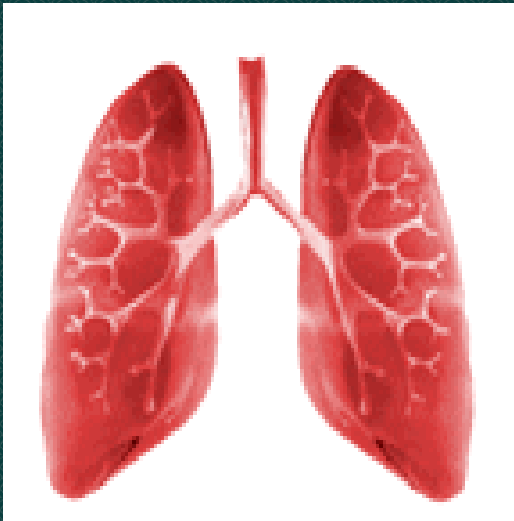


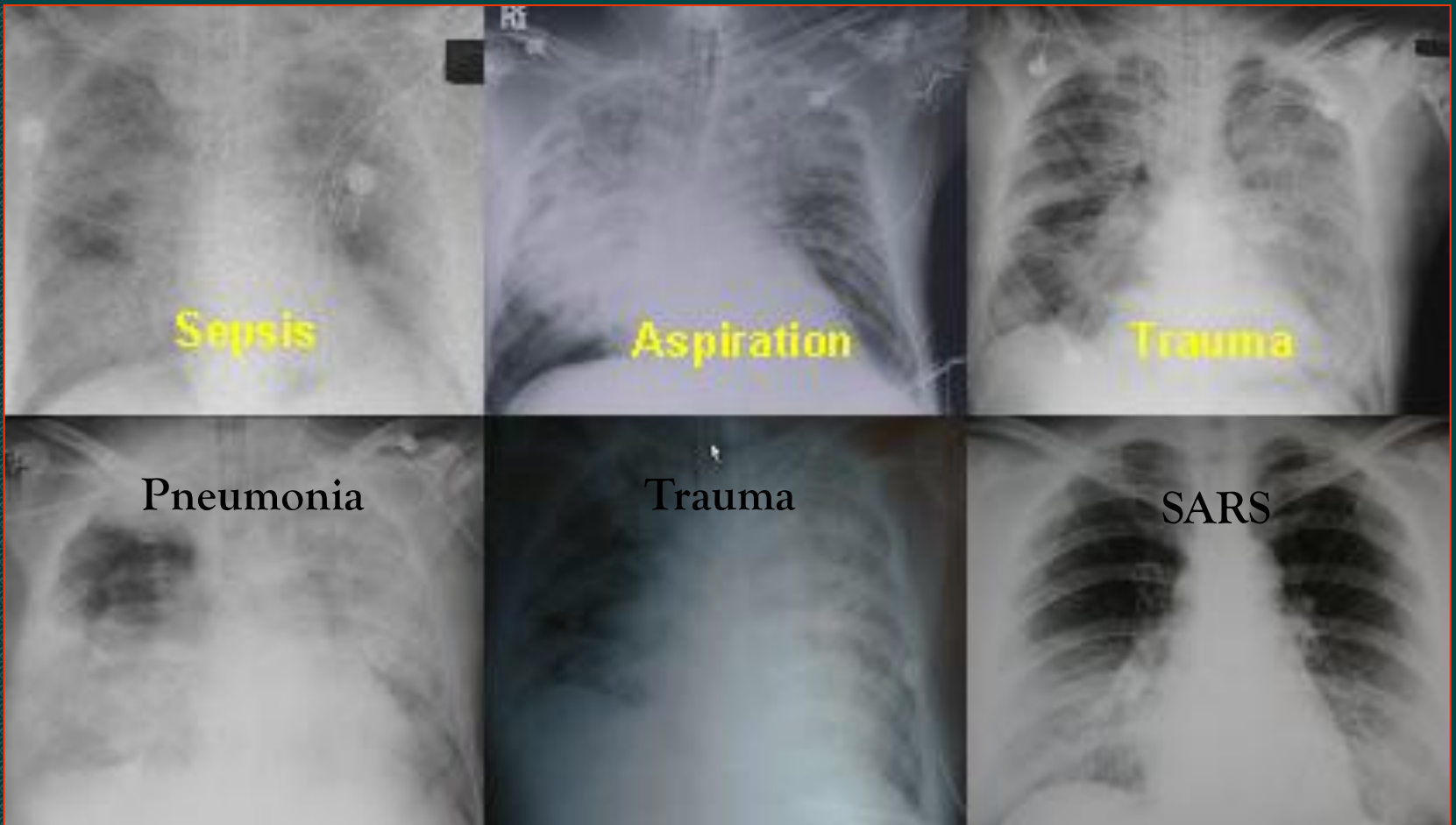
Acute Respiratory Disease Syndrome

Yuanlin Song, M.D.



Definition

- ◆ Clinical syndrome of severe dyspnea of rapid onset, hypoxemia, and diffuse pulmonary infiltrates leading to respiratory failure.



Diagnostic criteria

- ◆ $\text{PaO}_2/\text{fiO}_2 \leq 300$ (ARDS if ≤ 200)
- ◆ Bilateral alveolar or interstitial infiltrates
- ◆ $\text{PCWP} \leq 18$ mmHg, or no clinical evidence of increase left atrium pressure



Classification



Direct lung injury	Indirect lung injury
Pneumonia	Sepsis
Aspiration	Severe trauma
Pulmonary contusion	Multiple bone fracture
Near-drowning	Flail chest
Toxic inhalation injury	Head trauma
	Multiple transfusion
	Burns
	Drug overdose
	Pancreatitis
