CCM tutorial
--ARDS

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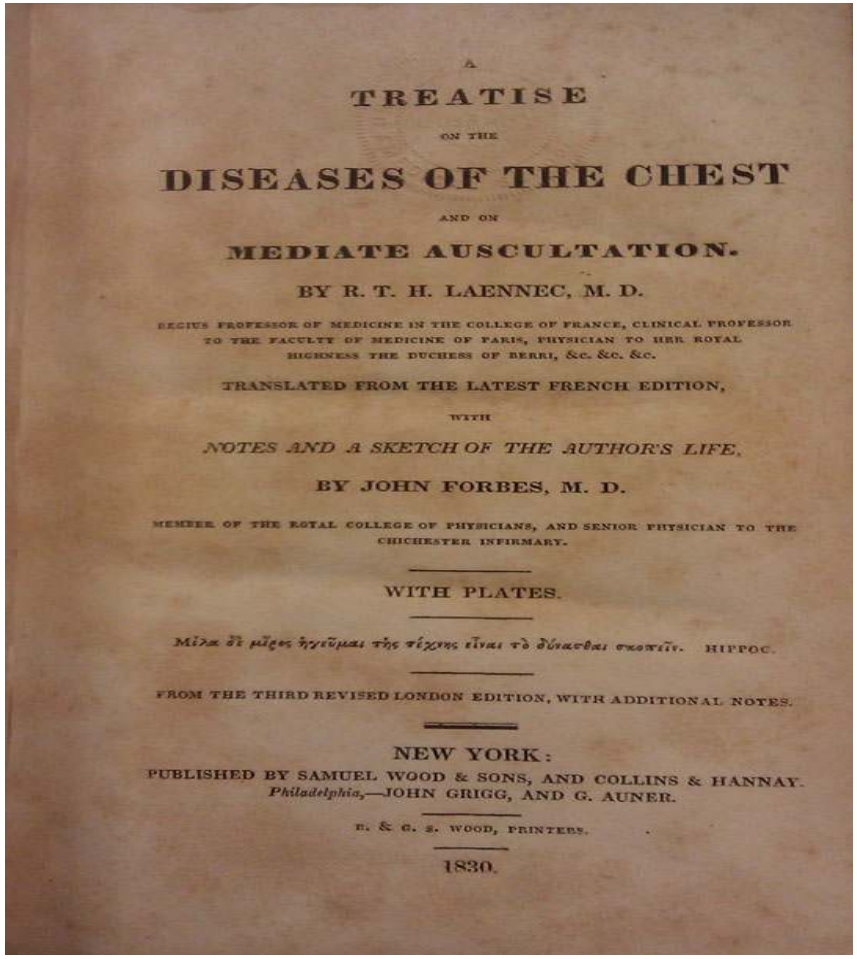
20th August 2013

In the beginning

- 1816, RTH Laennec invented the first stethoscope

In 1821

- Combining necropsy and physical finding, diseases of lung were described
- “Idiopathic anasarca of lung—pulmonary edema without heart failure”
- Universally fatal



A

TREATISE

ON THE

DISEASES OF THE CHEST

AND ON

MEDIATE AUSCULTATION.

BY R. T. H. LAENNEC, M. D.

REGIUS PROFESSOR OF MEDICINE IN THE COLLEGE OF FRANCE, CLINICAL PROFESSOR TO THE FACULTY OF MEDICINE OF PARIS, PHYSICIAN TO HER ROYAL HIGHNESS THE DUCHESS OF BERRI, &c. &c. &c.

TRANSLATED FROM THE LATEST FRENCH EDITION,

WITH

NOTES AND A SKETCH OF THE AUTHOR'S LIFE,

BY JOHN FORBES, M. D.

MEMBER OF THE ROYAL COLLEGE OF PHYSICIANS, AND SENIOR PHYSICIAN TO THE CHICHESTER INFIRMARY.

WITH PLATES.

Μέγα δὲ μέρος ἡγεῦμαι τῆς τέχνης εἶναι τὸ δύνασθαι σκοπεῖν. HIPPOC.

FROM THE THIRD REVISED LONDON EDITION, WITH ADDITIONAL NOTES.

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1830.

Ashbaugh 1967

- “Acute Respiratory Distress Syndrome”
- “Rapid onset of tachypnea and hypoxemia, with loss of lung compliance, diffuse CXR alveolar infiltrates”
- “Closely resembles respiratory distress seen in infants”
- Pathology is related to diminished surfactant
- PEEP may help

IDEAL DIFFERENCE BETWEEN CARDIOGENIC & NONCARDIOGENIC PULMONARY EDEMA

	CARDIOGENIC PULMONARY EDEMA	NONCARDIOGENIC PULMONARY EDEMA
History		
Acute cardiac event	Usually	Uncommon (but possible)
Physical Examination		
Cardiac output state	Low-flow state (cool periphery)	High-flow state (warm periphery, bounding pulses)
S_3 gallop	Present	Absent
Jugular venous distention	Present	Absent
Crackles	Wet	Dry
Underlying non-cardiac disease (e.g., peritonitis)	Usually absent	Present
Laboratory Tests		
Electrocardiogram	Ischemia/infarction	Usually normal
Chest x-ray	Perihilar distribution	Peripheral distribution
Cardiac enzymes	May be elevated	Usually normal
Pulmonary capillary pressure	>18 mm Hg	<18 mm Hg
Intrapulmonary shunting	Small	Large
Edema fluid/serum protein	<0.5	>0.7

Sibbald WJ et al. Chest 84:460, 1983.

American European Consensus Conference (AECC) 1994

- Acute onset
- Hypoxemia
  - ARDS → $PaO_2/ FiO_2 \leq 200$
  - Acute Lung Injury → $PaO_2/ FiO_2 \leq 300$
- Bilateral infiltrates on CXR consistent with odema
- No evidence of left atrial hypertension
  - PCWP ≤ 18 mmHg

Problems unanswered by AECC

- Heterogeneous disease
- Widely possible etiology

- Lacking gold standard to validate
  → pathology?
  → diffuse alveolar damage?

- Routine use of pulmonary artery catheter?

Specific issues unsettled

- “Acute” not defined explicitly
- Subsequent trials often arbitrarily fixed at ≤ 72 hours after pulmonary insults

Hypoxemia quantified

- Not standardized he conditions when the PaO_2/ FiO_2 should be calculated
- PaO_2/ FiO_2 ratio varied with ventilator setting and FiO_2 being used, and may improve with PEEP
- Other causes possible e.g. low cardiac output

