In the name of The Almighty God

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IN HOSPITAL TREATMENT OF ARDS & STEROIDS IN SEPSIS

Menderes Hazır ▶ **ATUDER Acil Görüntüleme**

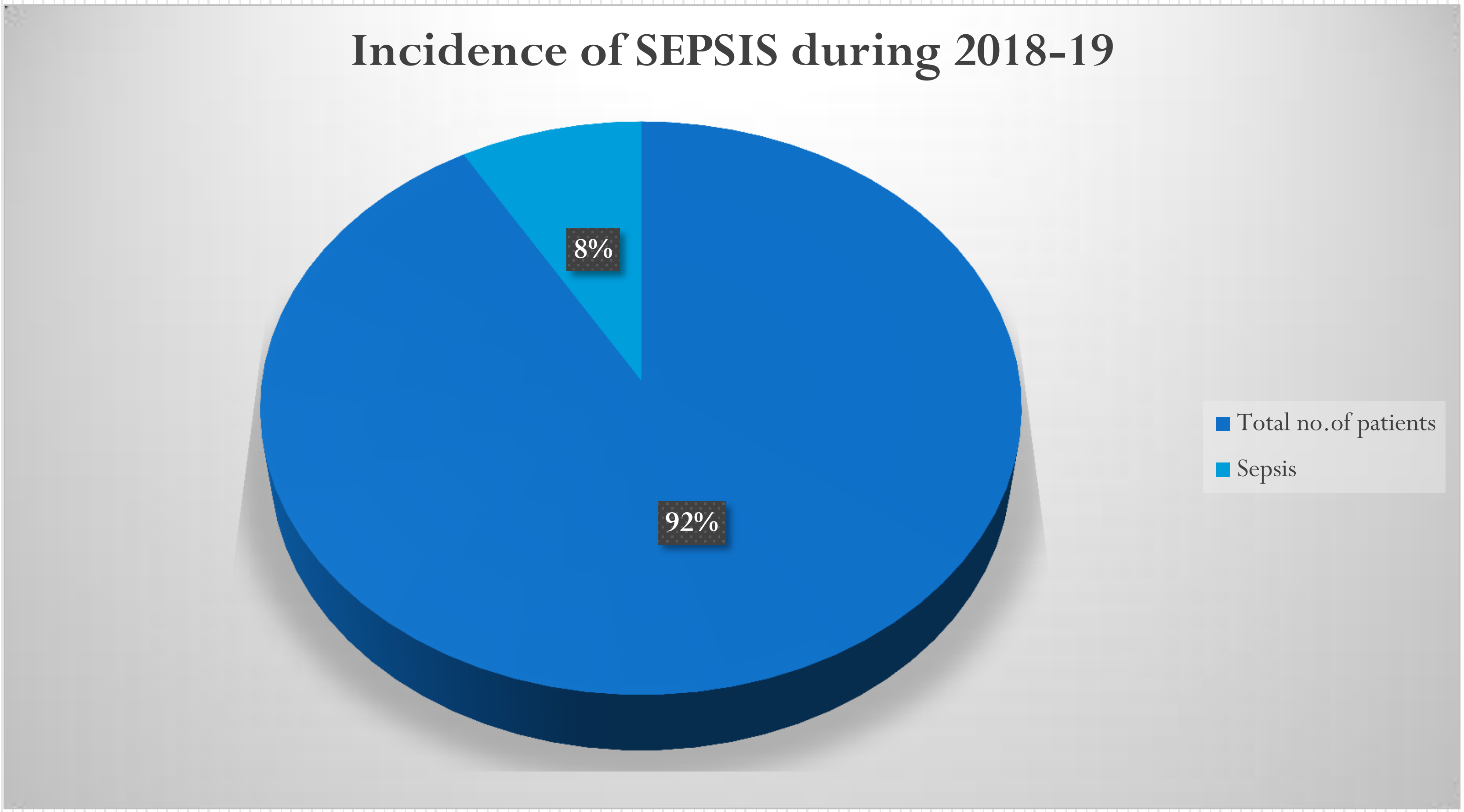
Sunday at 1:01 PM ·

ATUDER Başkanı Prof. Dr. Başar CANDER, Başkan Yardımcısı Prof. Zeynep ÇAKIR ve Genel Sekreterimiz Prof. Behçet AL 20th Annual Conference of Society for Emergency Medicine India (SEMI)'nin Kongresinde — with **Zeynep Gökcan Çakır** and **2 others**.

See Translation

Arif Karagoz and 12 others

3


Incidence of SEPSIS during 2018-19
8%
92%
Total no.of patients
Sepsis

History

- The first description in 1967,
- Ashbaugh and colleagues described 12 patients
  - acute respiratory distress,
  - cyanosis refractory to oxygen therapy,
  - decreased lung compliance, and
  - diffuse infiltrates evident on the chest radiograph.
- 1988, an expanded definition was proposed that quantified the physiologic respiratory impairment through the use of a four-point lung-injury scoring system

Table 2 Calculation of the lung injury score[4]

	Score
Chest radiograph	
No alveolar consolidation	0
Alveolar consolidation confined to 1 quadrant	1
Alveolar consolidation confined to 2 quadrants	2
Alveolar consolidation confined to 3 quadrants	3
Alveolar consolidation confined to 4 quadrants	4
Hypoxaemia score	
$PaO_2/FiO_2 \geq 300$	0
PAO_2/FiO_2 225–299	1
PaO_2/FiO_2 175–224	2
PaO_2/FiO_2 100–174	3
$PaO_2/FiO_2 < 100$	4
PEEP score (when mechanically ventilated)	
≤ 5 cm H_2O	0
6–8 cm H_2O	1
9–11 cm H_2O	2
12–14 cm H_2O	3
≥ 15 cm H_2O	4
Respiratory system compliance score (when available)	
≥ 80 ml/cm H_2O	0
60–79 ml/cm H_2O	1
40–59 ml/cm H_2O	2
20–39 ml/cm H_2O	3
≤ 19 ml/cm H_2O	4
The score is calculated by adding the sum of each component and dividing by the number of components used.	
No lung injury	0
Mild to moderate lung injury	0.1–2.5
Severe lung injury (ARDS)	>2.5

Table 2: The Lung Injury Prediction Score

Predisposing conditions	LIPS Score	Examples
Shock	2	(1) Patient with history of alcohol abuse with septic shock from pneumonia requiring $FIO_2 > 0.35$ Emergency room: sepsis + shock + pneumonia + alcohol abuse + $FIO_2 > 0.35$ 1 + 2 + 1.5 + 1 + 2 = 7.5 (2) Motor vehicle accident with traumatic brain injury, lung contusion, and shock requiring $FIO_2 > 0.35$ Traumatic brain injury + lung contusion + shock + $FIO_2 > 0.35$ 2 + 1.5 + 2 + 2 = 7.5 (3) Patient with history of diabetes mellitus and urosepsis with shock sepsis + shock + diabetes 1 + 2 − 1 = 2
Aspiration	2	
Sepsis	1	
Pneumonia	1.5	
High-risk surgery*		
Orthopaedic spine	1	
Acute abdomen	2	
Cardiac	2.5	
Aortic vascular	3.5	
High-risk trauma		
Traumatic brain injury	2	
Smoke inhalation	2	
Near drowning	2	
Lung contusion	1.5	
Multiple fractures	1.5	
Risk modifiers		
Alcohol abuse	1	
Obesity (BMI>30)	1	
Hypoalbuminemia	1	
Chemotherapy	1	
$FIO_2 > 0.35$ (>4 L/min)	2	
Tachypnoea (RR > 30)	1.5	
$SpO_2 < 95\%$	1	
Acidosis (pH < 7.35)	1.5	
Diabetes mellitus**	-1	

BMI = body mass index; RR = respiratory rate; SPO_2 = oxygen saturation by pulse oximetry
*Add 1.5 points in case of emergency surgery
**Only in cases of sepsis

Berlin definition

Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptom
Chest imaging	Bilateral opacities – not fully explained by effusions, lobar/lung collapse, or nodules
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload; need objective assessment (for example, a echocardiography) to exclude hydrostatic oedema if no risk factor present
Oxygenation	
Mild	$200 < PaO2/FiO2 \leq 300$, with PEEP ≥ 5 cmH2O
Moderate	$100 < PaO2/FiO2 \leq 200$, with PEEP ≥ 5 cmH2O
Severe	$PaO2/FiO2 \leq 100$, with PEEP ≥ 5 cmH2O

Etiology

Direct causes

- **Common causes**
  - Pneumonia
  - Aspiration of gastric contents
- **Less common causes**
  - Pulmonary contusion
  - Fat emboli
  - Near-drowning
  - Inhalational injury
  - Reperfusion pulmonary edema
  - after lung transplantation ora pulmonary embolectomy

Indirect causes

- **Common causes**
  - Sepsis
  - Severe trauma with shock and multiple transfusions
- **Less common causes**
  - Cardiopulmonary bypass
  - Drug overdose
  - Acute pancreatitis
  - Transfusions of blood products

Intensive Care Med (2001) 27: 457–460
DOI 10.1007/s001340100879

EDITORIAL

P. Pelosi
L. Gattinoni

Acute respiratory distress syndrome of pulmonary and extra-pulmonary origin: fancy or reality?