	Post-cardiopulmonary bypass

epidemiology



- ◆ Annual incidence: 30/100,000 for ALI and 10/100,000 for ARDS
- ◆ 10% ICU admission may have acute respiratory failure
- ◆ Morality: 40-70% worldwide
- ◆ In China, around 700,000 new cases per year
- ◆ In Shanghai, mortality was 70% in 2001
- ◆ Death number comparable to HIV, CI, breast cancer

Etiology of ALI/ARDS



Sepsis

Pneumonia

Trauma

Multiple transfusion

Aspiration

Drug over dose

Risk factors

Old age

Chronic alcohol abuse

Metabolic acidosis

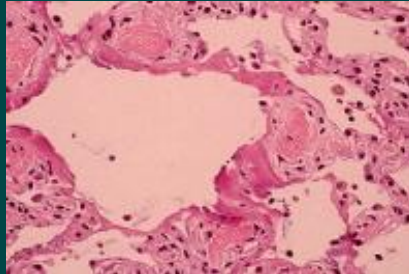
Severity of critical illness

Protective factors

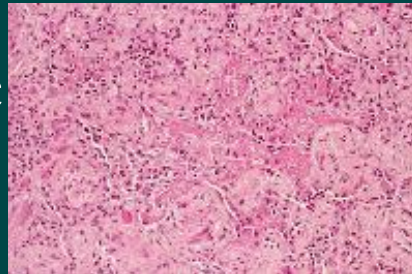
Diabetes

Pathology of ALI/ARDS

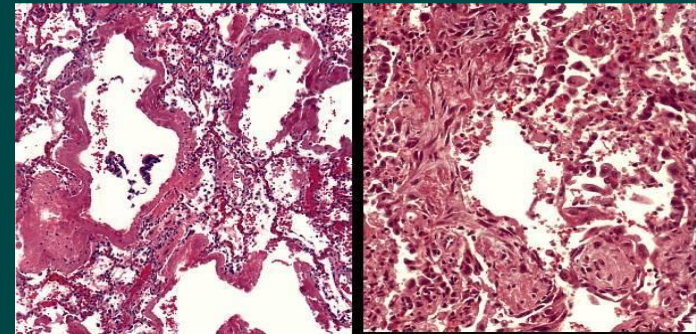
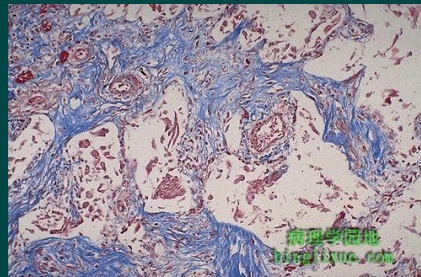
◆ Exudative phase