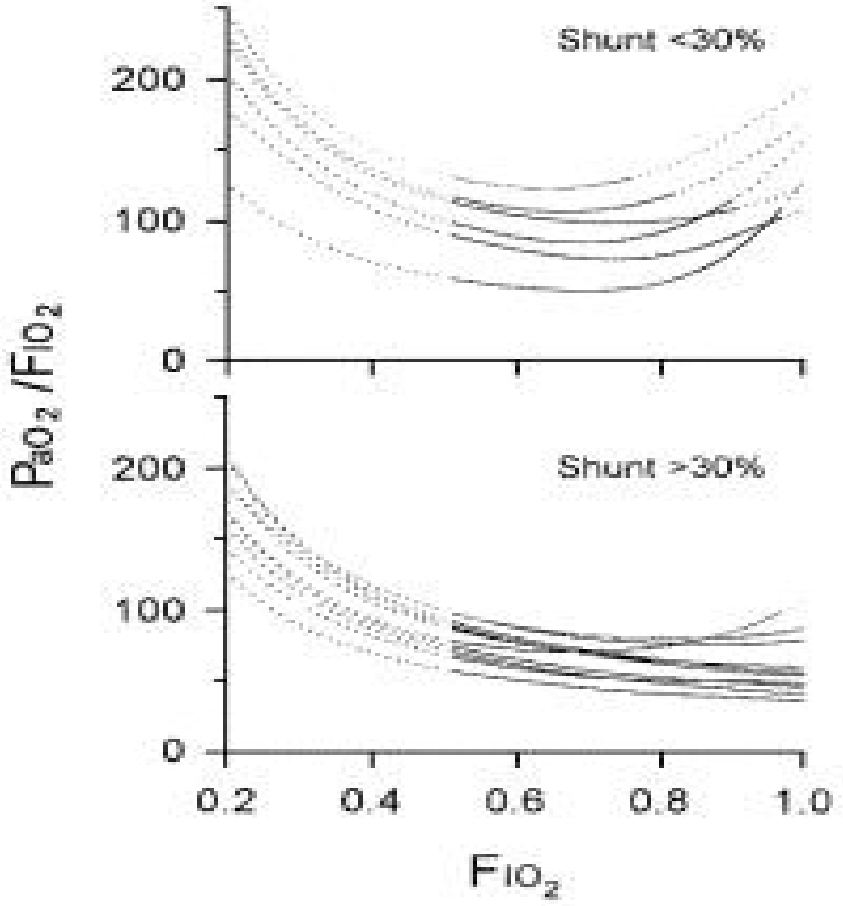
Analyzed published ARDS cases

- With relatively low shunt

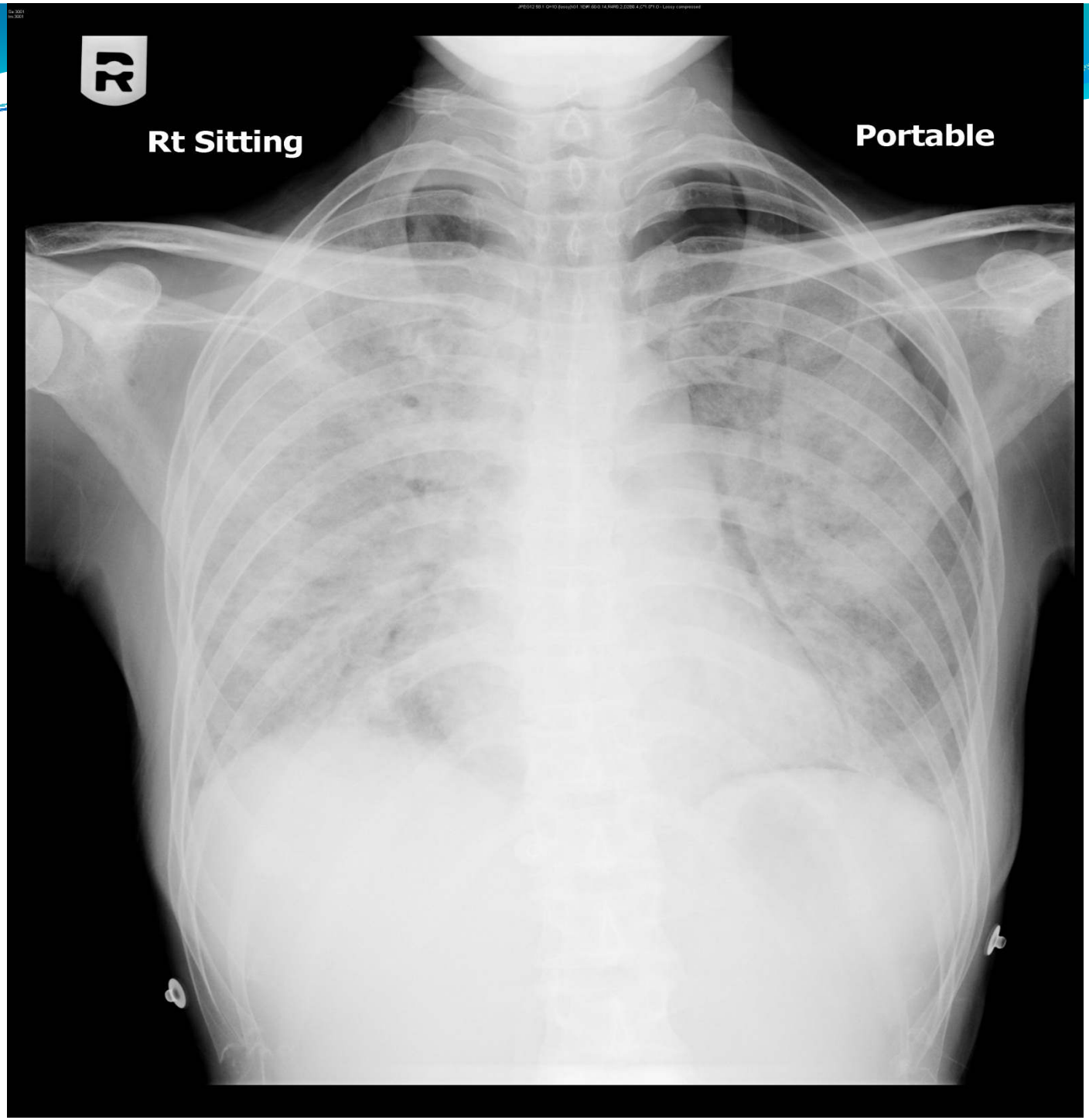
→higher PaO2/ FiO2 ratio at the extreme of FiO2

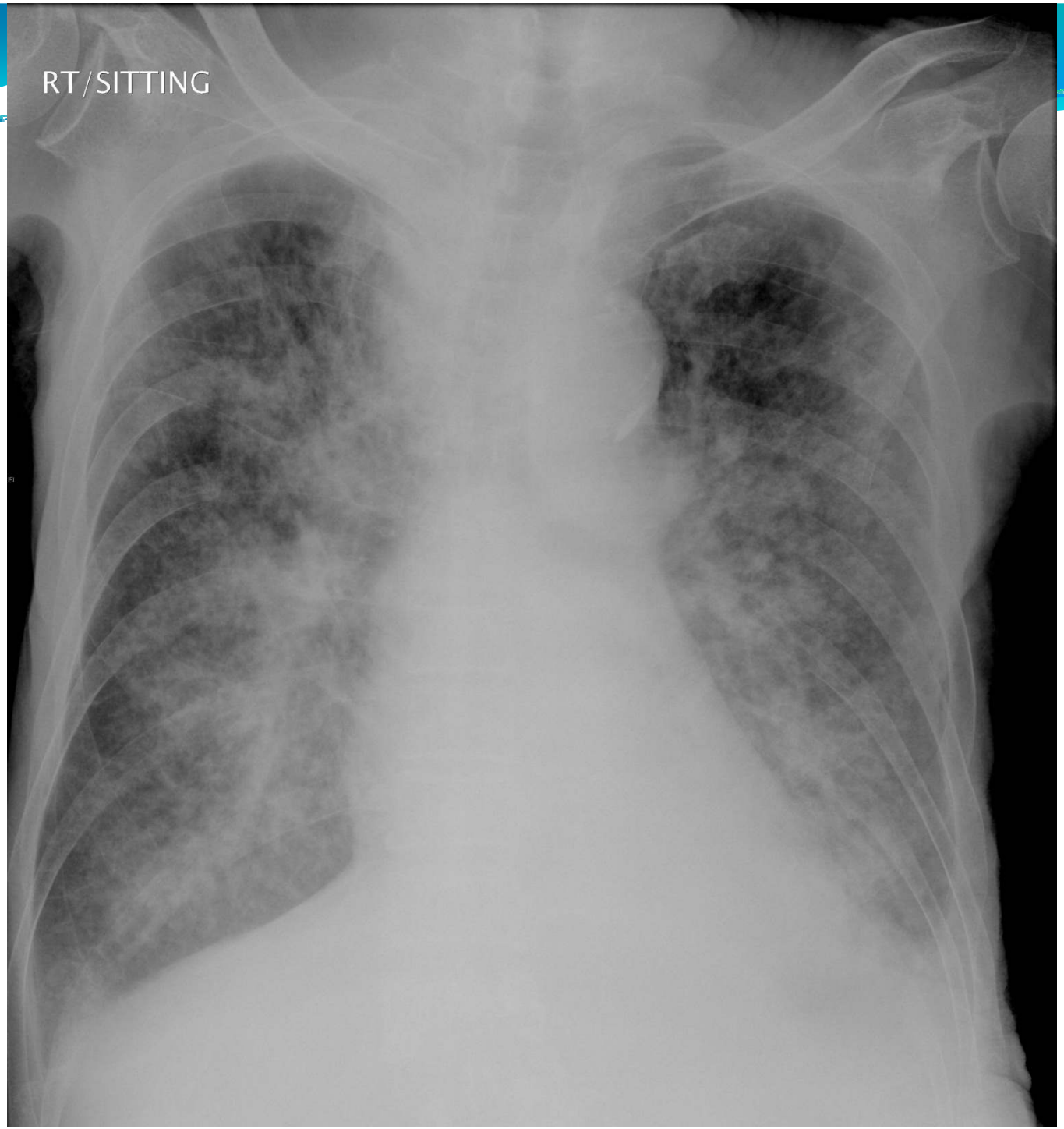
- With more shunt

→ Higher PaO2/ FiO2 at lower FiO2



Gowda et al. Crit Care Med 1997


Rt Sitting
Portable


RT/SITTING

Bilateral infiltrates

- Great inter-observer variability in interpretation
- Infiltrates are not static
- No specified features

Cardiogenic cause be excluded

- Left atrial hypertension is so common in critically ill patient, its presence not excluding ARDS
- PCWP being out of favor
- PA catheter issues

  → optimal site

  → variable readings as affected by airway pressure

Berlin definition (2012)

- Timing: Within one week from known insult
- Imaging: Bilateral infiltrates
- Cause of pulmonary edema: not fully explained by CVS
- Hypoxemia while assessed with PEEP ≥ 5 cm H_2O:
  → mild: PaO_2/ FiO_2 200 to 300 mmHg
  → moderate: PaO_2/ FiO_2 100 to 200 mmHg
  → severe: $PaO_2/ FiO_2 \leq 100$ mmHg

Predictive ability by Berlin definition

	ALI by AECC	ARDS by AECC	Mild by Berlin	Moderate by Berlin	Severe by Berlin
Progression from mild		34%		29%	4%
Progression from moderate					13%
Mortality	26%	37%	27%	32%	45%
Ventilator-free days	20 days	12 days	20 days	16 days	1 day
Ventilator-days for survivors	5 days	7 days	5 days	7 days	9 days

