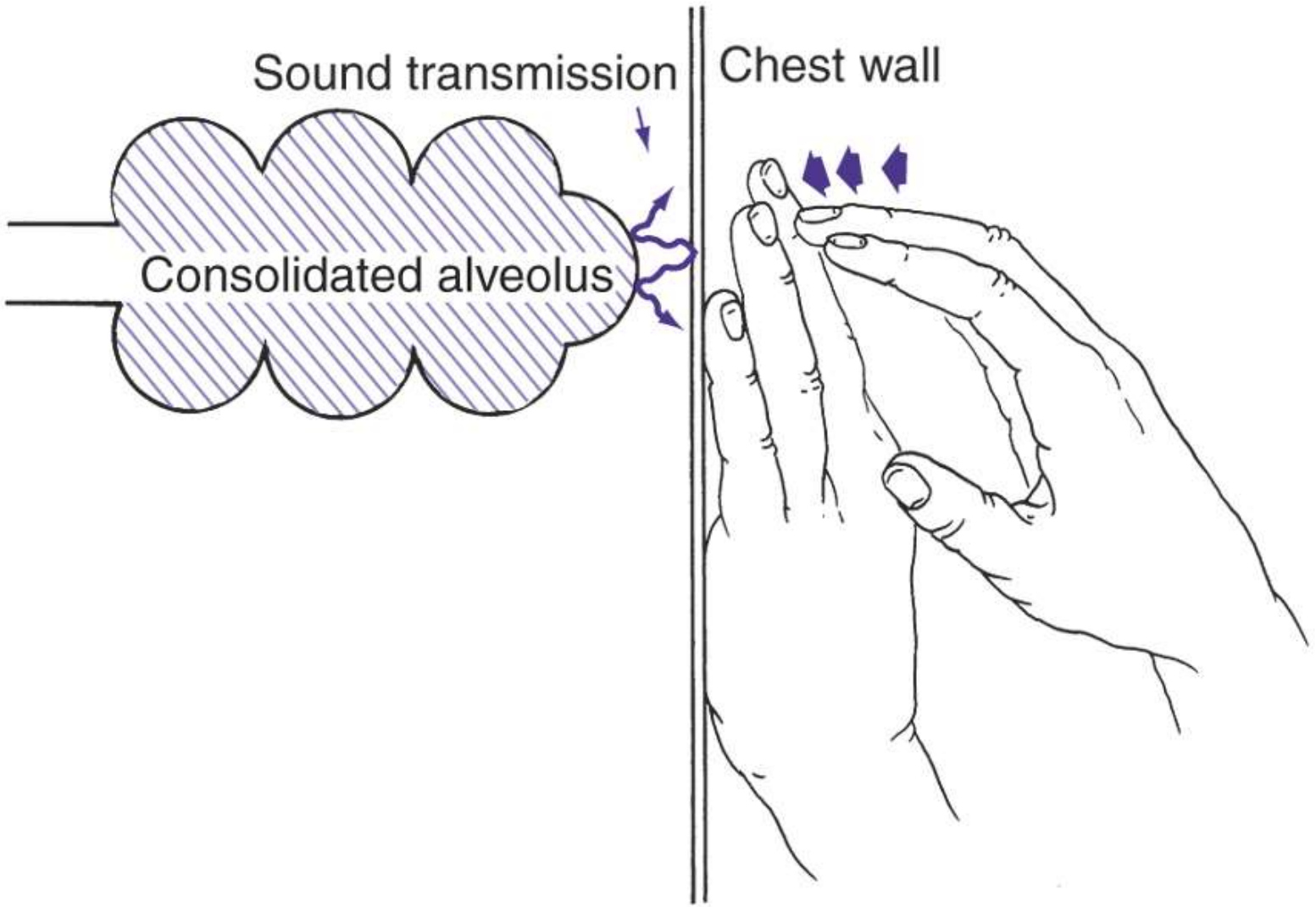


FIGURE 2-11. A SHORT, DULL, OR FLAT PERCUSSION NOTE IS TYPICALLY PRODUCED OVER AREAS OF ALVEOLAR CONSOLIDATION.