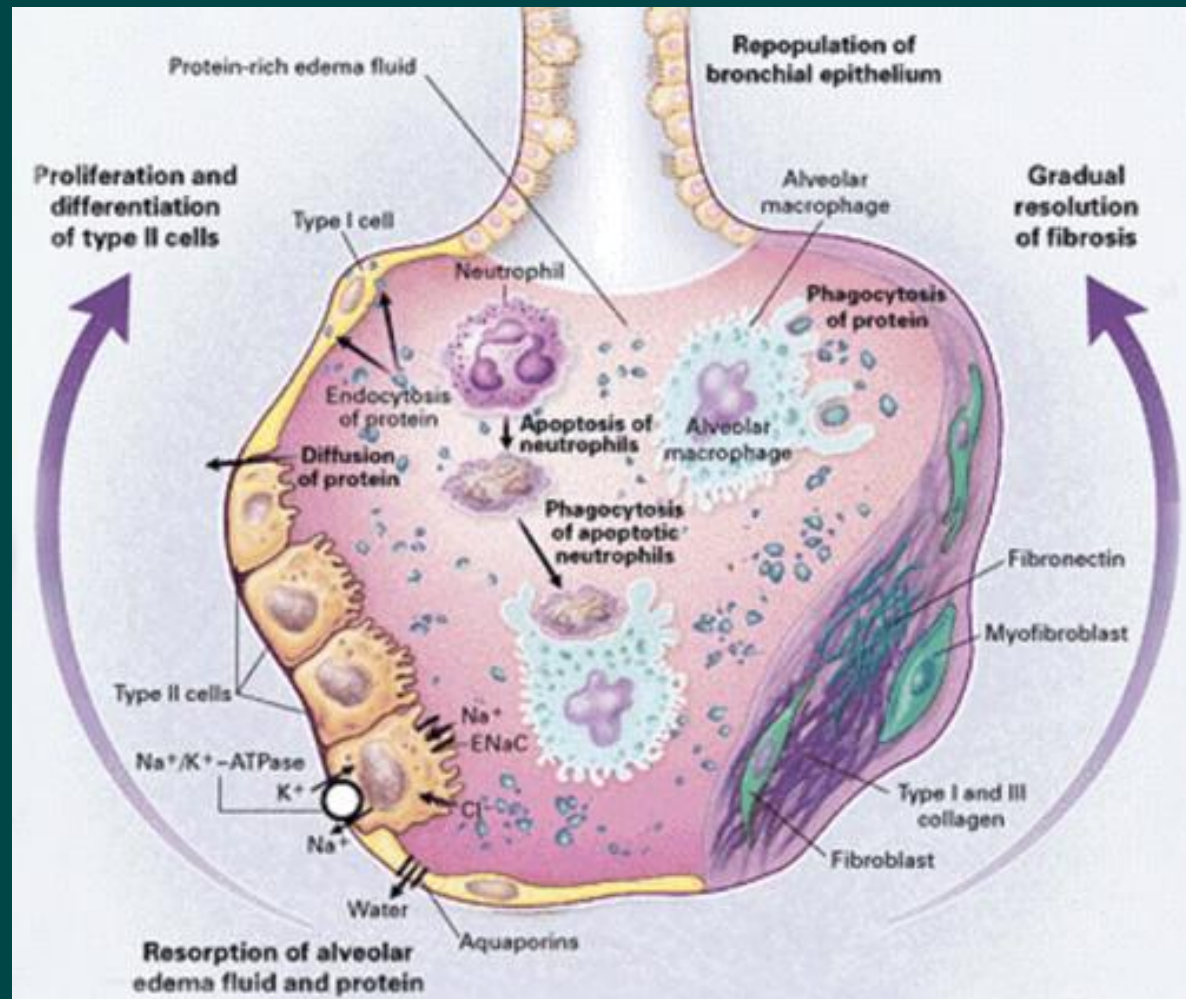
◆ Proliferative phase



◆ Fibrotic phase



Pathophysiology



Treatment

Principle:

1. Underlying disease control
2. Reduce Ventilator induced lung injury
3. Prevention of venous thromboembolism, GI bleeding, catheter infection
4. Prevent and recognition of HAP
5. Support therapy: nutrition, ventilation, fluid, antibiotics



Mechanical ventilation strategy principles



1. Selection of non-invasive and invasive ventilation
2. Management of artificial airways
3. Ventilation mode: IPPV, PSV, SIMV, PRV, NAVA,
4. PEEP:
5. Ventilation parameters: Volume, RR,
6. Other methods: HFV, ECMO, PLV

VILI

Original disease: sepsis, aspiration, pneumonia, and trauma etc

1

2

+

MV

High volume,
open-close

inflammation ↑

Immune
function ↓

ATPase ↓

Barrier
disruption

Local → systemic

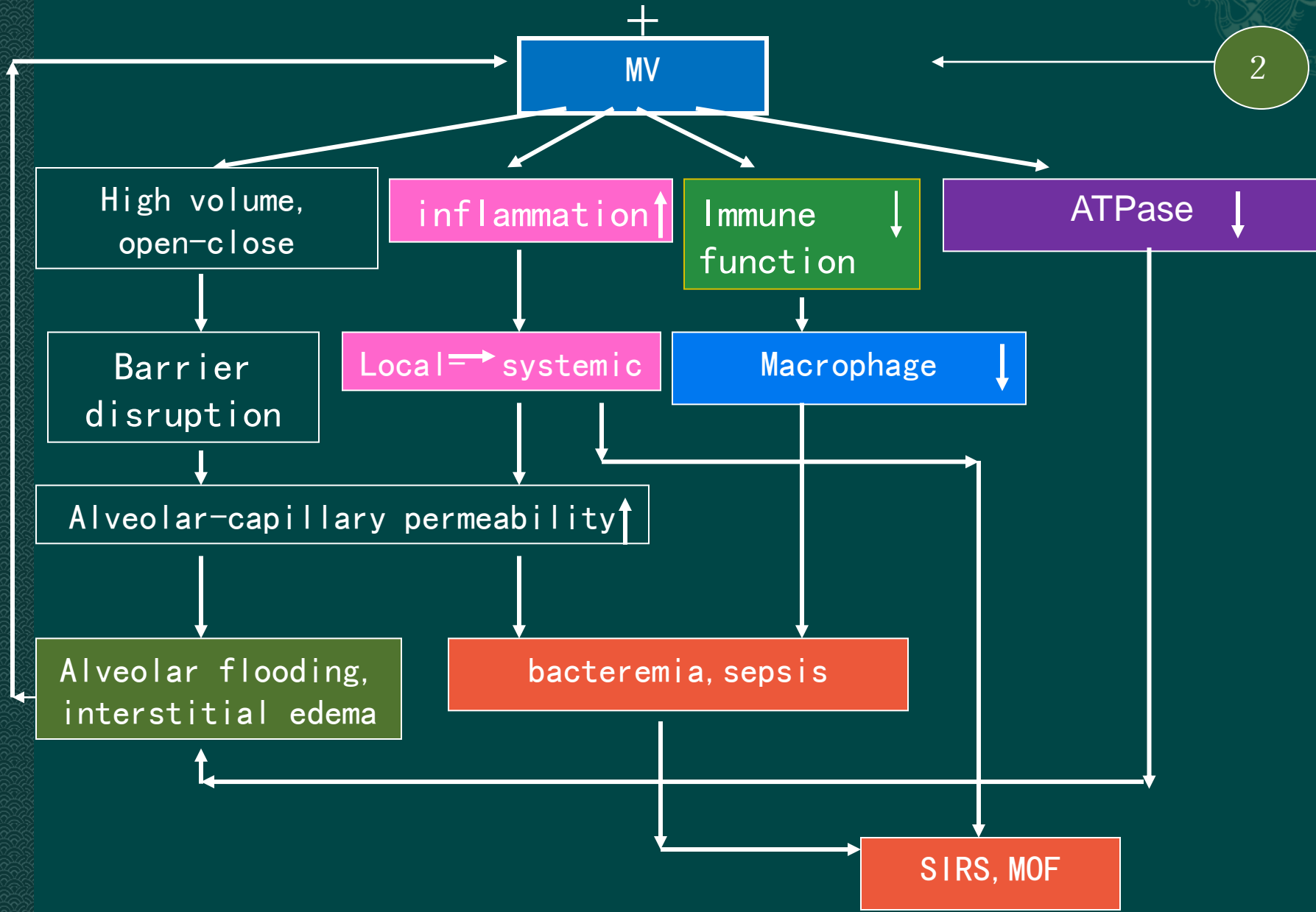
Macrophage ↓

Alveolar-capillary permeability ↑

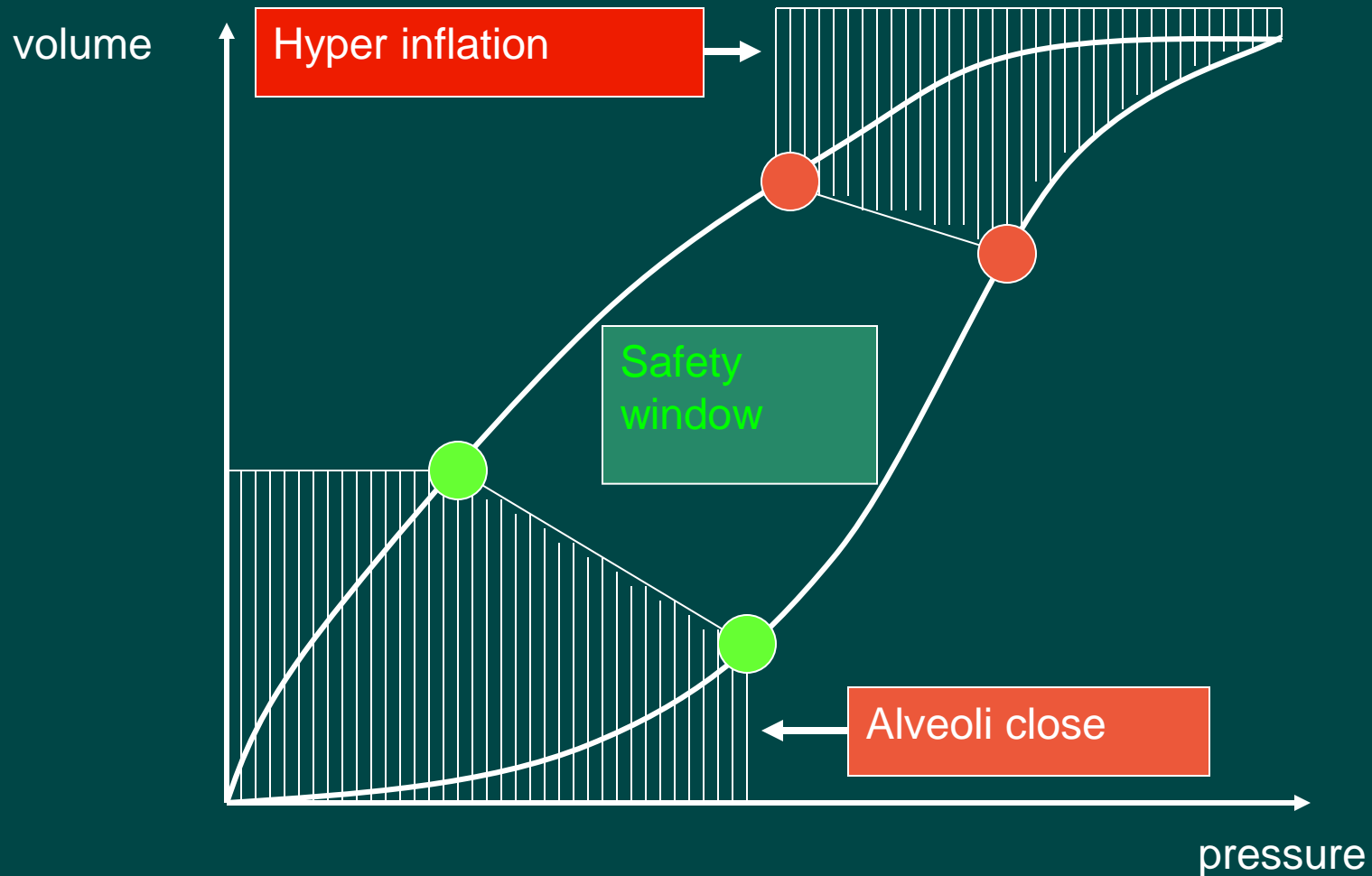