- Difference explained interms of
  - Pathophysiology
  - Respiratory mechanics
  - Ventillatory strategies
  - Effect of prone positioning

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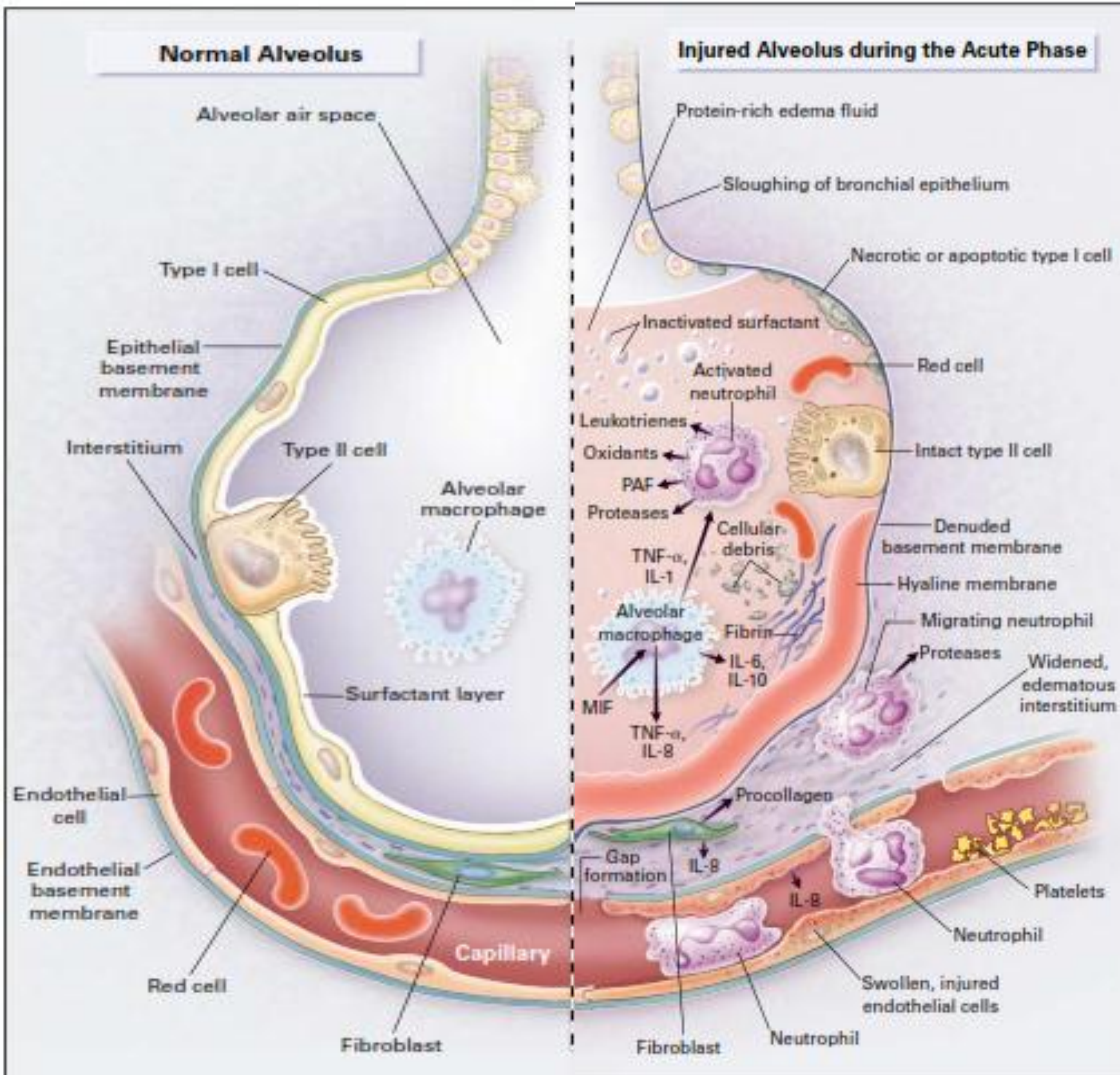
Pathophysiology

- **Endothelial and Epithelial Injury**
- Injury→ Increased permeability →Influx of protein-rich edema fluid →hypoxemia
  - Alveolar epithelium injury
  - Neutrophils and other pro inflammatory – cytokines are involved



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

Pathophysiology

- Refractory hypoxemia
  - Alveolar fluid→physiological shunt
  - Scatttered microthrombi → increaseig dead space
  - Pulmonary hypertension → hypoxic/thrombotic
- Decrease lung compliance
  - Increase surface tension
  - Alveolar oedema
  - Baby lung
- Propensity for alveolar closure

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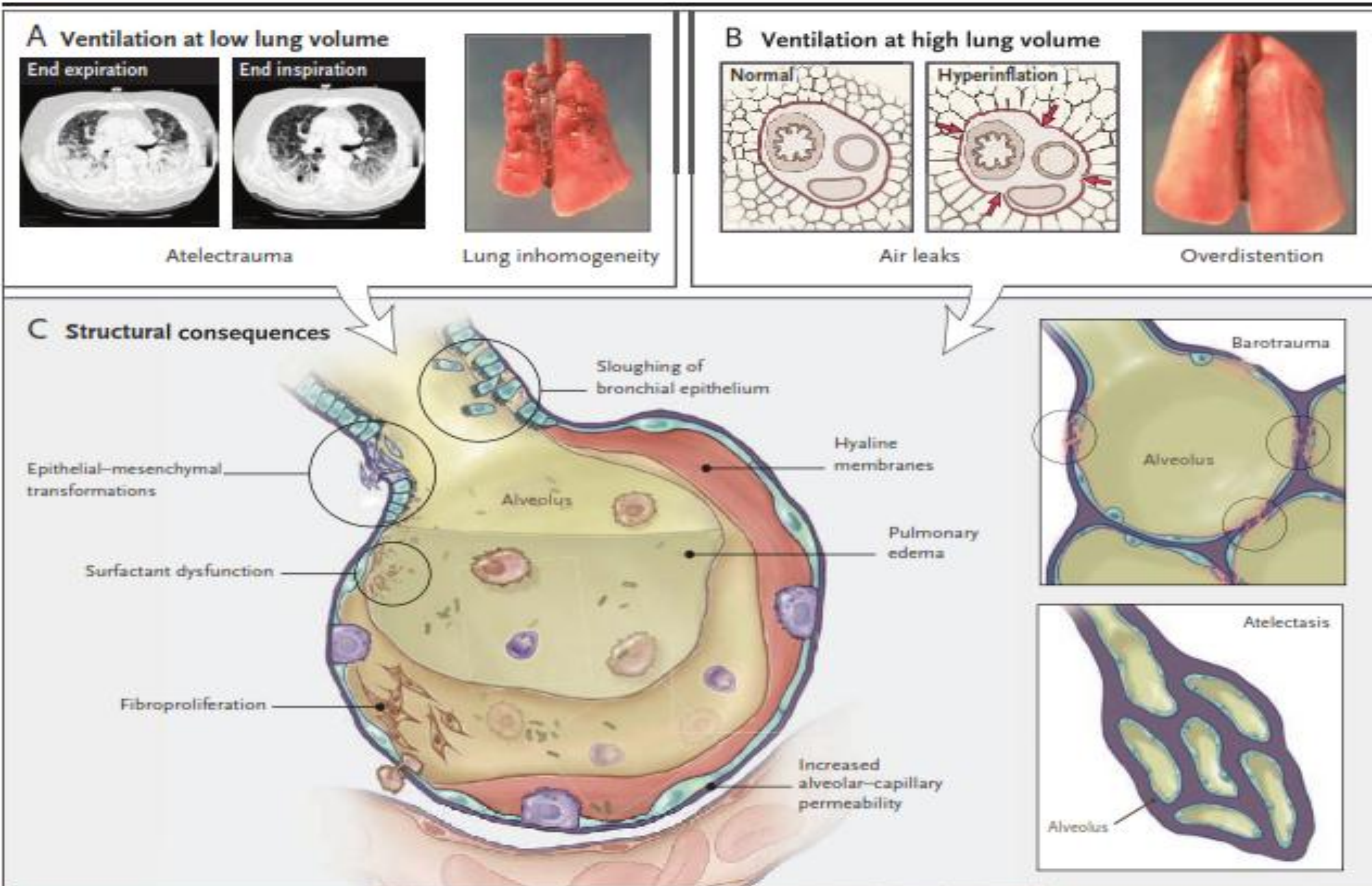
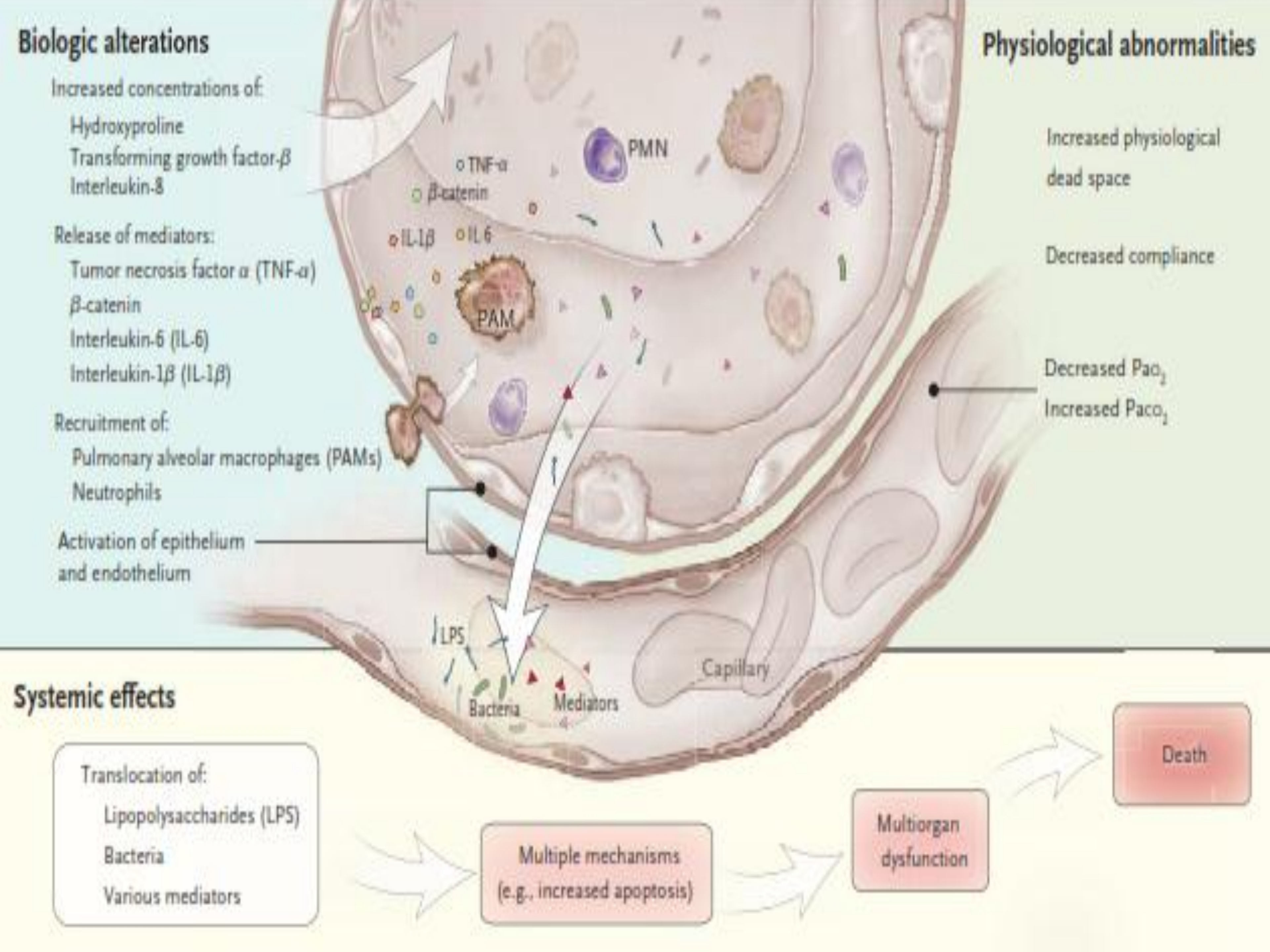
Ventilator associated lung injury