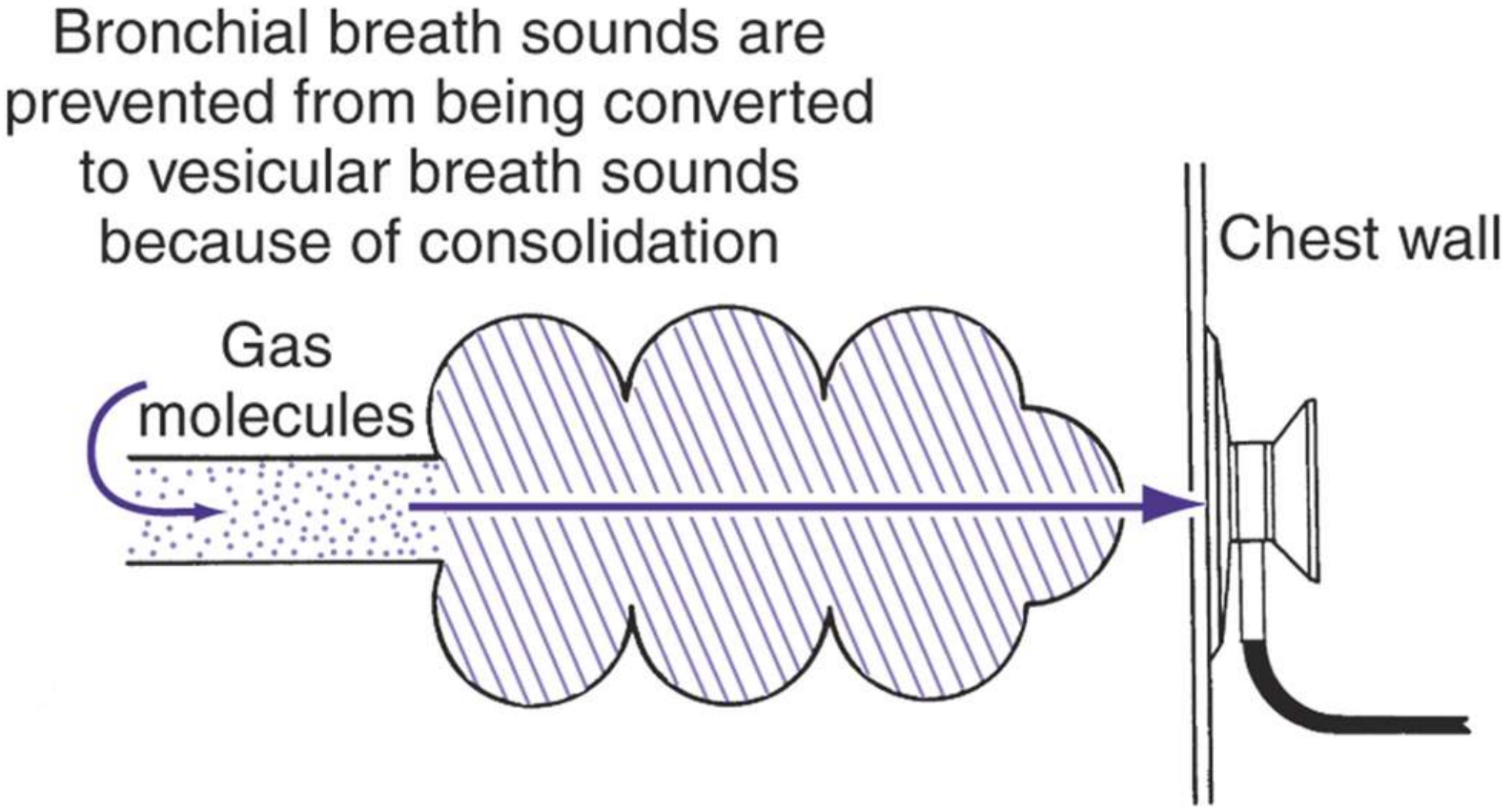


FIGURE 2-16. AUSCULTATION OF BRONCHIAL BREATH SOUNDS OVER A CONSOLIDATED LUNG UNIT.