Alveolar flooding,
interstitial edema

bacteremia, sepsis

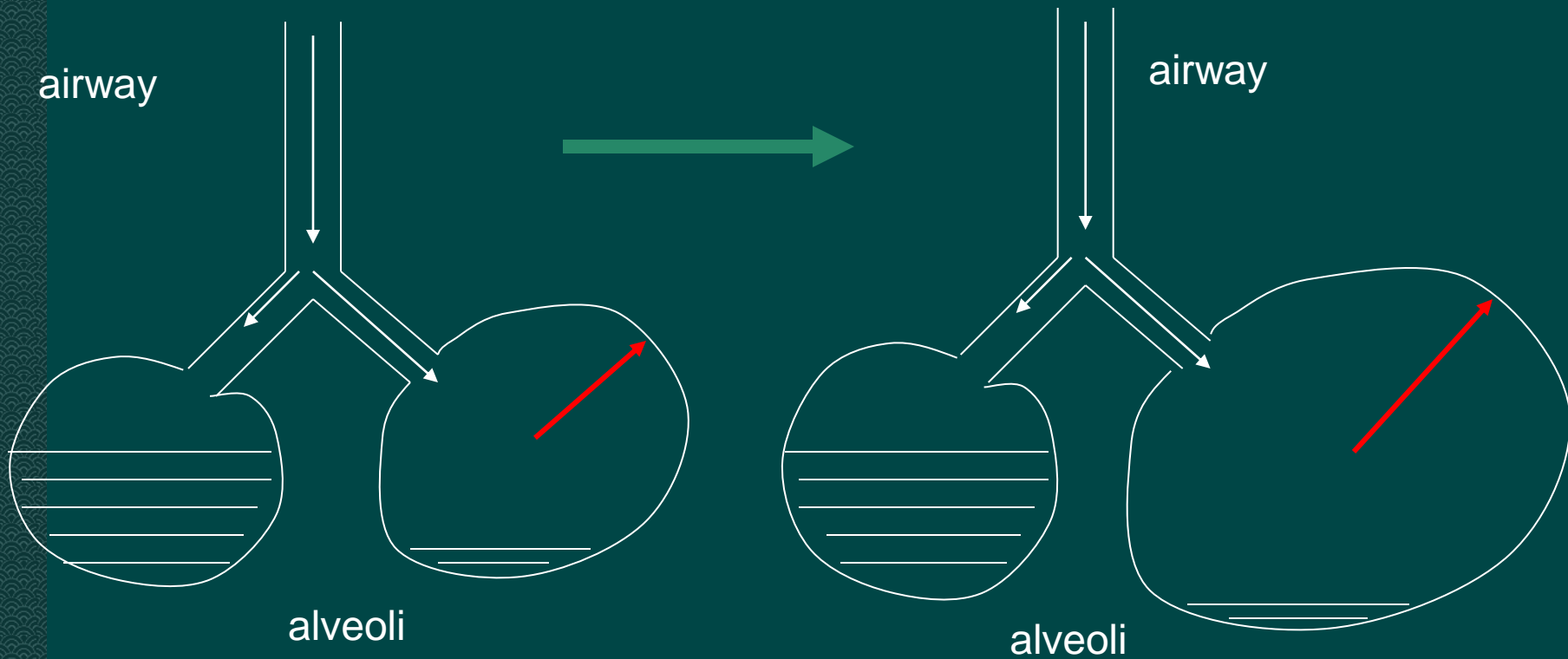
SIRS, MOF



Pressure-volume curve



Alveoli structure: stability



$$T_w = P_{TP} X r / 2$$

Lung recruitment maneuver



1. Selection of PEEP

2. Position

3. IRV

Other therapies



1. Steroid application
2. Fluid management
3. Anti-inflammation therapy: NAC, ambroxol
4. NO inhalation
5. APC infusion
6. Stem cell therapy