Pathophysiology

Occurs in stages

1. Exudative (Acute Phase)
2. Proliferative
3. Fibrotic
4. Recovery

Exudative Phase

- Damage to epithelia resulting in increased permeability of the barrier

  → influx of protein-rich fluid into alveoli

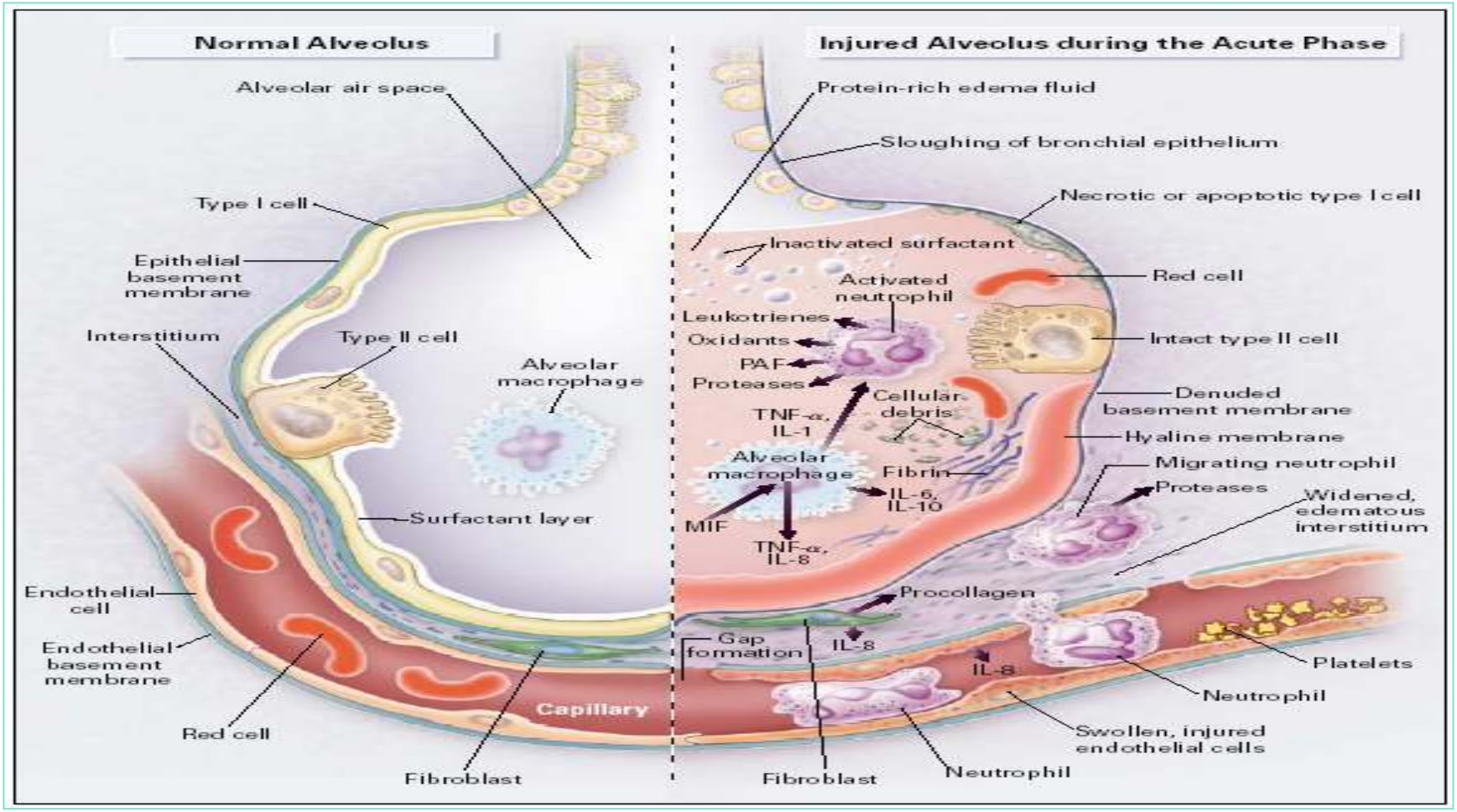
- Injury of Type I cells results loss of epithelial integrity and fluid extravasation (edema)

- Injury of Type II cells then impairs the removal of the edema fluid

Exudative Phase

- Dysfunction of Type II cells also leads to reduced production and turnover of surfactant which leads to alveolar collapse
- If severe injury to epithelium occurs – disorganized/insufficient epithelial repair occurs resulting in fibrosis
- Role of dys-coagulation

Exudative Phase



Fibrotic Phase

- After acute phase, some patient will have uncomplicated course and rapid resolution
- Some cases will progress to fibrotic lung injury
- Such injury occurs histologically as early as 5-7 days

Fibrotic Phase Characteristics

- Intense inflammation leads to obliteration of the normal lung architecture
- Alveolar space is filled with mesenchymal cells and their products
- Re-epithelialization and new blood vessel formation occurs in disorganized manner
- Fibroblasts also proliferate, collagen is deposited resulting in thickening of interstitium

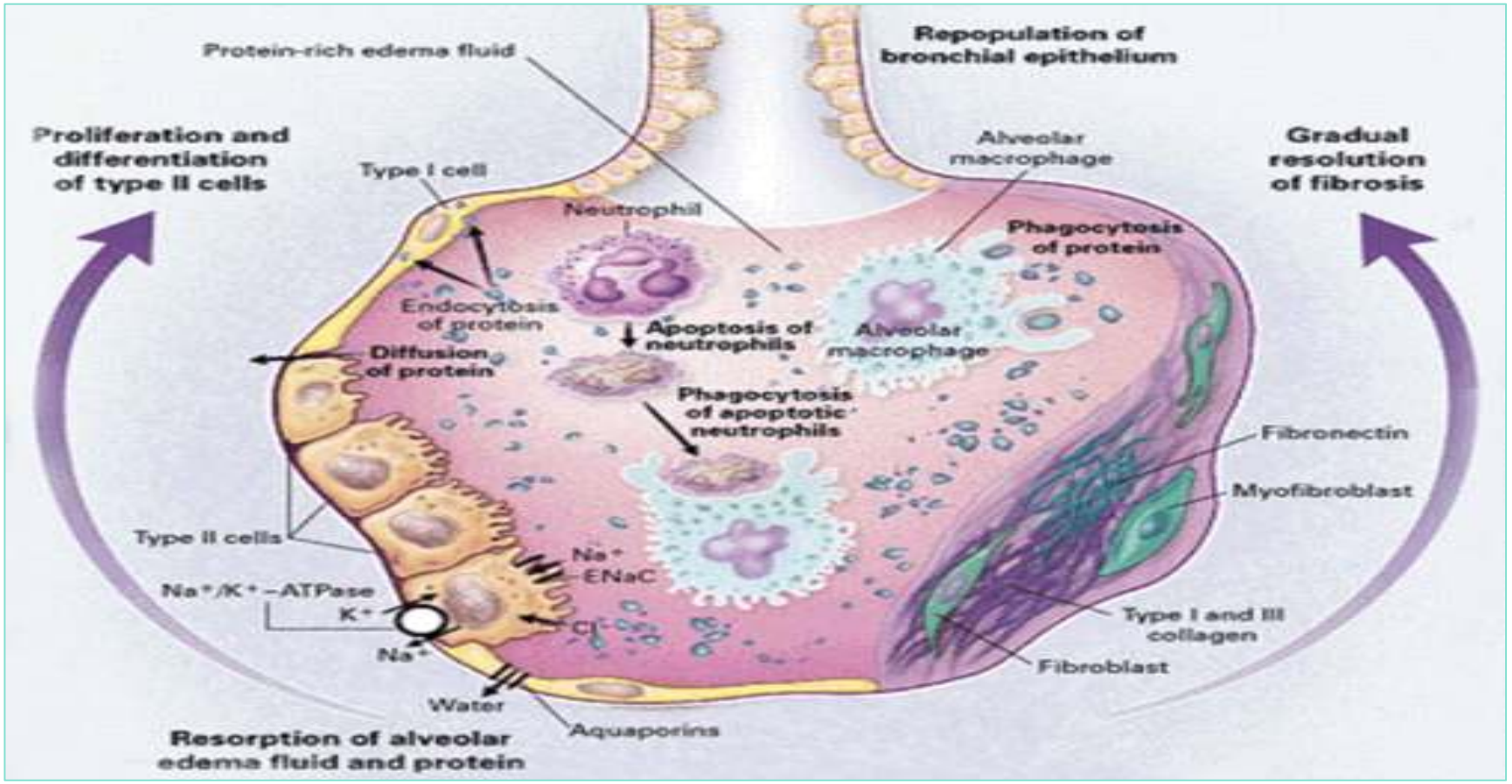
Proliferative Phase

- With intervention (mechanical ventilation) there is clearance of alveolar fluid
- Soluble proteins are removed by diffusion between alveolar epithelial cells
- Insoluble proteins are removed by endocytosis and transcytosis through *epithelial cells* and phagocytosis through *macrophages*