DIFFERENTIAL DIAGNOSIS

- CARDIOGENIC PULMONARY EDEMA
- Bronchopneumonia
- Hypersensitivity pneumonitis
- Pulmonary hemorrhage
- Acute interstitial pneumonia (Hamman-Rich Syndrome)

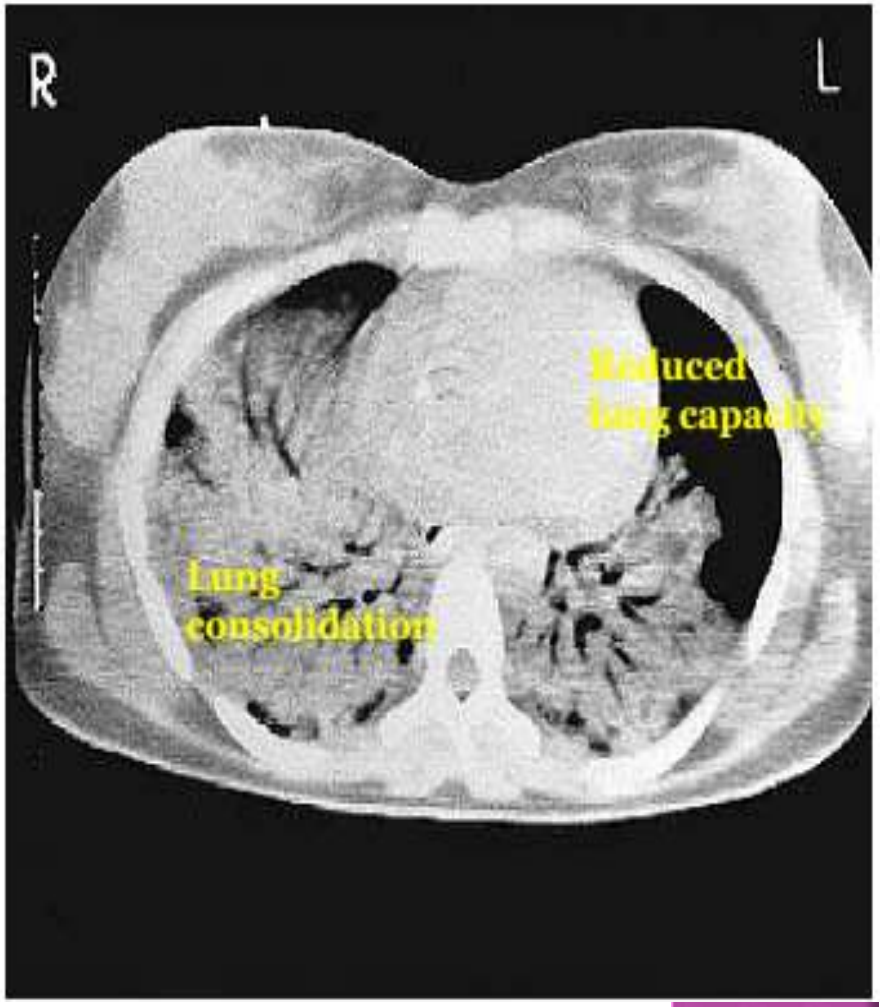
APPROACH TO CLINICAL DIAGNOSIS

1.Chest x ray

- Established cases-full blown pulmonary edema
- Not reliable :“normal” for a period of time (hours -days) following the precipitating event [e.g. sepsis]
- Progression to diffuse, bilateral alveolar infiltrates within 4 - 24 hours after the first abnormal radiographic signs appear
- Diagnostic confusion: cardiac failure, pneumonia, pulmonary embolism

2. CT Scan

- On CT imaging, the lung consolidation is confined to the posterior lung regions, which are dependent regions in supine position.
- The uninvolved lung in the anterior portion represents the functional portion of the lung.



3. Laboratory studies -

- **ABG**- Initial stages- hypoxemia with hypocapnia, respiratory alkalosis

  Later stages- hypoxia, hypercapnia, respiratory and metabolic acidosis
- Leukocytosis/Leucopenia/anemia are common
- Renal function / liver function abnormalities
- Acute phase reactants like ceruloplasmin or cytokine (TNF,IL-1,IL-6,IL-8) may be high
- NT PRO BNP>500-CHF

4. Echocardiography- method to detect cardiac causes of respiratory failure.

GOALS OF MANAGEMENT OF PATIENTS WITH ARDS

1. Treatment of respiratory system abnormalities-
   - Diagnose and treat the precipitating cause of ARDS
   - Maintain oxygenation.
   - Prevent VILI.
   - Keep pH in normal range without compromising goal to prevent VILI.
   - Enhance patient–ventilator synchrony and patient comfort by use of sedation, amnesia, analgesia
   - Liberate or wean from mechanical ventilation when patient can breathe without assisted ventilation