- Ventilation at High Lung Volumes(Volutrauma)
  - leading to alveolar rupture,
  - Air leaks
  - gross barotrauma
  - volume (i.e., lung stretching), not airway pressure, most important factor
- Ventilation at Low Lung Volumes(Atlectrauma)
  - Repetitive opening and closing of airways and lung units,
  - Effects on surfactant function,
  - regional hypoxia.
  - Epithelial sloughing, hyaline membranes



***Ventilator-Induced Lung Injury**, Arthur S. Slutsky, M.D., and V. Marco Ranieri, M.D,*
N Engl J Med 2013;369:2126-36



Biologic alterations
Increased concentrations of:
Hydroxyproline
Transforming growth factor-β
Interleukin-8
Release of mediators:
Tumor necrosis factor α (TNF-α)
β-catenin
Interleukin-6 (IL-6)
Interleukin-1β (IL-1β)
Recruitment of:
Pulmonary alveolar macrophages (PAMs)
Neutrophils
Activation of epithelium and endothelium
TNF-α
β-catenin
IL-1β
IL 6
PMN
PAM
LPS
Bacteria
Mediators
Capillary
Physiological abnormalities
Increased physiological dead space
Decreased compliance
Decreased Pa_{O_2}
Increased Pa_{CO_2}
Systemic effects
Translocation of:
Lipopolysaccharides (LPS)
Bacteria
Various mediators
Multiple mechanisms (e.g., increased apoptosis)
Multiorgan dysfunction
Death

Transpulmonary pressure and plateau pressure

- Transpulmonary pressure: principal force maintaining inflation (alveolar pressure minus pleural pressure)
- Measurement of pleural pressure is complicated & cumbersome
  - Estimated by esophageal pressure- yields only approximate results
- Plateau pressure as surrogate marker of lung over distension
- Nuances required in interpreting plateau pressure