ARDS pharmacotherapy



Drug name	Action	Results	Source
Prostaglandin E1	Pulmonary vasodilation Decrease neutrophils activation, decrease platelet aggregation	No difference for early mortality, inconclusive for later mortality	693 patients
N-acetylcysteine and procysteine	Antioxidant	No difference for early mortality	235 patients
Surfactant	Restore normal mechanical properties	No difference for early mortality	1416 patients
Ketoconazole			
Beta2-agonist		Iv injection showed decreased lung water, no changes for mortality	
indomethacin	Anti-inflammation		
Nitric oxide (inhalation)	Pulmonary vasodialator	Reduce shut, pulmonary artery pressure but no benefit for mortality	208 patients
Activated protein C (IV)	Inhibit PAI-1, promote fibrinolysis of hayline membrane	No difference for mortality, vent- free days	75
Corticosteroid	Multiple anti-inflammation	No difference for early mortality	1416 patients

ARDS ventilation/support therapy



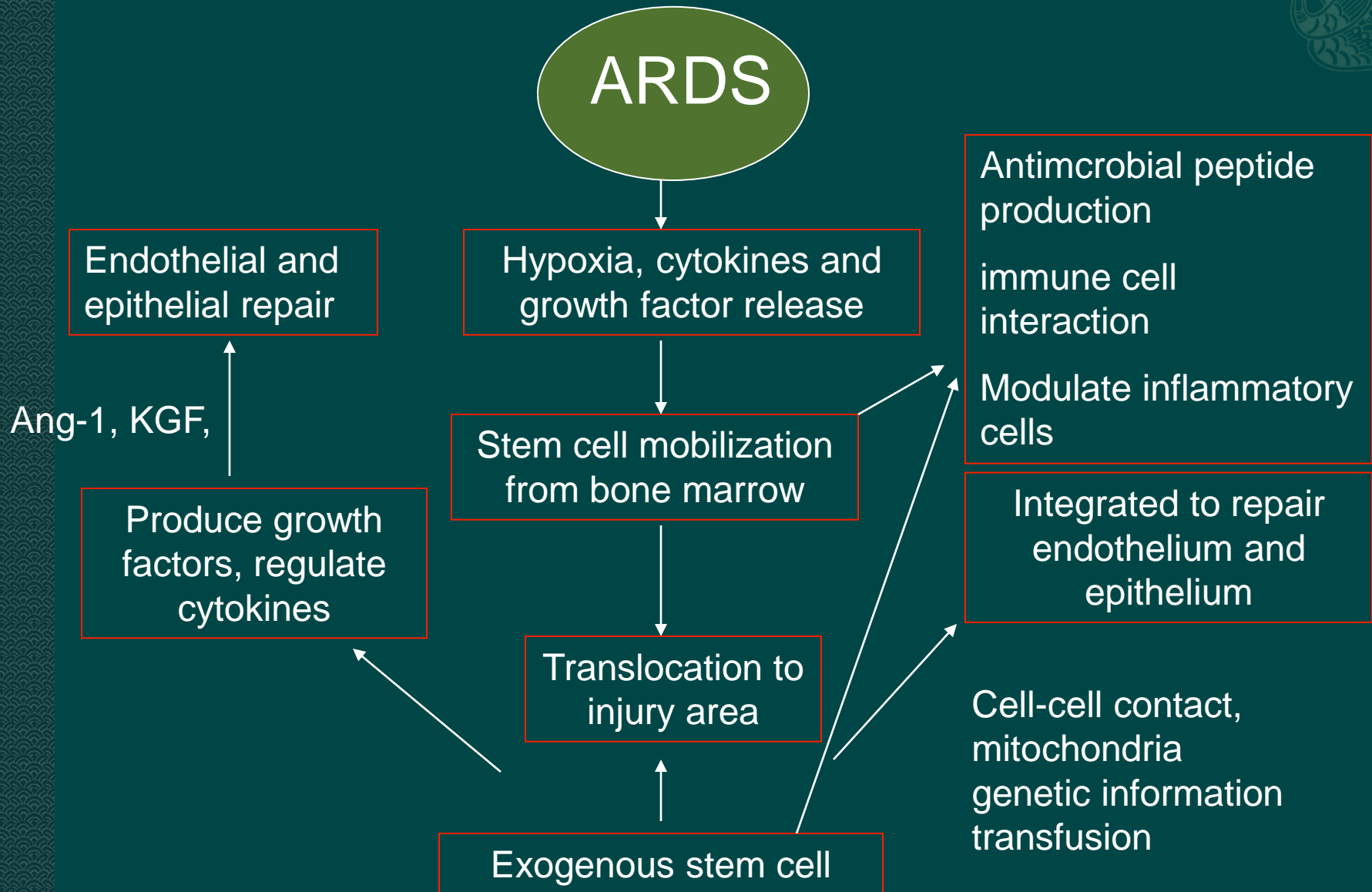
1. **Small tidal volume:** 6ml/kg vs 12 ml/kg, when applying 6ml/kg, Pplat set 25-30cmH₂O, decrease mortality (40% vs 31%), increase ventilation free days, reduce plasma cytokines, reduce organ failure days
2. **FiO₂/PEEP:** 0.3-1/5-24cmH₂O: high PEEP strategy: increase oxygen transfer function, increase lung compliance, but no difference in mortality. PEEP maybe not be more than 10 cmH₂O for a typical ARDS patients.
3. **NPPV:** early intervention, increase oxygenation, may reduce intubation rate (on going clinical trial in Chaoyang Hospital).
4. **Ventilation mode:** ARDSnet 6ml/kg, may reduce barotrauma, but may decrease alveoli recruitment. ARPV could maintain minimum airway pressure while keep alveoli recruitment. On going clinical trial