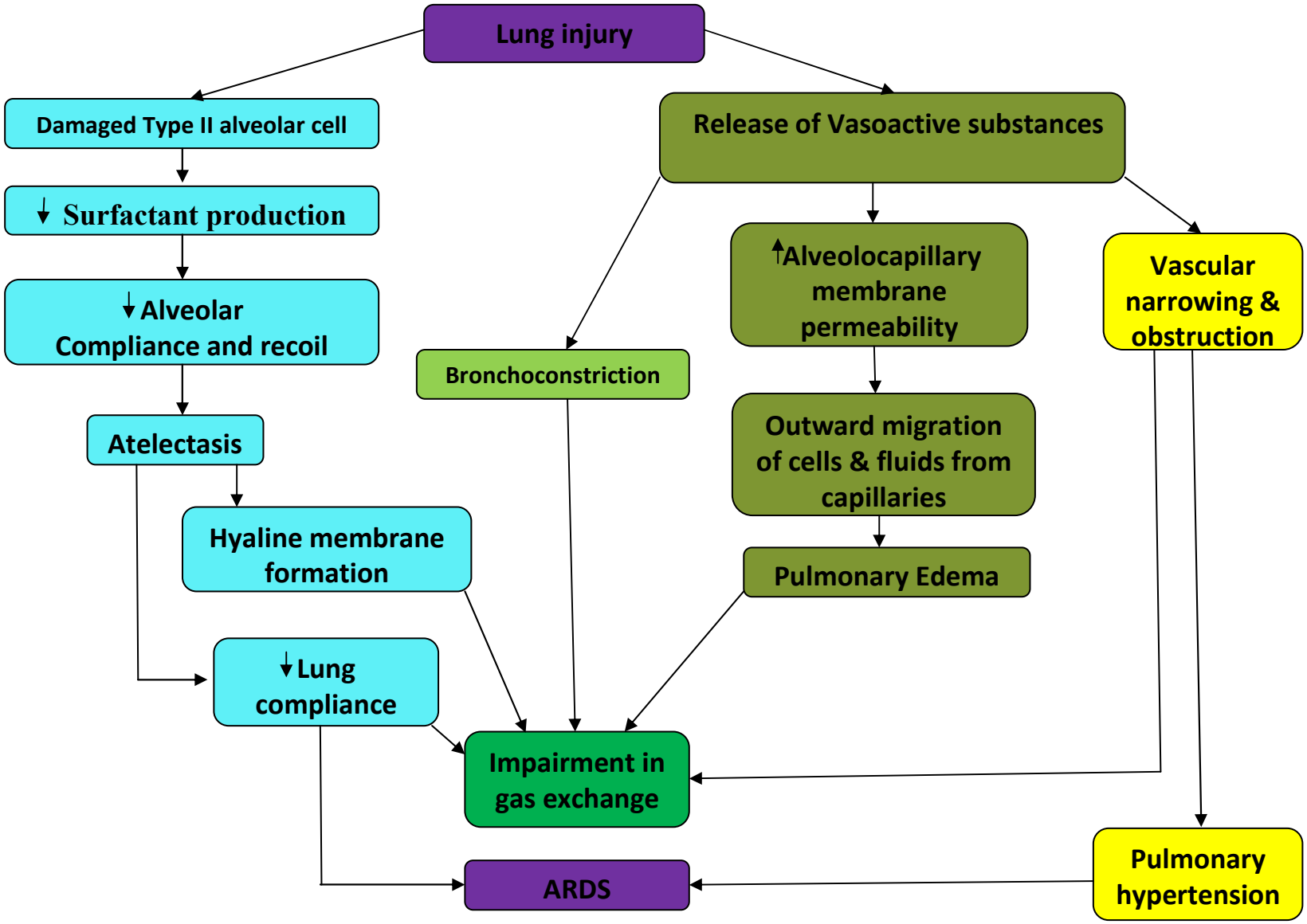
Proliferative Phase

- Type II cells begin to differentiate into Type I cells and re-epithelialize denuded alveolar epithelium
- Further epithelialization leads to increased alveolar clearance

Proliferative Phase



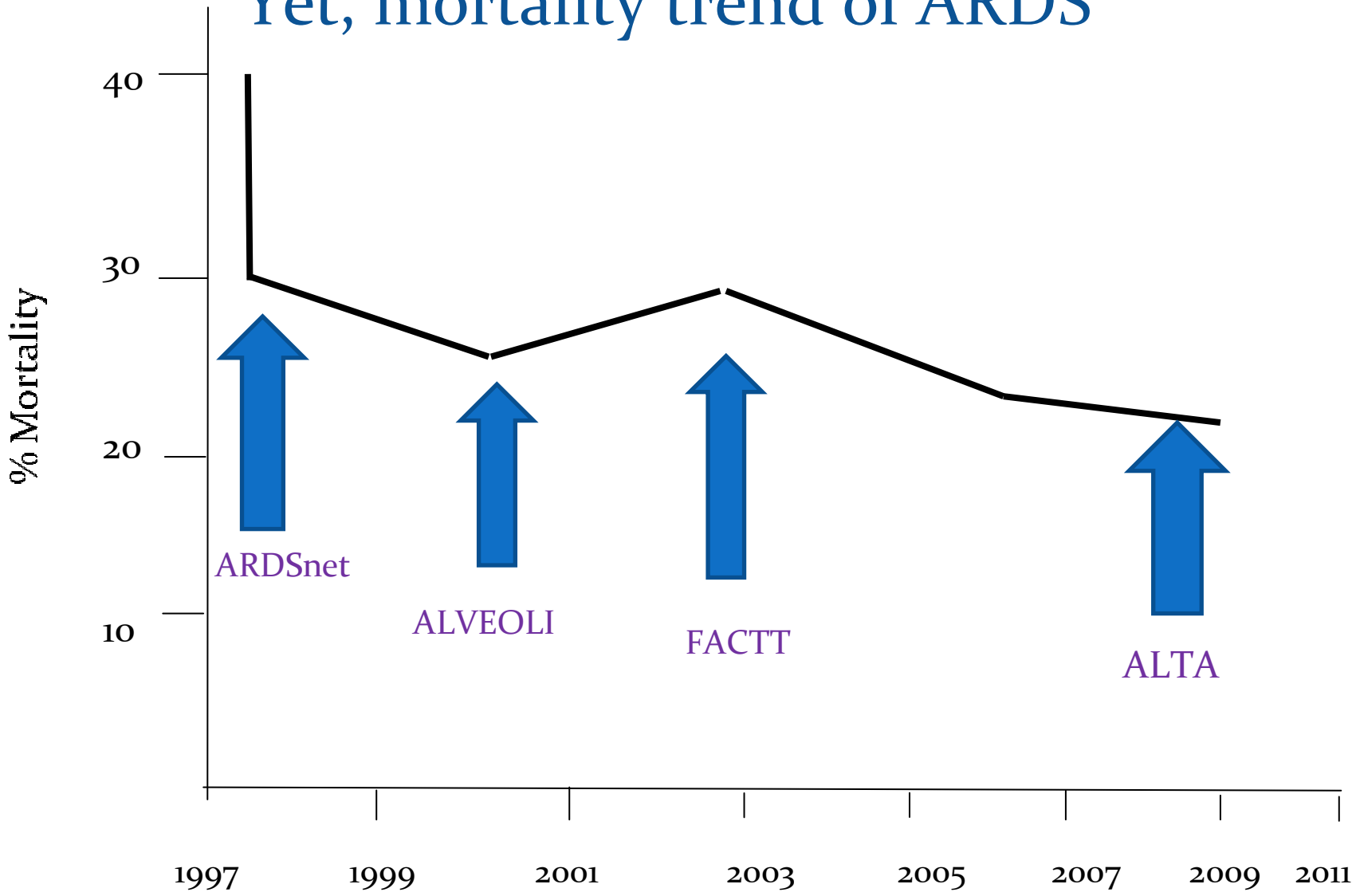
Simplified diagram of ARDS pathophysiology



Do something to retard process

- Surfactant replacement
- Ketoconazole
  - Inhibit thromboxane A2 which is important in platelet aggregation and neutrophil recruitment
- Lysofylline
  - Phosphodiesterase inhibitor with anti-inflammatory effect
- Sivelestat
  - Neutrophil elastase inhibitor
- N-acetylcysteine
  - Replenish Glutathionine
- Steroid??