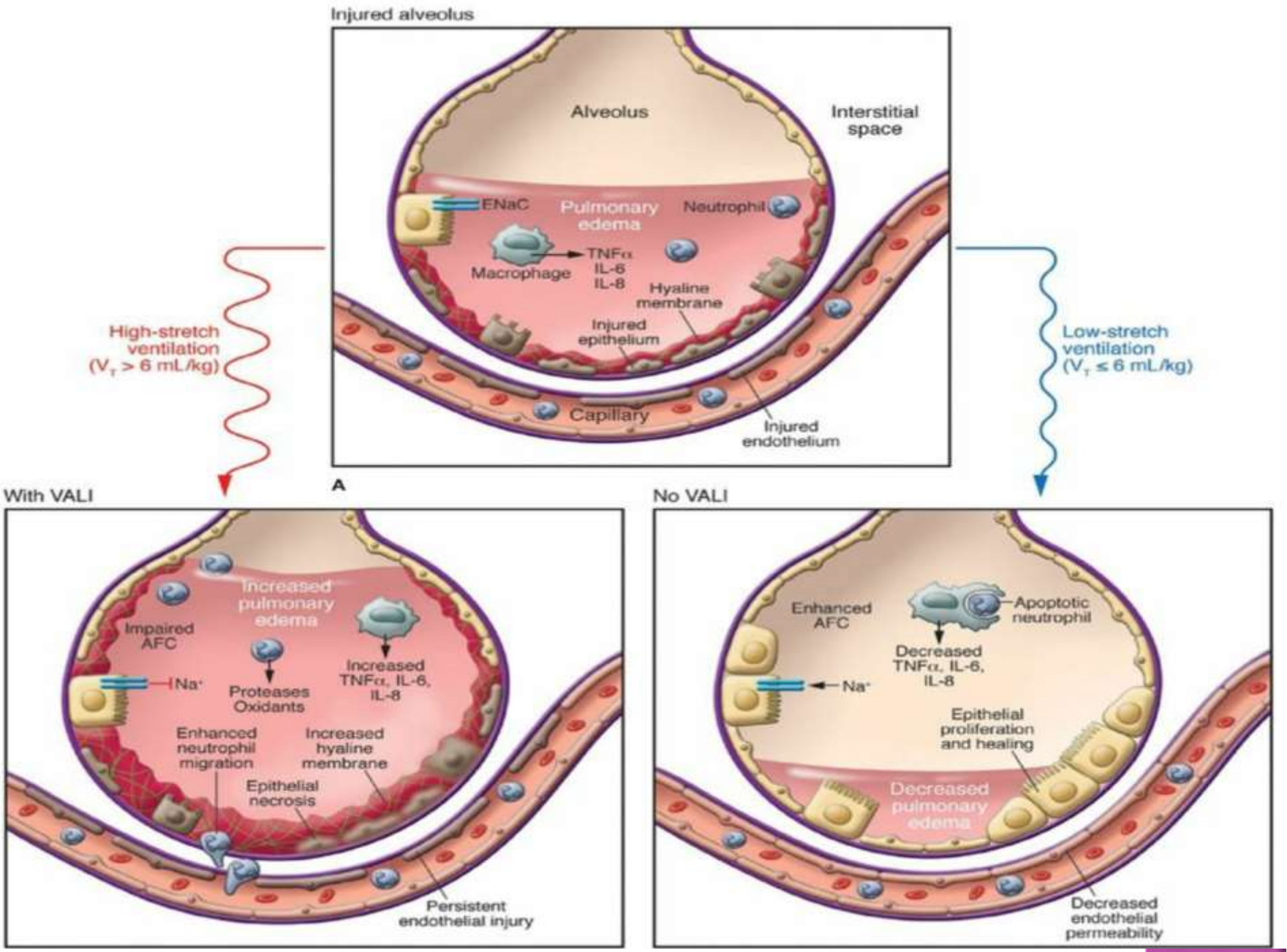
GOALS OF MANAGEMENT OF PATIENTS WITH ARDS

2. Treatment of nonrespiratory system abnormalities
   - Support or treat other organ system dysfunction or failure
   - General critical care (preventive and homeostatic measures)
   - Adequate early nutritional support