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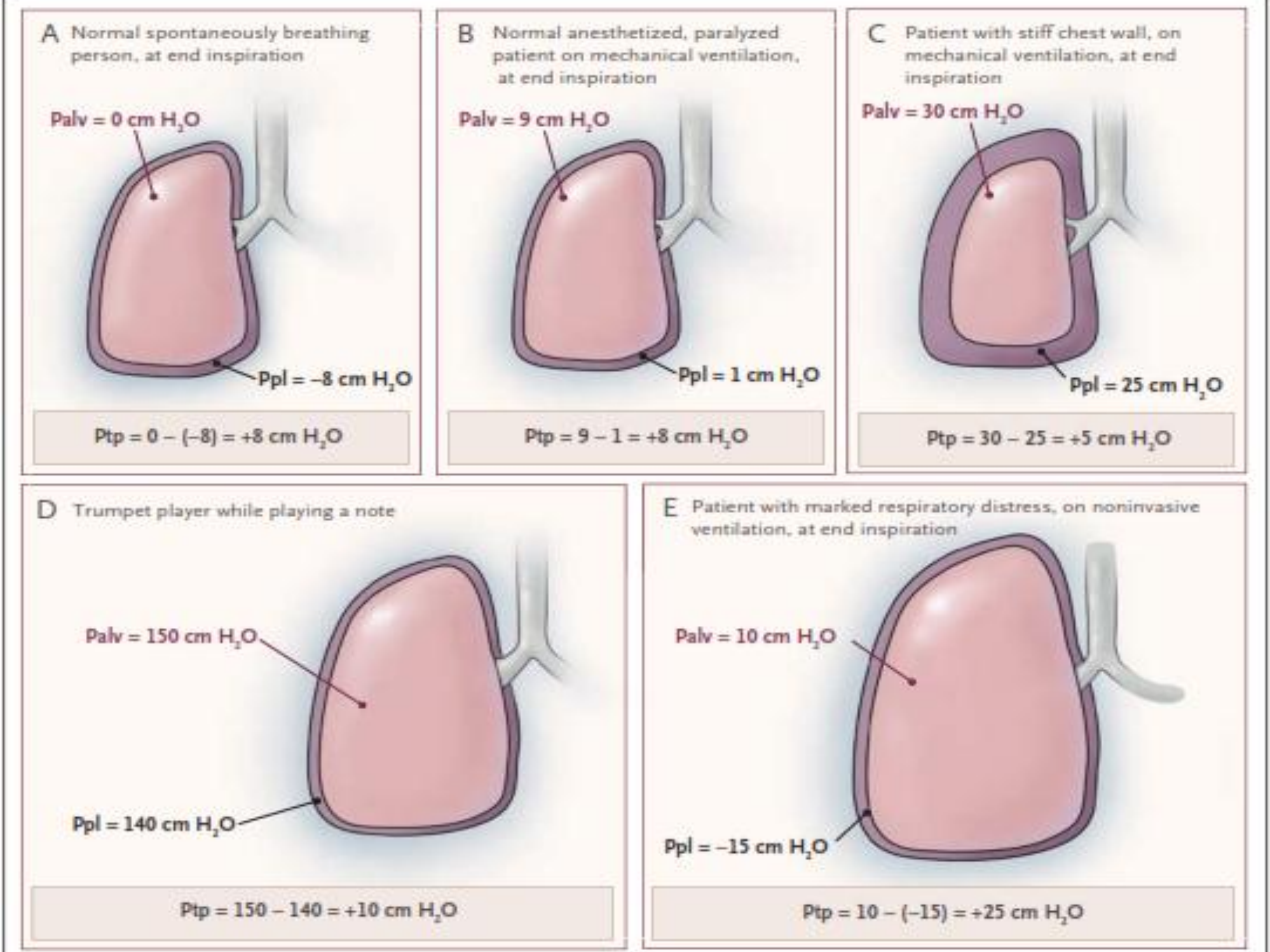
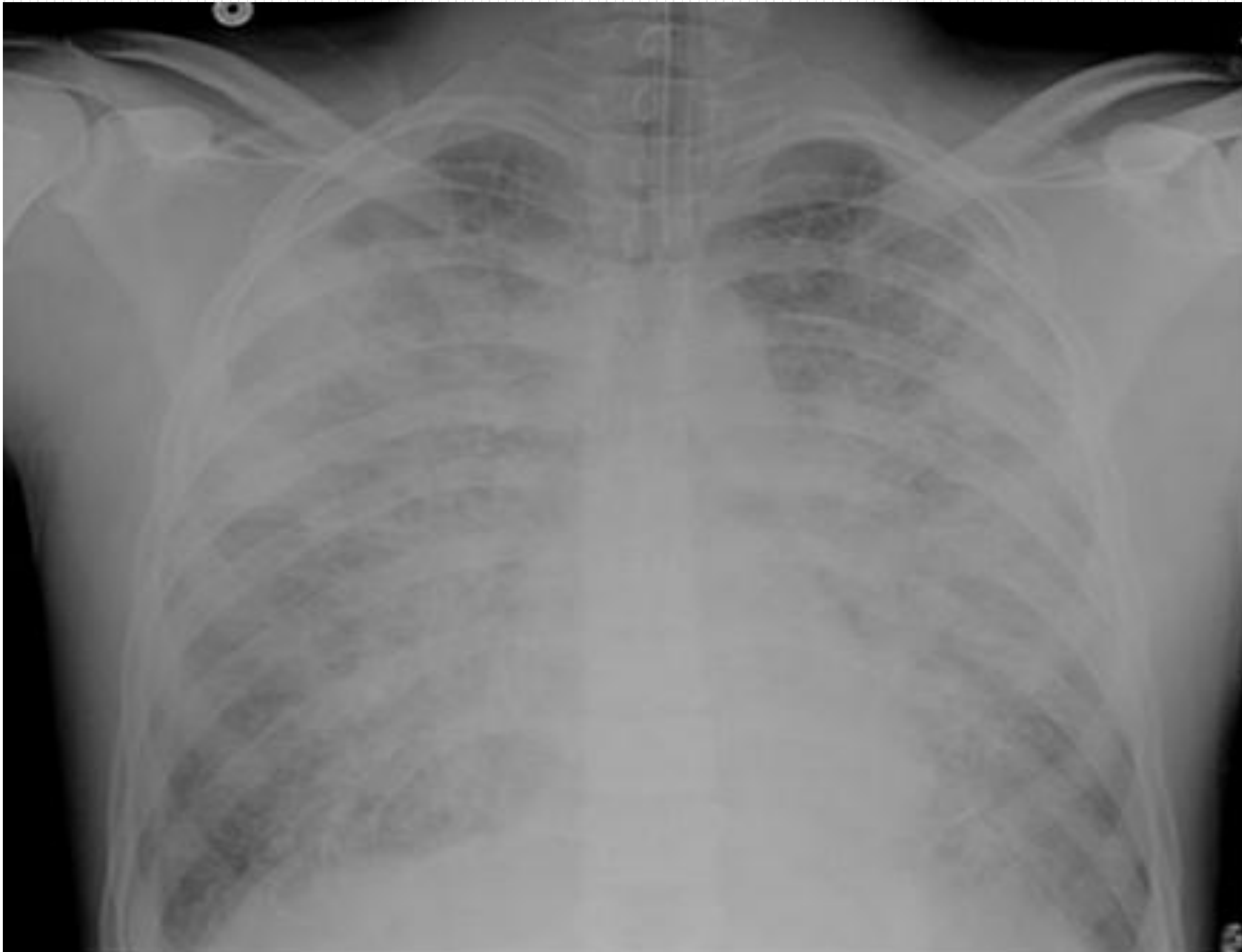


A Normal spontaneously breathing person, at end inspiration
Palv = 0 cm H_2O
Ppl = –8 cm H_2O
Ptp = 0 – (–8) = +8 cm H_2O
B Normal anesthetized, paralyzed patient on mechanical ventilation, at end inspiration
Palv = 9 cm H_2O
Ppl = 1 cm H_2O
Ptp = 9 – 1 = +8 cm H_2O
C Patient with stiff chest wall, on mechanical ventilation, at end inspiration
Palv = 30 cm H_2O
Ppl = 25 cm H_2O
Ptp = 30 – 25 = +5 cm H_2O
D Trumpet player while playing a note
Palv = 150 cm H_2O
Ppl = 140 cm H_2O
Ptp = 150 – 140 = +10 cm H_2O
E Patient with marked respiratory distress, on noninvasive ventilation, at end inspiration
Palv = 10 cm H_2O
Ppl = –15 cm H_2O
Ptp = 10 – (–15) = +25 cm H_2O

Baby lung concept

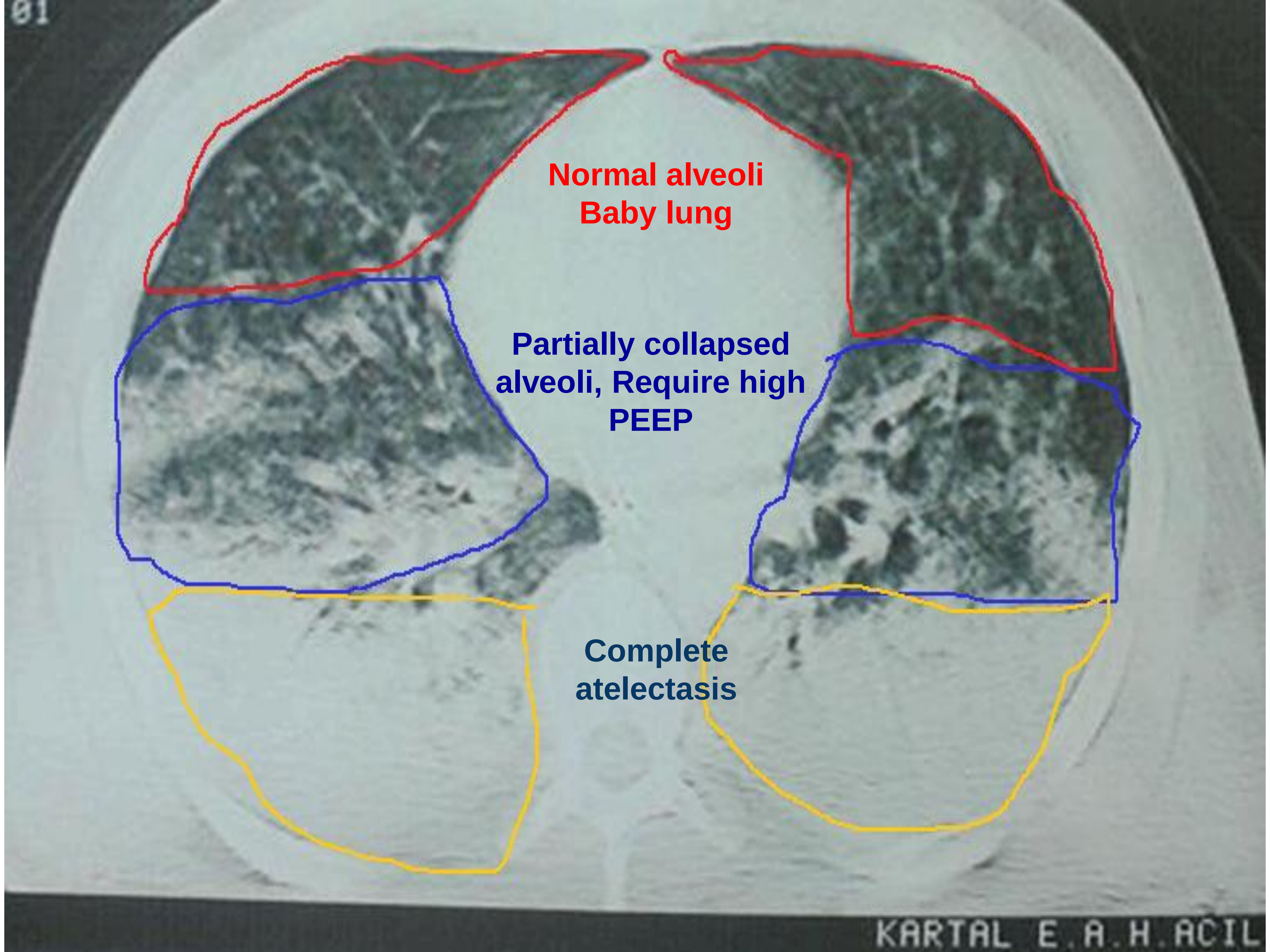
Earlier concept

- ARDS involves all the lung tissue homogeneously
- ARDS lungs were regarded as homogeneously heavy and stiff
- To achieve normal $PaCO_2$ high tidal volume ventilation was used
- To achieve normal PaO_2 PEEP was employed