Yet, mortality trend of ARDS



Study Participants	ARDSNet 2000	Amato et al , 1998	Brochard et al , 1998	Stewart et al , 1998	Brower et al , 1999
No.	861	53	116	120	52
Mean age, y	52	35	57	59	49
Target Tidal volume (mL/kg)	6 vs. 12 PBW	≤6 vs. 12 ABW	6-10 vs. 10-15 DBW	≤8 vs. 10-15 IBW	≤8 vs. 10-12 PBW
Plateau pressure (cm H2O)	30≥vs.50 ≥	20>vs. unlimited	30-25vs.60 ≥	30≥vs.50≥	30≥vs.55-45≥
Actual Tidal volume (ml/ kg)	6.2vs. 11.8	384 vs. ‡ 768	7.1vs. 10.3	7.0vs. 10.7	7.3vs. 10.2
Plateau pressure (cm H2O)	25vs. 33	30vs. 37	26vs. 32	22vs. 27	25vs. 31
mortality% ,	31 vs. 40	38 vs. 71 .	47 vs. 38	50 vs. 47	50 vs. 46
P value	0.007	0.001	0.38	0.72	0.61

The New England
Journal of Medicine

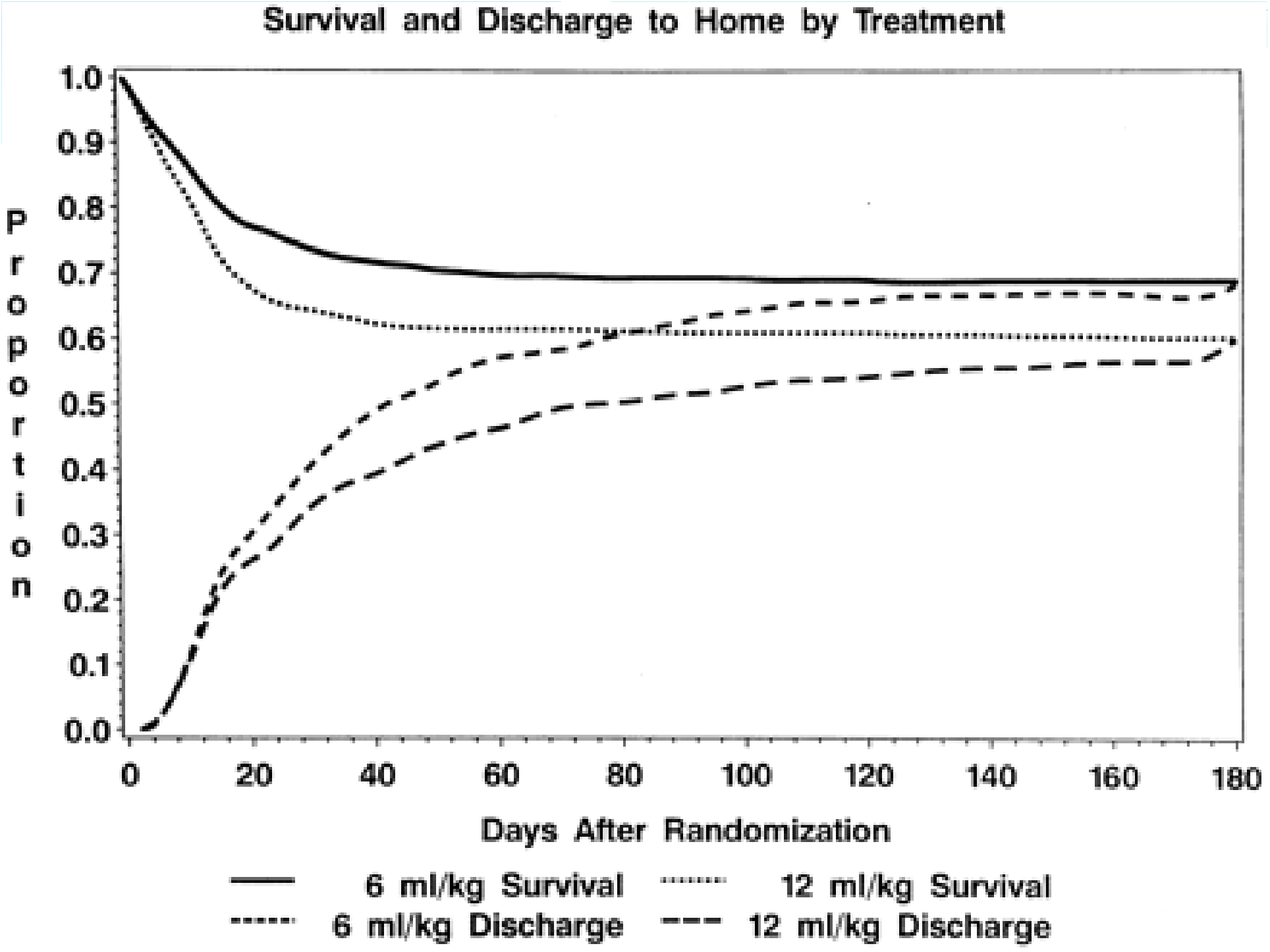
VOLUME 342 MAY 4, 2000 NUMBER 18

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*

- 861 patients with ALI and ARDS
- multicenter, randomized trial
- Tidal volume : 6 ml/kg vs. 12 ml/kg

- Mortality rate:31.0% vs. 39.8% (P=0.007)
- The number of days without ventilator use in the first 28 days: mean 12 ± 11 days vs. 10 ± 11 days (P=0.007)


Survival and Discharge to Home by Treatment
Proportion
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
20
40
60
80
100
120
140
160
180
Days After Randomization
6 ml/kg Survival
12 ml/kg Survival
6 ml/kg Discharge
12 ml/kg Discharge

Details of ARMA protocol

- Initial tidal volume of 8 mL/kg of predicted body weight which is calculated by: [2.3 *(height in inches - 60) + 45.5 for women or + 50 for men]
- Set respiratory rate up to 35 breaths/min to deliver the expected minute ventilation requirement
- Set PEEP to at least 5 cm H_2O, and FiO_2 to maintain SaO_2 of 88-95%
- Over a period of less than 4 hours, reduce tidal volumes to 7 mL/kg, and then to 6 mL/kg.

Why low tidal volume helps

- In rats, more rapid resolution of alveolar edema

  Frank AJRCCM 2002

- Down-regulate pro-inflammatory pathways, as evidenced by lower plasma levels of markers