- Infectious etiologies
  - Bacterial or other sepsis, e.g., fungemia, responsive to antimicrobial therapy
  - Diffuse bacterial pneumonias, e.g., Legionella species
  - Diffuse viral pneumonias, e.g., cytomegalovirus, influenza A
  - Diffuse fungal pneumonias, e.g., Candida species, Cryptococcus
  - *Pneumocystis jiroveci* pneumonia
  - Other diffuse lung infections, e.g., military tuberculosis
- Noninfectious etiologies
  - Diffuse alveolar hemorrhage post–bone marrow transplantation
  - Diffuse alveolar hemorrhage due to vasculitis, e.g., Goodpasture syndrome
  - Acute eosinophilic pneumonia
  - Lupus pneumonitis
  - Toxic drug reactions, e.g., aspirin

VENTILATORY MANAGEMENT IN ARDS

- **Conventional** mechanical ventilation-
- Tidal volumes are **12-15ml/kg**
- In ARDS, the functional portion of the lungs is greatly reduced
- High inflation volumes results in overdistension and rupture of the distal airspaces.
- Ventilator associated lung injury:
  - High inflation pressure - Barotrauma
  - Over distension - Volutrauma
  - Repetitive opening & closing of alveoli - atelectrauma
  - SIRS & cytokines release - Biotrauma.


Injured alveolus
Alveolus
Interstitial space
ENaC
Pulmonary edema
Neutrophil
Macrophage
TNFα
IL-6
IL-8
Hyaline membrane
Injured epithelium
Capillary
Injured endothelium
High-stretch ventilation (V_T > 6 mL/kg)
Low-stretch ventilation (V_T ≤ 6 mL/kg)
A
With VALI
Increased pulmonary edema
Impaired AFC
Na+
Proteases Oxidants
Increased TNFα, IL-6, IL-8
Enhanced neutrophil migration
Increased hyaline membrane
Epithelial necrosis
Persistent endothelial injury
No VALI
Enhanced AFC
Apoptotic neutrophil
Decreased TNFα, IL-6, IL-8
Na+
Epithelial proliferation and healing
Decreased pulmonary edema
Decreased endothelial permeability

LUNG PROTECTIVE VENTILATION

- Tidal volumes – ***6ml/kg***
- Limits risk of volutrauma and biotrauma
- Uses positive end expiratory pressure to limit the risk of atelectrauma.

- *Currently, the only therapy that has been proven to be effective at reducing mortality in ALI/ARDS in a large, randomized, multi-center, controlled trial is a protective ventilatory strategy.*

LUNG PROTECTIVE VENTILATORY STRATEGY

Ventilator mode	Volume assist-control
Tidal volume	≤6 mL/kg PBW
Plateau pressure	≤30 cmH_2O
Ventilation set rate, pH goal	6–35, adjusted to achieve arterial pH ≥7.30, if possible
Inspiratory flow, I:E	Adjust flow to achieve I:E = 1:1–1:3
Oxygenation goal	$55 \leq Pa_{O_2} \leq 80$ mm Hg or $88 \leq Sp_{O_2} \leq 95\%$

F_{IO_2}/PEEP Combinations

F_{IO_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, cmH_2O	5	5	8	8	10	10	10	12	14	14	14	16	18	18, 22, 24

(further increases in PEEP to 34 cmH_2O allowed, but not required)

Weaning	Attempts to wean by pressure support required when F_{IO_2}/PEEP ≤0.40/8

ROLE OF PEEP IN ARDS

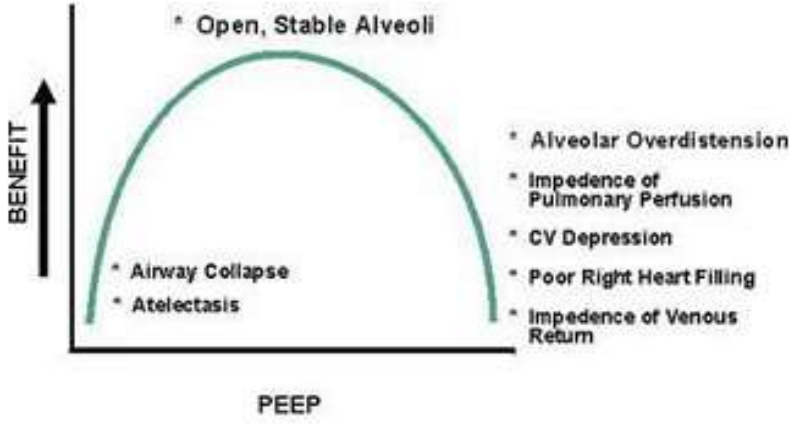
- PEEP avoids repetitive opening and collapse of atelectatic lung units – could protect against VILI
  - Improves arterial oxygenation
  - Lung is kept open by using PEEP to avoid end expiratory collapse
  - Preserves inspiratory recruitment
  - Re-establish end expiratory lung volume
  - Prevent surfactant loss in airway
  - Decreases intrapulmonary shunt