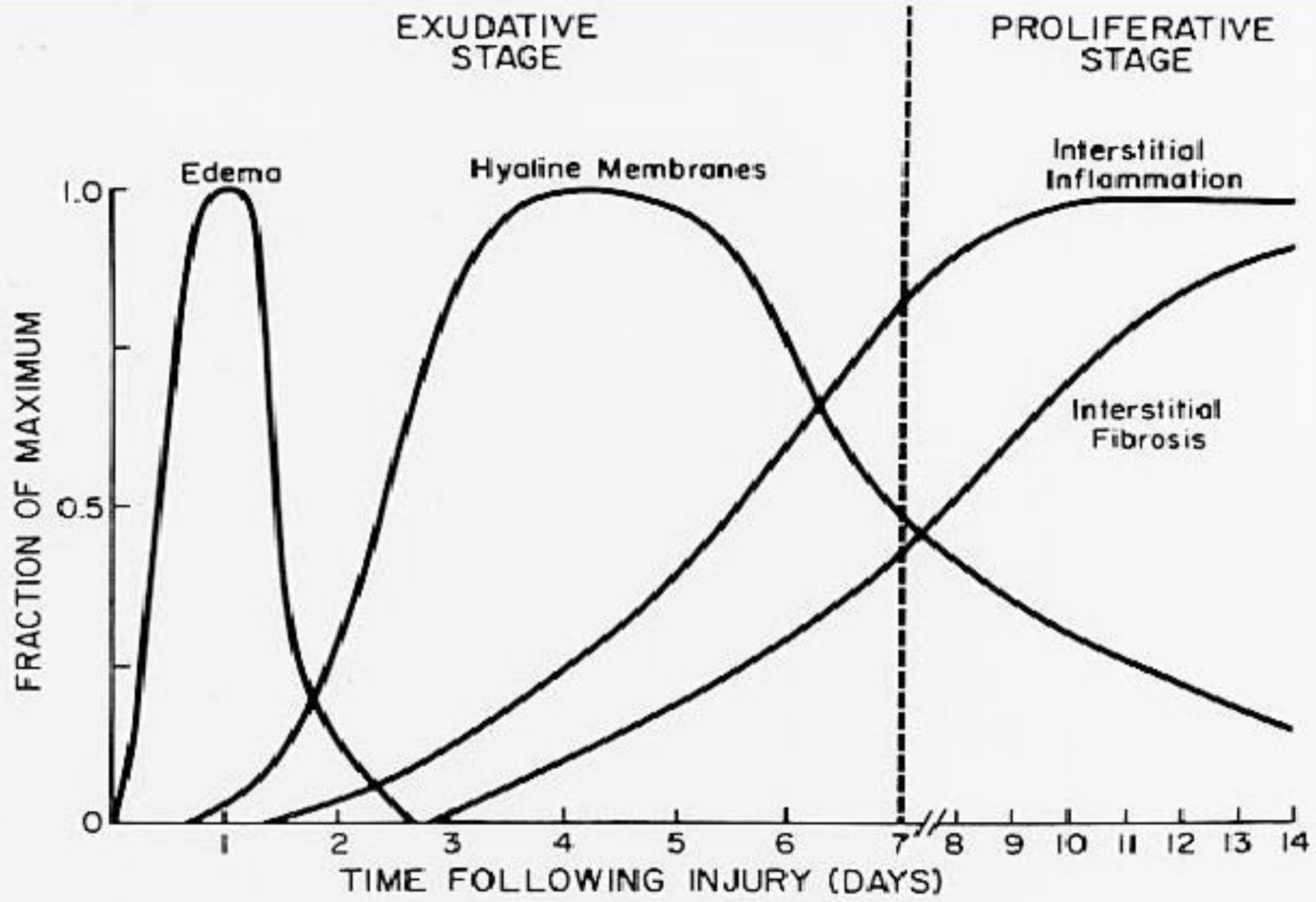


Baby lung

- CT findings in ARDS in mid1980
- ARDS appears non-homogeneous on CT, with the densities concentrated primarily in the most dependent regions
  - normally aerated,
  - poorly aerated,
  - overinflated, and nonaerated tissue
- Normally aerated tissue only foms a fraction of the whole lung- **Baby lung**


01
Normal alveoli
Baby lung
Partially collapsed
alveoli, Require high
PEEP
Complete
atelectasis
KARTAL E.A.H.ACIL

Stages of ARDS



Management of ARDS- Ventilation

- Calculate predicted Body weight
  - Male 50+2.3(height in inches-60)
  - Females 45.5+2.3(height in inches-60)
- Select any ventilator mode
- Set initial ventilator settings to achieve V_T 8ml/kg
- Reduce V_T by 1 ml/kg at intervals $\leq$ 2 hours until V_T = 6ml/kg
- Set initial rate to approximate baseline minute ventilation (not > 35 bpm)
- Adjust V_T and RR to achieve pH and plateau pressure goals below

The New England Journal of Medicine

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VOLUME 342 MAY 4, 2000 NUMBER 18

VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

- RCT comparing V_T of 6ml/kg and 12ml/kg
- 861 patients were enroled
- Mortality in low V_T 31% as compared to 39.8% in control
- Ventilator free days were more in study group

Setting up of PEEP

Start with initial PEEP of atleast 5 and target SPO2 of 88-95%

Lower PEEP/higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 22, 2004 VOL. 351 NO. 4

Higher versus Lower Positive End-Expiratory Pressures in Patients with the Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute ARDS Clinical Trials Network*

Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

Alain Mercat, MD

Context The need for lung protection is universally accepted, but the optimal level

Ventilation Strategy Using Low Tidal Volumes, Recruitment Maneuvers, and High Positive End-Expiratory Pressure for Acute Lung Injury and Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

Maureen O. Meade, MD, MSc

Context Low-tidal-volume ventilation reduces mortality in critically ill patients with

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

Systematic Review and Meta-analysis

- Meta analysis of 3 trials(ALVEOLI, LOVS, EXPRESS)
- Mortality benefit seen in patients with ARDS
- Patients with acute lung injury may not benefit or may actually experience harm from higher PEEP levels
- Small increase in risk of pneumothorax

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PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.

If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H_2O.

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pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)

If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCO_2$ < 25 (Maximum set RR = 35).

.

If pH < 7.15: Increase RR to 35.

If pH remains < 7.15, V_T may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