  Parsons CCM 2005

- May attenuate insult to other major organ

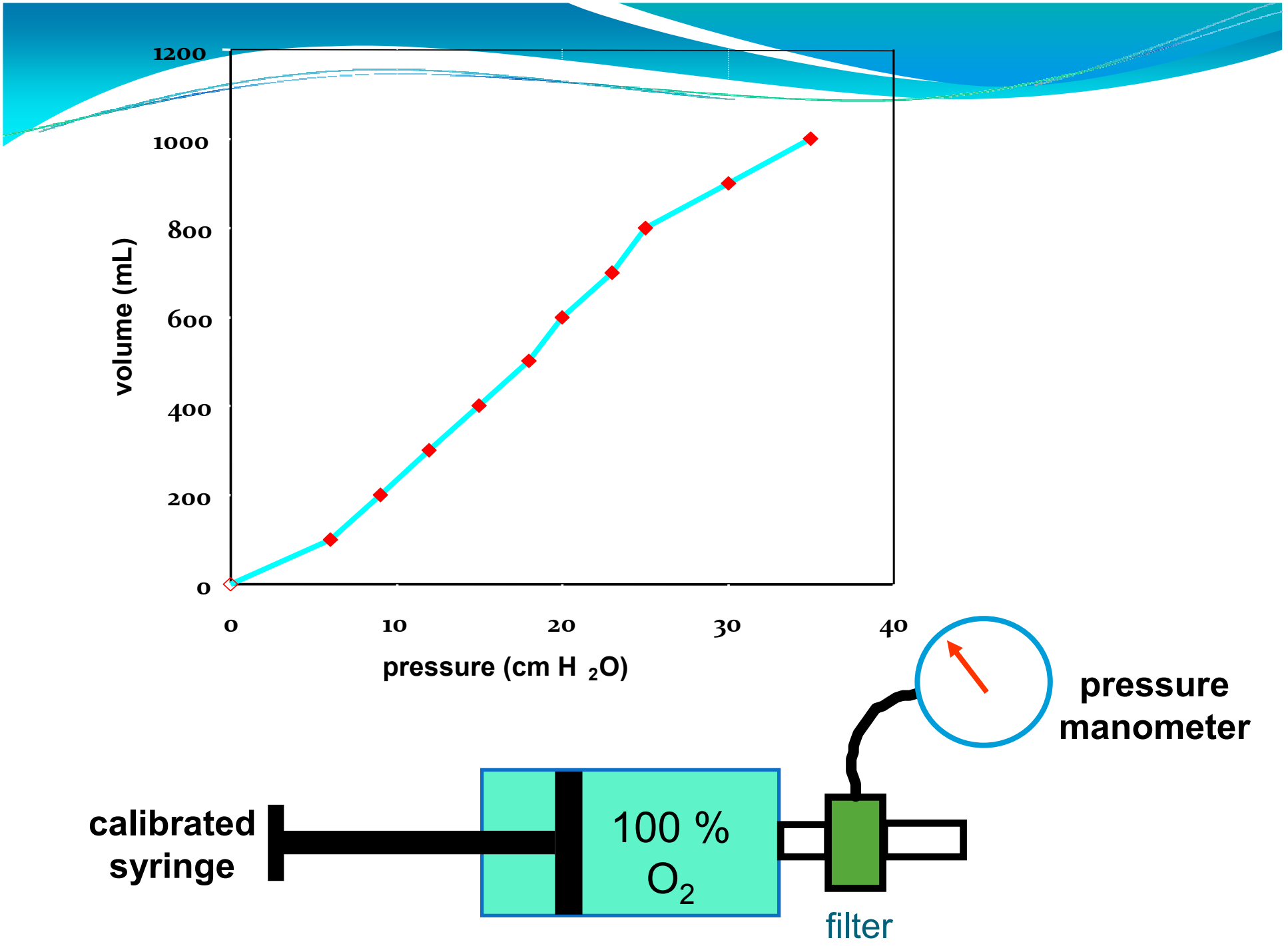
  Imai JAMA 2003

Apart from small tidal volume

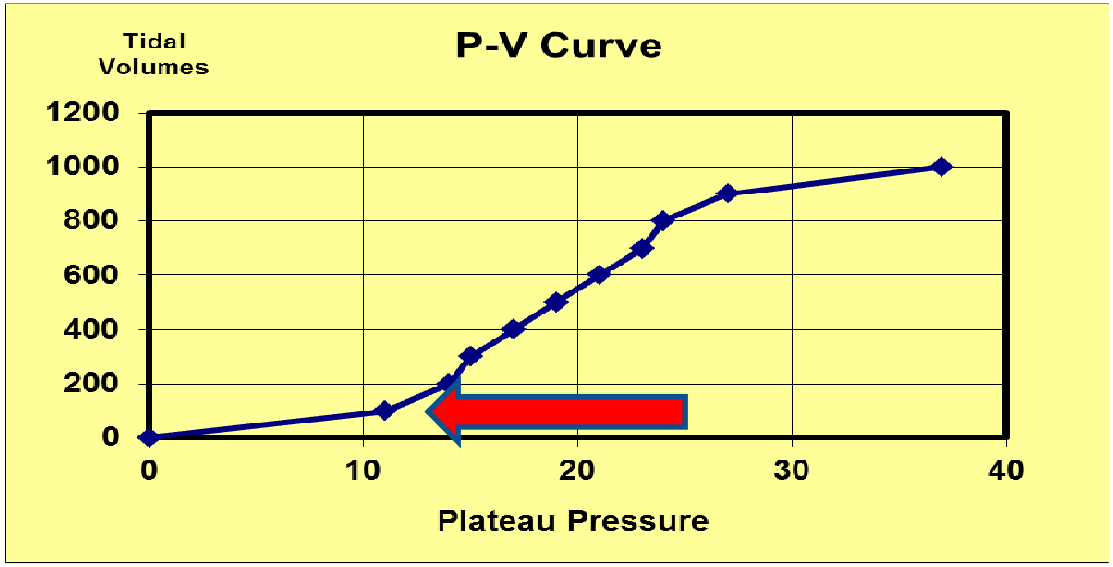
- High PEEP
  - Help prevent atelectasis
  - Help prevent alveolar collapse on exhalation
  - May cause over-distension
  - Improve oxygenation $\neq$ survival benefit
  - Difficulty to obtain an optimal PEEP
  - Haemodynamics concern

Obtaining the static P-V Curve

1. Pre-oxygenate
2. Set resp. rate to 5 per minute
3. Set PEEP to 0
4. Adjust peak flow
5. Change tidal volume (alternate small-large)
6. Set plateau for 1-2 sec. interval
7. Record plateau pressure
8. Return to previous vent settings and wait 1 min.


1200
1000
800
600
400
200
0
volume (mL)
0
10
20
30
40
pressure (cm H 2O)
pressure
manometer
calibrated
syringe
100 %
O2
filter

LIP represents the critical opening pressure of a large number of alveoli



- Set PEEP ≥ 2 cmH2O above LIP

Problem of static PV curve

- Requires sedation and paralysis
- Rather labor-intensive
- The “Inflection points” may not be easily seen
- Problem to get rid of chest wall compliance
- Inter-observer variability can be as great as 11 cmH2O

Scott AJRCCM 2000

What is the extent of the patient's lung injury?	What is the patient' chest wall (C_w) compliance?	
Target PaO_2>60-80 What FiO_2 is required to achieve this?	**NORMAL**	**LOW** -obesity -edema -abdominal hypertension
FiO_2	**Normal C_w Compliance PEEP in cmH_2O**	**Low C_w Compliance PEEP in cmH_2O**
0.3	**5**	**10**
0.4	**8**	**12**
0.5	**10**	**14**
0.6*	**12**	**16**
0.7*	**14**	**18**
0.75*	**16**	**20**
0.8*	**18**	**22**
0.9*	**20**	**22**
1*	**22**	**24**

High PEEP ?evidence

Studies	Sample size	Low PEEP	High PEEP	Death low PEEP	Death high PEEP	Ventilator-free days low PEEP	Ventilator-free days high PEEP
Brower 2004	549	8.3 ± 3.2	13.2 ± 3.5	24.9 %	27.5 %	14.5 ± 10.4	13.8 ± 10.6
Meade 2008	983	9.8 ± 2.7	14.6 ± 3.4	40.4 %	36.4 %	—	—
Mercat 2008	767	8.1 ± 2.0	15.1 ± 4.3	39.0%	35.4 %	7	3

High PEEP in conclusion

- Lacking consensus
- Physiology improvement
- Earlier weaning
- Mortality unaltered

Permissive hypercapnea

- How “permissive” can one be ?
  - Ventilated patients with ARDS appear to tolerate very low blood pH and very high pCO_2
  - Safe to allow pH to fall to at least 7.20.
  - The actual pCO_2 is of little importance.
  - Cautious in presence of
  - Cerebral edema, mass lesions or seizures;
  - Active coronary artery disease; arrhythmias;
  - Hypovolemia; GI bleeding

ADJUNCTS IN TREATMENT OF ARDS

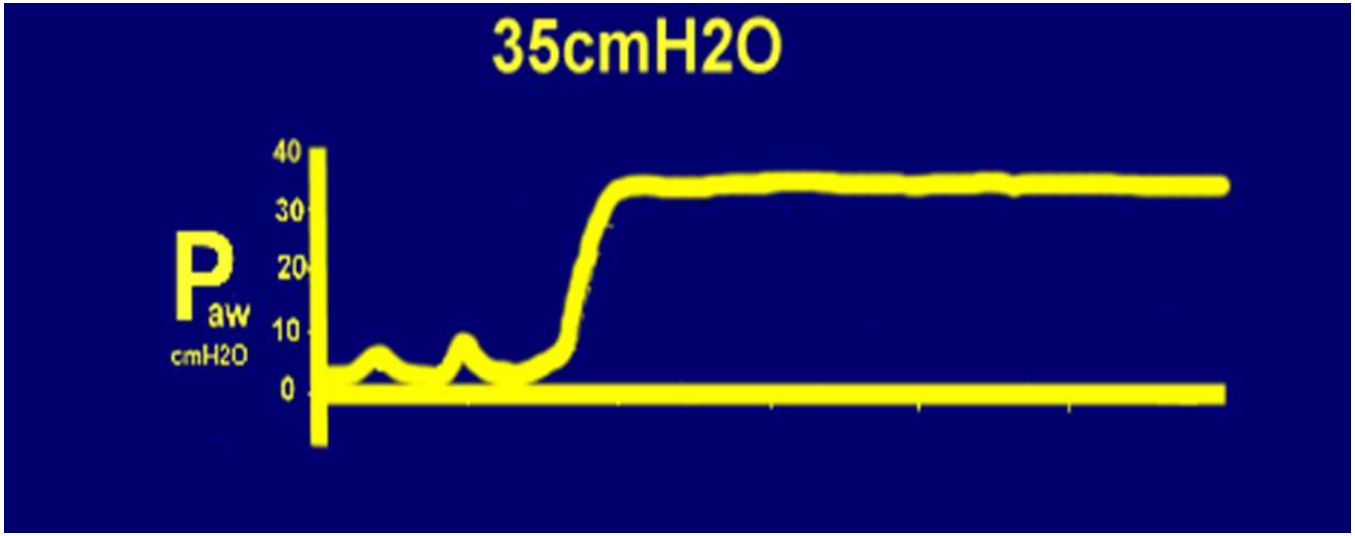
1. Ventilatory Strategies other than Lung Protective Strategy.
   - Recruitment/ NM blocker
   - Prone Ventilation
   - Liquid Ventilation
   - High Frequency Ventilation
   - Tracheal Gas Insufflation
   -
2. Hemodynamic Management – Fluids, Vasopressors
3. Surfactant replacement therapy.
4. Antioxidants – NAC
5. Anti-inflammatory Strategies.
   a) Corticosteroids.
   b) Cycloxygenase & lipoxygenase inhibitors.
   c) Lisofylline and pentoxifylline.

Adjunct: recruitment Maneuvers

- Apneic TLC maneuvers
- Non-apneic TLC maneuvers
- Sigh
- Inverse Ratio Ventilation
- Prone positioning

Apneic TLC maneuvers

- CPAP of 30 cm H2O for 30 - 40 seconds.
- Monitor tidal volume and oxygenation for 15 - 30 min
- May repeat at 35-40 cmH2O if needed



Non- apneic Lung Recruitment

- Resp rate 10/min
- I:E ratio = 1:1.
- PEEP 20 - 40 cm H_2O.
- PCV pressure 10-20 cm H_2O
- Apply for 45 sec. to 2 min.
- Monitor tidal volume and oxygenation for 15 - 30 min.
- If unresponsive, repeat at higher PEEP.