ROLE OF PEEP IN ARDS

- **Optimal /Best PEEP:**

  It is the minimum PEEP necessary to maintain adequate PaO2 at non toxic FIO2 .

- It is required for optimization of arterial oxygenation without introducing risk for oxygen toxicity and VILI, with least effect on haemodynamics, oxygen delivery and airway pressures.



RECRUITMENT MANEUVER

- Lung recruitment maneuvers are defined as the application of CPAP aimed at “recruiting” or opening totally or partially collapsed alveoli.
- The alveoli are then kept inflated during expiration using an appropriately high level of PEEP.
- No good evidence that it helps patient outcomes.
- Consider in specific circumstances such as for salvage therapy

RECRUITMENT MANEUVER

- No controlled clinical trial supports the efficacy of recruitment maneuvers alone to improve clinically important outcomes, such as mortality or ventilator-free days.
- Studies of recruitment maneuvers have generally used physiologic end points, for example, improvement in oxygenation.

SPONTANEOUS BREATHING DURING POSITIVE PRESSURE VENTILATION

- Two ventilatory modes of modern, microprocessor-based devices that permit spontaneous breathing to occur at any phase of the respiratory cycle during assisted ventilation include
- biphasic airway pressure (BIPAP) and
- airway pressure release ventilation (APRV).

AIRWAY PRESSURE RELEASE VENTILATION (APRV)

- A mode of ventilation in which the spontaneous breaths are at elevated baseline.
- This elevated baseline is periodically released to facilitate expiration.
- Mandatory inspiration begins with time-triggered closing of release valve, airway pressure then rapidly increases to baseline CPAP and is maintained for the duration of inspiration.
- Time triggered opening of release valve causes expiration.
- Here the patient is allowed to inspire spontaneously at any point during mandatory breath.

TABLE 141-12 "Rescue" or "Salvage" Interventions Used in Patients with ARDS and Severe Hypoxemia Resistant to Conventional Mechanical Ventilation and PEEP

Corticosteroids
Extracorporeal CO_2 removal ($ECCO_2R$)
Extracorporeal membrane oxygenation (ECMO)
High-frequency oscillatory ventilation (HFOV)
Inhaled nitric oxide (NO) or inhaled prostacyclin (epoprostenol/iloprost)
Pressure-controlled inverse ratio ventilation (PC-IRV)
Prone positioning
Recruitment maneuvers
Tracheal gas insufflation (TGI)

INVERSE-RATIO VENTILATION

- IRV causes shunt reduction and improved arterial oxygenation
- Short exhalation time may cause increased auto-PEEP which may account for the improved oxygenation
- Many patients require heavy sedation and paralysis