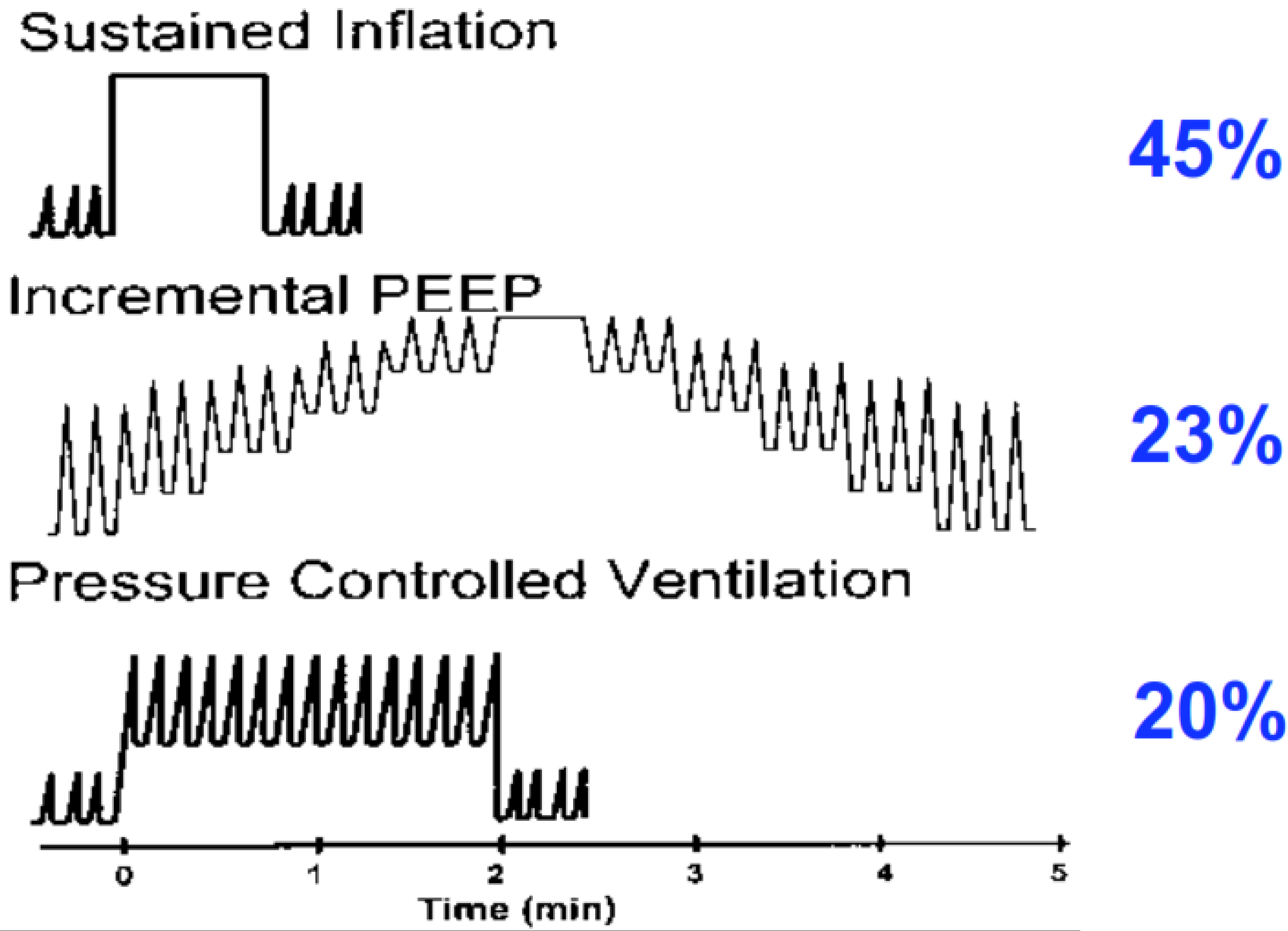
May give $NaHCO_3$

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

Role of recruitment maneuvers

- Clinical studies of RMs in ALI/ARDS have yielded variable results
- Factors such as the
  - Duration and
  - Underlying etiology of ARDS
  - Methods of the RM (e.g., sustained inflation versus incremental positive end-expiratory pressure [PEEP])
- may be important determinants of the potential for alveolar recruitment
- Optimal pressure, duration, and frequency of RMs have not been determined or tested in large clinical trials.

- Transient increase in oxygenation
- No effect on PEEP values or FiO_2 concentration
- No mortality benefit
- May be used when
  - After suctioning
  - Disconnections
  - At initial stage before setting optimal PEEP
  - Rescue maneuver


Sustained Inflation
45%
Incremental PEEP
23%
Pressure Controlled Ventilation
20%
0
1
2
3
4
5
Time (min)

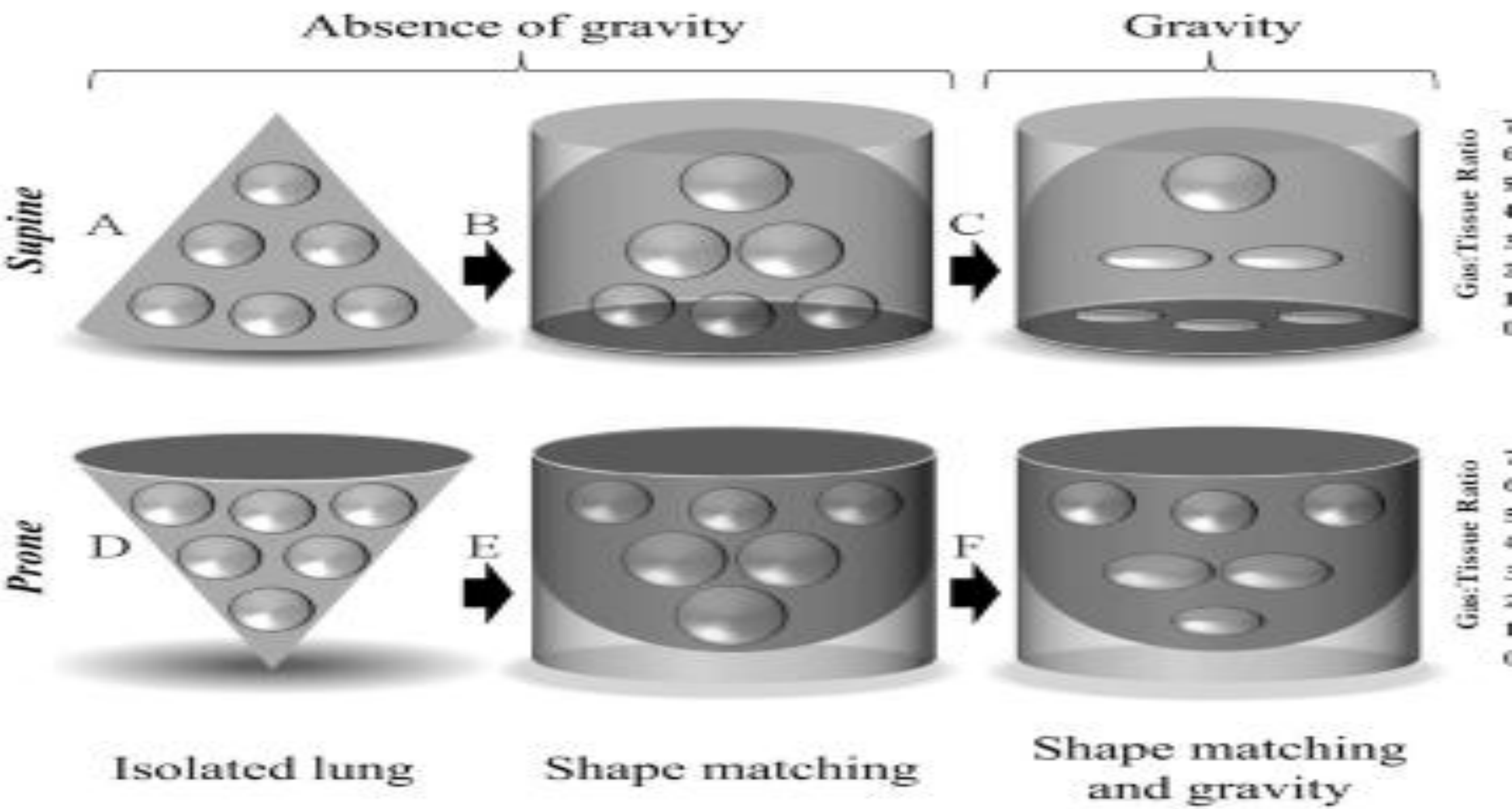
Disadvantages

- 3 randomized, controlled trials were not able to demonstrate a beneficial effect of RMs on oxygenation in routine practice
- Some safety concerns
- Large variability of oxygenation response across the patients.
- Relevant end-points in assessment of RMs have moved from oxygenation improvement toward VILI prevention.
- Not recommended for routine practice

Prone Ventilation

- Prone positioning, first proposed in 1974
- Sponge model" of lung.
- Increase in oxygenation and improved lung mechanics
- CT scan shows a more homogeneous distribution of gas throughout lung parenchyma in prone ventilation
- In experimental models of ARDS, there is evidence that prone positioning prevents or significantly delays development of VILI.

Physiology


Absence of gravity
Gravity
Supine
A
B
C
Prone
D
E
F
Gas:Tissue Ratio
Gas:Tissue Ratio
Isolated lung
Shape matching
Shape matching and gravity

- More tissue of lung in dorsal side for ventilation
- Shifting of heart weight
- Decrease effect of intraabdominal pressure

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

Prone Positioning in Severe Acute Respiratory Distress Syndrome

- Prone position given for atleast 16hrs
- 28 day mortality in prone group was 16% compared to 32% in supine
- No difference in adverse events b/w groups
- Participating hospitals had adequate experience to prone patients before study

Hu *et al. Critical Care* 2014, **18**:R109
http://ccforum.com/content/18/3/R109

CRITICAL CARE

RESEARCH Open Access

The effect of prone positioning on mortality in patients with acute respiratory distress syndrome: a meta-analysis of randomized controlled trials