Use of Sighs

- 3 times hour
- Use a fixed tidal volume which produces a Plateau Pressure of 45 cm H2O.
- Help resolve atelectasis in poorly ventilated lung
- May open units with opening pressures > 35 cmH2O.

Pelosi, et al. AJRCCM 1999

Adjunct: Neuromuscular blocker

- Achieve better patient-ventilator synchrony
- Facilitate lung-protective mechanical ventilation
  - Easier adjustment tidal volume and pressure
- Reduced pro-inflammatory process and less systemic cytokine release
- ?Aggravates muscle weakness and prolongs weaning

RCT with NMB for 48 hours

- Papazian NEJM 2010
- Multi-center double-blind
- 340 patients randomized within 48 hours ARDS
- Cisatracurium for 48 hours as intervention arm
- Hazard ratio to die within 90 days 0.68, p 0.04
- Among those PaO2/ FiO2 <150, crude 90-day mortality 30.8% vs. 44.6% for control (p 0.04)
- No difference for acquired paralyisis

PRONE VENTILATION

- Improves oxygenation – allows decrease Fio_2 and PEEP
  - But benefit Variable and not predictable

- Response rate – 50-70%

- Proposed mechanism

  1) Increase FRC
  2) Improved ventilation of previously dependent regions.
     → Weight of heart ?affect ventilation
     → Difference in diaphragmatic movement
     supine : dorsal and ventral portion move symmetrically
     prone : dorsal > ventral
  3) Improvement in Cardiac output
  4) Improves damaged lymphatics

Details of prone

- Consider if ARDS > 24 hrs./ 2nd day of ventilation
- Usually one time per day
- 2 to 20 hours/day.
- Outcome:
  - Improvement in oxygenation
  - Improvement in survival still needs evaluation

PROSEVA Study Group

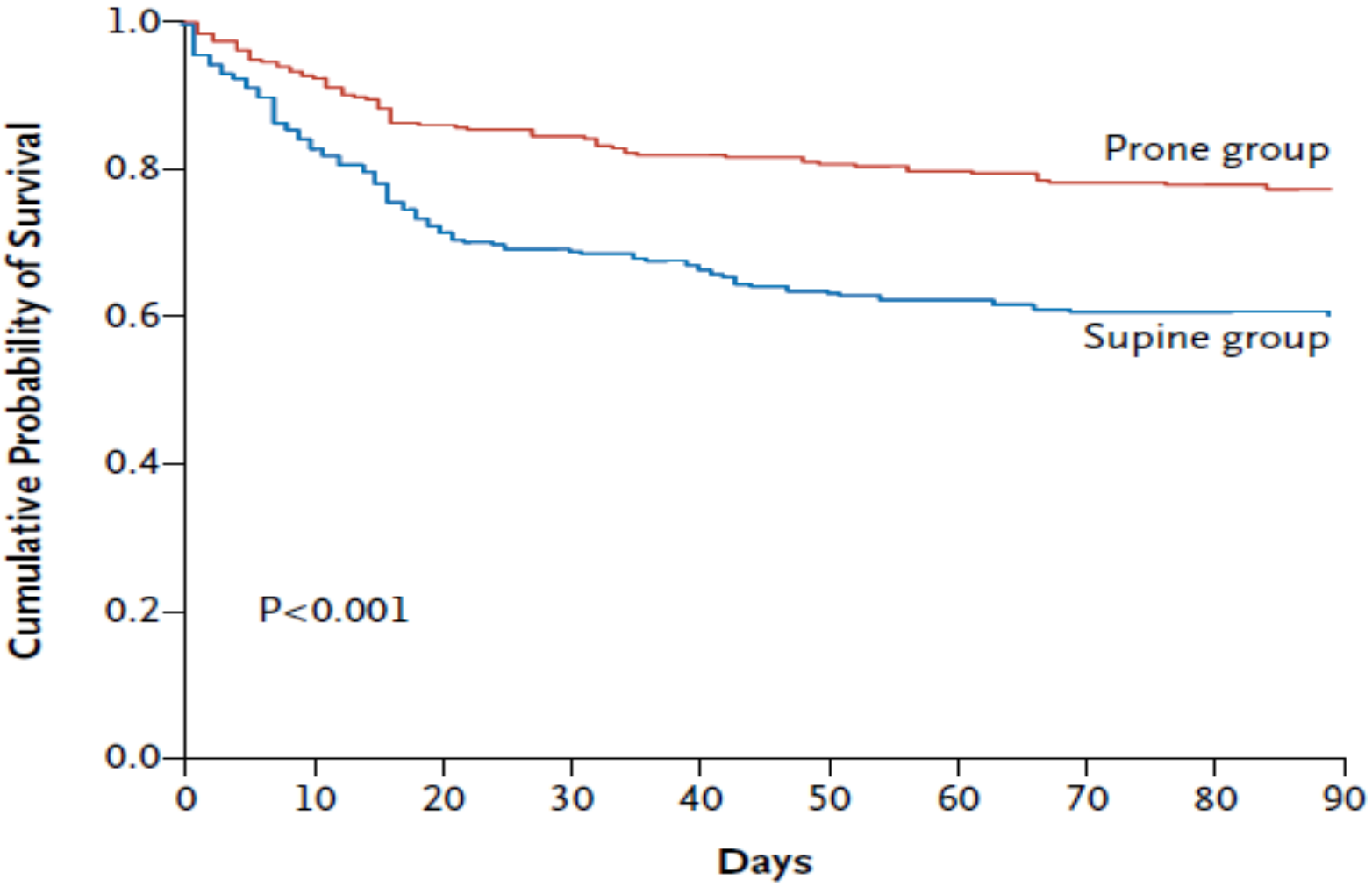
- N Engl J Med 2013; 368:2159-2168
- ARDS patients ventilated for less than 36 hours;
- Severe cases (defined as a PaO2:FiO2 ratio of <150 mm Hg, with an FiO2 of ≥0.6, a PEEP of ≥5 cm of water, and a tidal volume of about 6 ml/ kg of BW
- Prone position for at least 16 consecutive hours
- Criteria for stopping prone treatment :
  - improvement in oxygenation (defined as a PaO2:FiO2 ratio of ≥150 mm Hg, with a PEEP of ≤10 cm of water and an FiO2 of ≤0.6;
  - Decrease in the PaO2:FiO2 ratio of more than 20%, relative to the ratio in the supine position;
  - complications occurring during a prone session
- 229 in the supine group and 237 in the prone group

Results of PROSEVA Study

- Average number of prone sessions was 4±4 per patient, and the mean duration per session was 17±3 hours
- Use of rescue therapies in the supine and prone groups were 2.6% versus 0.8% for ECMO (P=0.14)
- Mortality at day 28 was significantly lower in the prone group than in the supine group: 16.0% (38 of 237 participants) versus 32.8% (75 of 229) (P<0.001)
- After adjustment for the SOFA score and the use of neuromuscular blockers and vasopressors at the time of inclusion, mortality remained significantly lower in the prone group than in the supine group

Table 2. Ventilator Settings, Respiratory-System Mechanics, and Results of Arterial Blood Gas Measurements at the Time of Inclusion in the Study.*

Variable	Supine Group (N = 229)	Prone Group (N = 237)
Tidal volume (ml)	381±66	384±63
Tidal volume (ml per kg of PBW)	6.1±0.6	6.1±0.6
Respiratory frequency (breaths per min)	27±5	27±5
PEEP (cm of water)	10±4	10±3
FIO_2	0.79±0.16	0.79±0.16
$Pplat_{RS}$ (cm of water)	23±5	24±5
Cst_{RS} (ml per cm of water)	35±15	36±23
PaO_2 (mm Hg)	80±18	80±19
PaO_2:FIO_2 (mm Hg)	100±20	100±30
$PaCO_2$ (mm Hg)	52±32	50±14
Arterial pH	7.30±0.10	7.30±0.10
Plasma bicarbonate (mmol per liter)†	25±5	25±5



No. at Risk					
Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

Figure 2. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.