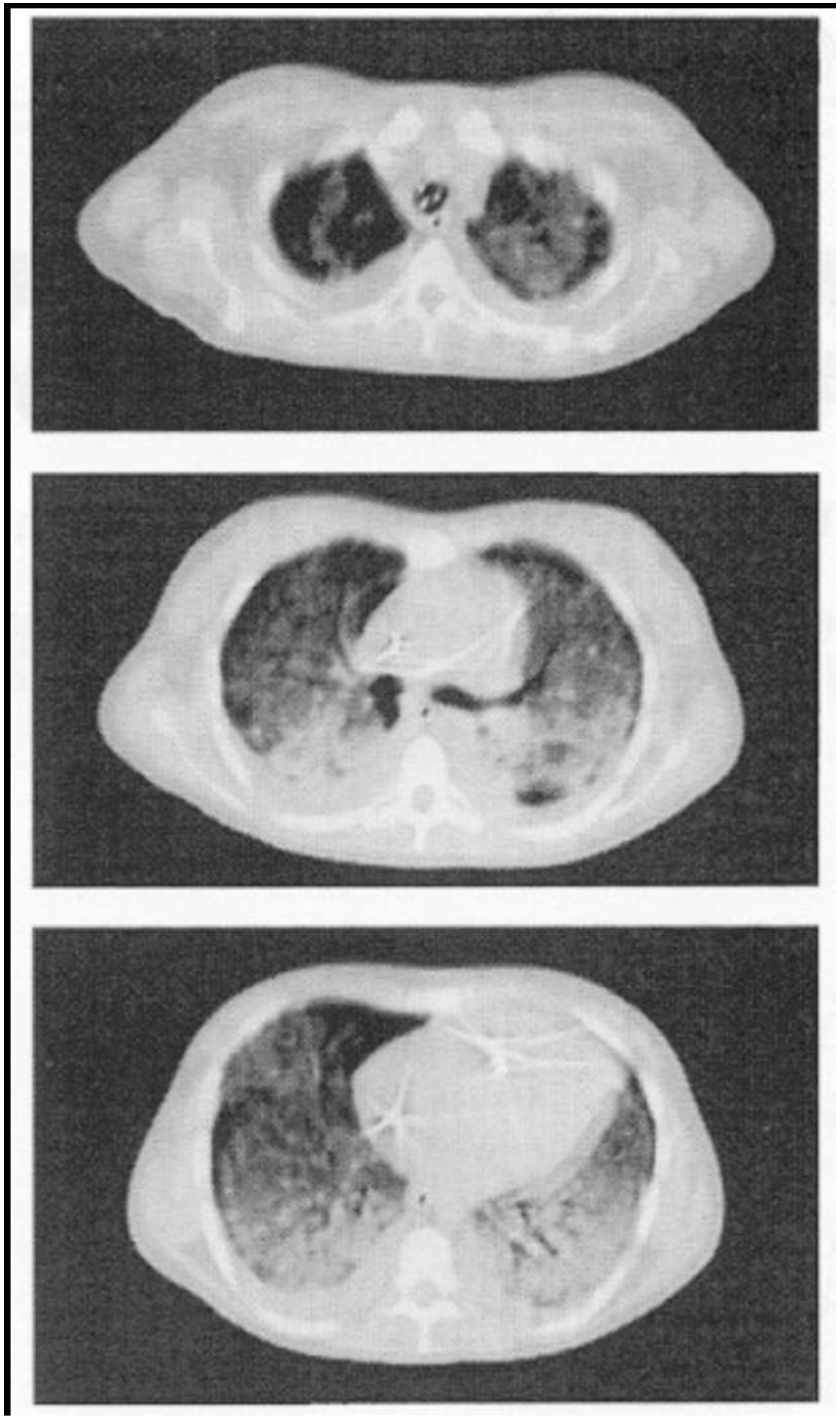
PRONE POSITIONING

- Improves ventilation to previously dependent regions of the lung
- Leads to substantial improvement in oxygenation in 65% of ARDS patients
- Prevents ventilator-associated lung injury by promoting more uniform distribution of tidal volume and by recruiting dorsal lung regions
- Clinical outcome did not improve in ARDS patients randomized to prone positioning for at least 6h/d vs patients randomized to remain supine*

*Gattinoni L et al. *Lancet* 1997;350:815

PRONE POSITION EFFECTS

- (1) increased functional residual capacity;
- (2) change in regional diaphragmatic motion;
- (3) perfusion redistribution; and
- (4) improved clearance of secretions



PERMISSIVE HYPERCAPNIA

TABLE 141-11 Contraindications to Permissive Hypercapnia and Acute Respiratory Acidosis

Increased intracranial pressure from any cause (trauma, mass lesion, malignant hypertension)
Acute cerebrovascular disorders, e.g., stroke
Acute or chronic myocardial ischemia
Severe pulmonary hypertension
Right ventricular failure
Uncorrected severe metabolic acidosis
Sickle cell anemia
Tricyclic antidepressant overdose
Patients taking beta-blockers
Pregnancy (due to potential for decreased fetal blood flow from vasodilation-induced steal syndrome; in addition, shift to the right of the O_2 dissociation curve decreases the maternal-fetal

THANQ..