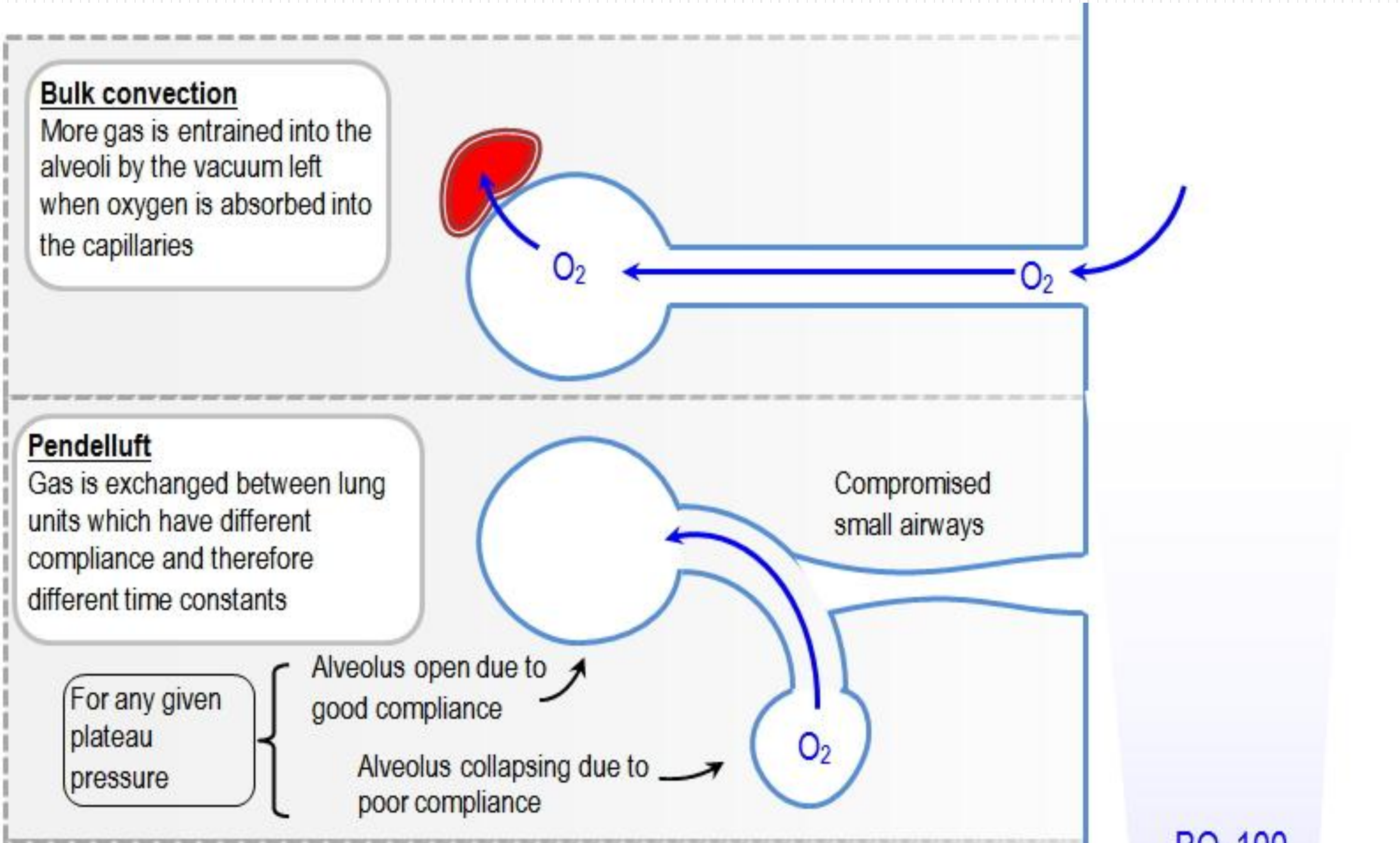
Shu Ling Hu, Hong Li He, Chun Pan, Ai Ran Liu, Song Qiao Liu, Ling Liu, Ying Zi Huang, Feng Mei Guo, Yi Yang and Hai Bo Qiu*

- Meta analysis of 9 RCT
- Decrease in mortality (28days, 60 days and 90 days) in prone position
- Prone position has to be done ≥12hrs

HFOV

- Ventilator strategy – small VT @1ml/kg at high frequencies 10-15hz
- Gas is actively pushed in and actively withdrawn
- Vt less than dead space
- Rescue measure when conventional ventilation fail

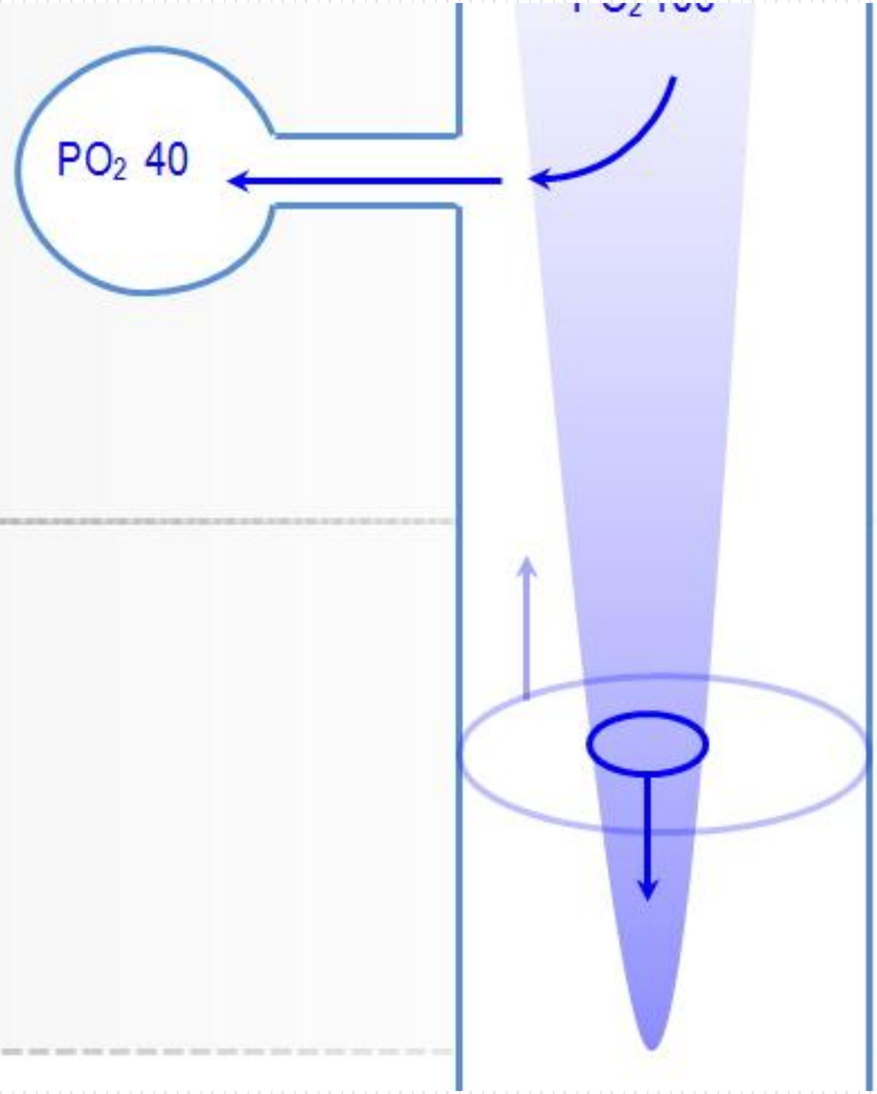
Mechanism of gas exchange



Taylor dispersion

Gas is exchanged between the central rapid jet of oxygenated gas, and the relatively oxygen-poor gas at the periphery of airways.

The force behind this central jet allows it to penetrate deeper into the bronchial tree, allowing oxygenation of distal units



Coaxial flow

A bi-directional flow of gas exists, with a central rapidly moving inspiratory column and a slower moving peripheral expiratory sleeve, pushed out of the lung by the force of the incoming gas.

Values to be set in HFOV

- Mean airway pressure
- FiO2
- Amplitude or Delta P
- % inspiration
- Frequency

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 28, 2013 VOL. 368 NO. 9

High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

CONCLUSIONS

In adults with moderate-to-severe ARDS, early application of HFOV, as compared with a ventilation strategy of low tidal volume and high positive end-expiratory pressure, does not reduce, and may increase, in-hospital mortality. (Funded by the Canadian Institutes of Health Research; Current Controlled Trials numbers, ISRCTN42992782 and ISRCTN87124254, and ClinicalTrials.gov numbers, NCT00474656 and NCT01506401.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D., Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D.,

CONCLUSIONS

The use of HFOV had no significant effect on 30-day mortality in patients undergoing mechanical ventilation for ARDS. (Funded by the National Institute for Health Research Health Technology Assessment Programme; OSCAR Current Controlled Trials number, ISRCTN10416500.)

Role of ECMO

- Donald Hill and colleagues described the first use of an ECMO device for acute respiratory failure in humans
- They reported on a 24-year-old polytrauma patient
- The National Institutes of Health (NIH) performed the first multicenter trial in the 1970s,
- 90 patients with severe ARDS refractory to conventional ventilation
- 42 received ECMO.
- Survival was extremely low (<10%)

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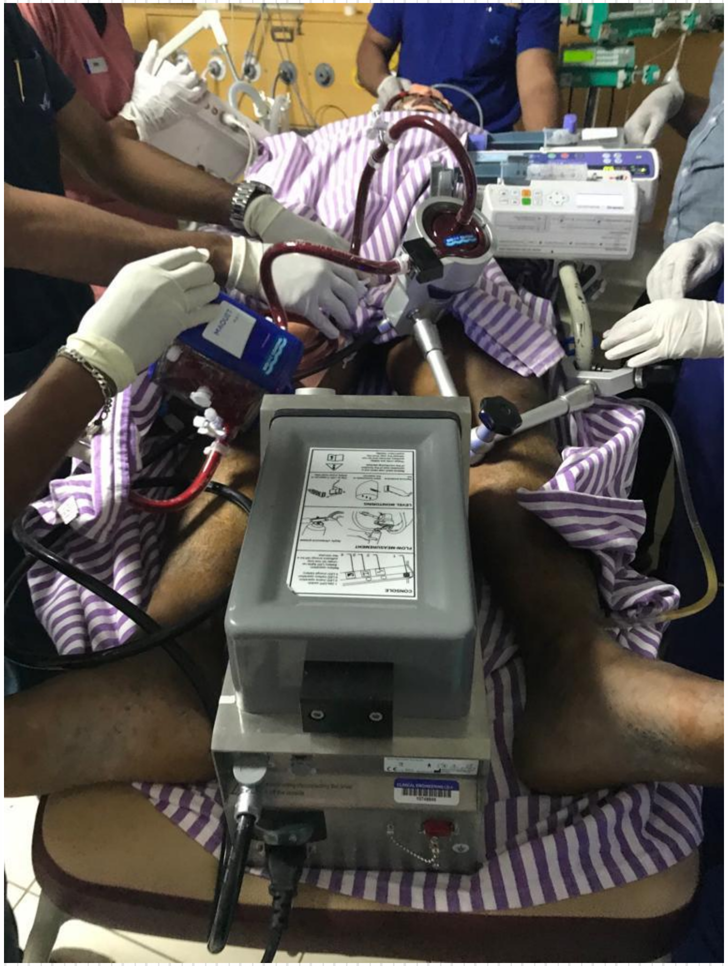

In our Hospital we had 6 adult patients on ECMO in 2018 for ARDS – 50% was the results.