Ventilation/support therapy



1. **Liquid ventilation:** both low dose (10mg/kg) and high dose (20ml/kg) of perfluorocarbon does not provide any benefit compared to CMV.
2. **High frequency ventilation:** no clear benefit compared to CMV mode.
3. **Prone-position ventilation:**
improve oxygenation, maybe useful
in severe ARDS patients.
4. **Nutrition:**
Ongoing clinical trial including OMGA-3
5. **Fluid:** 1000 patients, main finding: no difference in clinical outcome, but fluid conservative trial significantly increased ventilation-free days.
6. **Control infection:**

Stem cell therapy



Prognosis

- 1.Mortality
- 2.Biomarker study
- 3.Long term follow up



Biomarker and lung injury

Biomarkers for: cardiac infarction-LDH, Procalcitonin; liver cancer: FP;

Why no biomarkers for lung injury? Complexity, non-specific inflammation.....

We need good biomarkers for ARDS diagnosis, prognosis, indication for therapy.

Potential biomarkers:

- Cell specific receptor/antigen:KL-6, RAGE
- Released or synthesized during injury/repair: SPA-D, MMP, CRP
- Cytokines: IL-1,6, 8, 10

Cell adherence molecules: ICAM-1,

Biomarkers for ALI/ARDS



name	Significance	Source	author
VWF	Independent predictor for hospital mortality in ALI	CCM, 2001, AJCCM 2004	Ware
ICAM-1	May predict outcomes(cut off)	AJCCM 2001	kayal
SPA,SPD	SPA-predict ARDS Dev SPD-correlates with LTV	Chest 1999 Thorax 2003	Greene Eisner
RAGE	Associated with mortality	Thorax, 2008	Griffts
PC	Reduced PC Correlates with increased mortality	AJP 2003	Ware
PAI-1	Independent predictor for mortality	Ajp, 2003	Prabhak aran
KL-6 (mucin like protein expressed on ATII cell)	Increased plasma level associated with severe lung injury and high mortality	ERJ, 2004	Sato

Quiz (correct answer is yellow one)



◆ The typical feature of ARDS

1. Increased vascular permeability
2. Increased alveolar epithelium permeability
3. Heterogeneous Lung damage
4. Un-controlled lung inflammation
5. All above

◆ Which is the most beneficial treatment of ARDS

1. Fluid restriction
2. Anti-coagulation
3. Steroid application
4. Protective ventilation strategy
5. Nutrition and support therapy