Karnataka: Mobile ECMO retrieval team of Narayana Health City saves a life

Acute respiratory syndrome (ARDS) is a life-threatening lung condition wherein the flow of oxygen into the lungs and blood is prevented.

ANI | March 29, 2019, 10:22 IST

Bengaluru: Compassion has no boundaries and that's what happened with Nagesh. He was given a new lease of life at a city hospital by the ECMO (Extra Corporeal Life Support) retrieval

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

- 63% (57/90) of patients allocated to consideration for treatment by ECMO survived to 6 months without disability compared with 47%
- Pitfalls
  - 22 patients randomized to the ECMO arm did not receive ECMO
  - No standardized protocol for lung-protective mechanical ventilation existed in the control group
  - Third, more patients received corticosteroids in the ECMO group

Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

The Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators*

Context The novel influenza A(H1N1) pandemic affected Australia and New Zealand during the 2009 southern hemisphere winter. It caused an epidemic of critical illness and some patients developed severe acute respiratory distress syndrome (ARDS) and were treated with extracorporeal membrane oxygenation (ECMO).

Conclusions During June to August 2009 in Australia and New Zealand, the ICUs at regional referral centers provided mechanical ventilation for many patients with 2009 influenza A(H1N1)–associated respiratory failure, one-third of whom received ECMO. These ECMO-treated patients were often young adults with severe hypoxemia and had a 21% mortality rate at the end of the study period.

JAMA. 2009;302(17):1888-1895 www.jama.com

- 63 patients kept on ECMO compared with 133 on mechanical ventilation
- Patients were younger, low apache score on admission in ECMO group

PART II: WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:

1. $FiO_2 \leq 0.40$ and $PEEP \leq 8$ OR $FiO_2 \leq 0.50$ and $PEEP \leq 5$.
2. PEEP and $FiO_2 \leq$ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP $\geq$ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

B. SPONTANEOUS BREATHING TRIAL (SBT):

If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with $FiO2 \leq 0.5$ and $PEEP \leq 5$:

1. Place on T-piece, trach collar, or CPAP $\leq$ 5 cm H_2O with PS $\leq$ 5
2. Assess for tolerance as below for up to two hours.
   - a. $SpO_2 \geq 90$: and/or $PaO_2 \geq 60$ mmHg
   - b. Spontaneous $V_T \geq 4$ ml/kg PBW
   - c. RR $\leq$ 35/min
   - d. pH $\geq$ 7.3
   - e. No respiratory distress (distress= 2 or more)
     - ➢ HR > 120% of baseline
     - ➢ Marked accessory muscle use
     - ➢ Abdominal paradox
     - ➢ Diaphoresis
     - ➢ Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.

4. If not tolerated resume pre-weaning settings.

Non ventilatory strategies for ARDS- Fluid balance

- Adequate fluid resuscitation to treat the initial shock
- Once patient is our of shock conservative fluid strategy
- No mortality benefit but reduced on ventilation, no organ failure

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ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

NMB in ARDS

- Early use of NMB in severe ARDS
  - Reduces mortality
  - Increased ventilator free days
  - No residual muscle weakness

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ESTABLISHED IN 1812 SEPTEMBER 16, 2010 VOL. 363 NO. 12

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Steroids in ARDS

- Role of steroid is controversial
- Points to note
  - When to start
  - Dose
  - When to stop complications
  - Contraindications

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ESTABLISHED IN 1812 APRIL 20, 2006 VOL. 354 NO. 16

Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

- Steroid started after 7 days
- No mortality benefit in steroid group
- Increase complications when started after 14 days
- Mortality benefit when started b/w 7-14days

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Glucocorticoid Treatment in Acute Lung Injury and Acute Respiratory Distress Syndrome

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Table 2
Prolonged glucocorticoid treatment initiated before day 14 of acute lung injury/acute respiratory distress syndrome

Study	Hospital Mortality[a]	Reduction in Inflammation	Improvement in PaO_2:FiO_2	Reduction in Duration of MV	Reduction in ICU stay	Rate of Infection
Early ALI/ARDS (≤3 d)	38% vs 62%	3 of 3	4 of 4	4 of 4	3 of 3	.30 vs .39
Confalonieri et al,[51] 2005 (n = 46)	0.0% vs 30%[b]	Yes	Yes	Yes	Yes	0 vs .17
Lee et al,[50] 2005 (n = 20)	8% vs 88%[b]	NR	Yes	Yes	Yes	.33 vs 0
Annane et al,[53] 2006[c] (n = 177)	64% vs 73%[c]	Yes	Yes	Yes	NR	14 vs .13
Meduri et al,[16] 2007 (n = 91)	24% vs 43%[b]	Yes	Yes	Yes	Yes	.63 vs 1.43
Unresolving ARDS (≥5 d)	26% vs 45%	5 of 5	5 of 5	2 of 3	2 of 3	.48 vs .51
Meduri et al,[6] 1998 (n = 22)	13% vs 57%[b]	Yes	Yes	Yes	Yes	0 vs NR
Varpula et al,[36] 2000 (n = 31)	19% vs 20% (30 days)	Yes	Yes	No	No	.56 vs .33
Huh et al,[54] 2002 (n = 48)	43% vs 74%[b]	Yes	Yes	NR	NR	NR
Steinberg et al,[15] 2006 (n = 132)	27% vs 36% (60 days)	Yes	Yes	Yes	Yes	.31 vs .47
Early and Unresolving ARDS	34% vs 55%	8 of 8	9 of 9	6 of 7	5 of 6	.38 vs .44

- Meta analysis of 8 studies
- Shows definitive mortality benefit
- No higher risk of infection
- Dose 1-2mg/kg/day
- Most of the trials started steroids early
- Evidence regarding use in H1N1 controversial
- Not to be combined with other drugs causing neuromuscular weakness

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Source FICM – 2018 document

- Treatment Harms

  Potential harms of treatment with steroids included excess hospital acquired infections, neuromyopathy and delirium. The only available MA reported a composite analysis of infection, neuromyopathy, diabetes, gastrointestinal bleeding and other complications21. The RR reported was 0.82 (0.5 to 1.36) but the quality of the trials was low.

- GRADE Recommendation Statement

  The use of corticosteroids in established ARDS should be the subject of a suitably powered multicentre RCT with long term follow up, that focuses on both potential benefits and harms. (GRADE Recommendation: research recommendation).

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Nutrition

- Standard supportive care for the patient with ALI/ARDS includes providing adequate nutrition
- The enteral route is preferred to the parenteral route and is associated with fewer infectious complications
- Immunomodulation via dietary manipulation has been attempted, using various combinations of omega-3 fatty acids, ribonucleotides, arginine, and glutamine
- The ARDS Network -large, multicenter, randomized placebo-controlled study of omega-3 fatty acid and antioxidant supplementation in patients with ALI/ARDS. Study was stopped early for a trend towards excess mortality in patients receiving the omega-3 fatty acid supplement
- Overall, there is still no compelling evidence to support the use of anything other than standard enteral nutritional support, with avoidance of overfeeding, in ALI/ARDS

Others

- Inhaled nitric oxide
  - Transiently improves oxygenation but does not improve mortality
  - Increase chance of rrenal dysfunction
- Prostaglandins
  - Inhaled prostaglandins improves oxygenation in small trials
  - Larger trials are awaited

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- Where mechanical ventilation is required, the use of low tidal volumes (< 6 ml/kg ideal body weight) and airway pressures (plateau pressure < 30 cmH2O) was recommended. For patients with moderate/severe ARDS (PF ratio < 20kPa), prone positioning was recommended for at least 12 hours per day.
- high frequency oscillation is not recommended and it is suggested that inhaled nitric oxide is not used. The use of a conservative fluid management strategy was suggested for all patients, whereas mechanical ventilation with high positive end-expiratory pressure (PEEP) and the use of the neuro-muscular blocking agent cisatracurium for 48 hours was suggested for ARDS patients with PF ratios less than or equal to 27 and 20 kPa respectively.

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