Optimization of fluid

- Dilemma between adequate tissue perfusion of other vital organs and aggravating alveolar fluid accumulation/ pulmonary edema in ARDS

- Defective alveolar fluid clearance is one key pathophysiology process

Fluid and Catheter Treatment Trial

- NEJM 2006; 354: 2564-75
- ARDS clinical trials network
- Prospective randomized multi-center trial
- Included intubated patients with $PaO_2/FiO_2 < 300$
- Excluded patients with established ARDS more than 48 hours, and those with chronic conditions which may independently affect survival

Randomization

- One group with liberal fluid and another with conservative fluid management
- Simultaneously randomly assigned to receive PA catheter or central venous pressure monitor
- Hemodynamics management for 7 days or until 12 hours post-extubation
- Ventilated according to ARDS network protocol
- Weaning protocol used

Results of FACTT

- 503 patients in conservative fluid group and 498 patients in liberal fluid management
- Comparable demographics, percentage of pulmonary cause, APACEH III score and ventilation strategy
- 91% compliance rate to protocol in conservative fluid group, comparing to 88% in liberal group
- Seven-day cumulative fluid balance was –136±491 ml in the conservative-strategy group, as compared with 6992±502 ml in the liberal-strategy group ($P<0.001$)
- Lower MAP for conservative group (81 vs. 84 mmHg)

Outcomes

	Conservative	Liberal	P value
60d Mortality (%)	25.5	28.4	0.30
Ventilator-free day (Day 1 – 28)	14.6 ± 0.5	12.1 ± 0.5	< 0.001
ICU-free day (Day 1 – 28)	13.4 ± 0.4	11.2 ± 0.4	< 0.001
60d Dialysis days	11.0 ± 1.7	10.9 ± 1.4	0.96
60d Dialysis patient (%)	10	14	0.06

What we learnt from FACTT

- Conservative fluid strategy led to insignificant reduction of mortaliuty

- Conservative strategy improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing non-pulmonary organ failures

- Choice between PA catheter and central venous pressure line is not the key issue

Role of beta2-agonist

- Beta-2 agonist acts on many cellular pathways involved in ARDS, reducing neutrophil sequestration and pro-inflammatory cytokines in vivo
- Epithelial cells beta-2 receptors activation leads to acceleration of sodium transport thus fluid absorption

- BALTI showed reduction of extravascular lung water and plateau airway pressure after salbutamol infusion
- ALTA prematurely stopped as aerosolized Albuterol led to futility in ventilator-free days reduction

BALTI 2

- Multi-center double-blinded, placebo-controlled
- 46 ICUs in UK
- Included intubated patients within 72 hour of ARDS
- Intervention group: 15 microgram/ kg ideal BW/ hour. Rate adjusted according to protocol if tachycardia >140. Aim at 7 days infusion
- Intention to treat analysis
- Primary outcome: mortality within 28 days

BALT 2 results

- Recruitment was stopped because interim analysis suggested more death in treatment group
- 162 patients at intervention and 164 at placebo group
- Median PaO_2/ FiO_2 in salbutamol infusion group is 103.5 ± 36.75 vs. 103.5 ± 36.75 for placebo
- Comparable demographics, APACHE II and percentage of pulmonary cause of ARDS

BALT 2 Outcomes

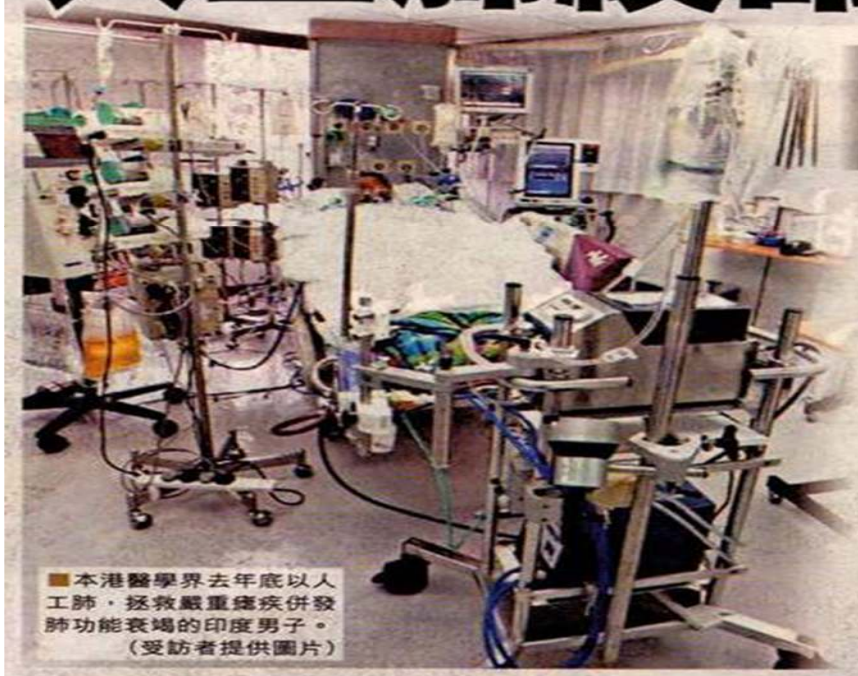
	Salbutamol	Placebo	RR or difference
28d mortality	34%	23%	**1.47**
Death in ICU	36%	28%	1.31
Ventilator-free days	8.5 ± 8.8	11.1 ± 9.3	**-2.7 ± 2.0**
Organ failure-free days	16.2 ± 10.7	18.5 ± 9.8	**-2.3 ± 2.2**
ICU stay	17.6 ± 14.3	17.1 ± 14.0	0.5
Tachycardia to stop treatment	14%	1%	11.71
Arrhythmia to stop treatment	9%	2%	4.75

What we learnt from BALT 2

- Early intravenous salbutamol infusion unlikely to help in ARDS
- Poorly tolerated
- Possible dose-related toxicity
- Causes of death uncertain

將血液體外加氧送回　讓心肺暫休息

人工肺續命 存活增兩成



■本港醫學界去年底以人工肺，拯救嚴重瘧疾併發肺功能衰竭的印度男子。（受訪者提供圖片）

受嚴重肺炎、肺纖維化或禽流感侵襲的病人，可出現急性肺功能衰竭，導致氧氣無法進入血液，最終因多重器官衰竭死亡。本港近年引入俗稱「人工肺」的體外膜氧合器（ECMO），將病人血液於體外加氧再送回體內，暫代心肺功能，病人存活率可提高近兩成。

香港港安醫院呼吸系統科專科醫生曾華德指，若肺部嚴重纖維化，或感染禽流感、豬流感、沙士及瘧疾等併發嚴重肺炎，可致肺部喪失功能，阻礙氧氣進入血液，引發多重器官衰竭。

以往此類病人只可「插喉」，以呼吸機將氧氣泵入肺部，惟若肺部已嚴重損壞，插喉未必有用，甚至可能「泵爆肺」。

四公院用於10病人

本港醫學界自沙士後引入人工肺以治療嚴重肺病患者，曾華德解釋，人工肺可模擬心肺循環系統，先將病人血液引流體外，利用氧合器及氣體混合器將氧氣溶入血液及抽出二氧化碳，再將血液加熱送回體內。

人工肺雖無直接治療作用，但可替病人「買時間」，讓心肺得以暫時休息，務求撐至心肺功能恢復或接受心肺移植。

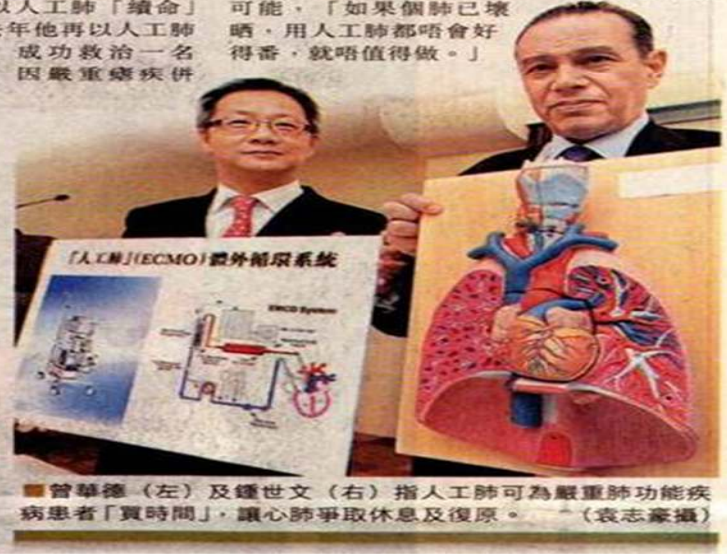
他在〇七年進行本港首宗以人工肺治療急性肺炎個案，患者以人工肺「續命」四星期，惜最終不治；去年他再以人工肺成功救治一名因嚴重瘧疾併發肺、肝及腎衰竭的印度男子，為全球首宗案例。公立醫院方面，威爾斯親王醫院、東區醫院、屯門醫院及伊利沙伯醫院已引入人工肺，至今用於約十名病人。

英國一項橫跨六年的研究指，一百八十名嚴重肺病病人中，使用人工肺的患者存活率為六成三，比沒用人工肺的患者高近兩成。

去年人類豬流感肆虐期間，澳洲及新西蘭六十八名急性呼吸窘迫症患者使用人工肺後，存活率由五成提升至七成一，惟分別有五成四及六成二人有出血性及感染性併發症。

私院兩例無併發症

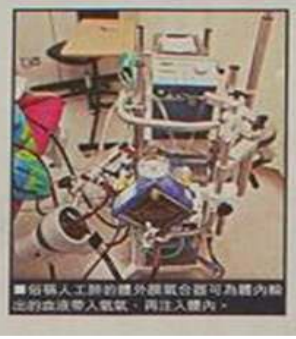
曾華德指併發症風險與各地使用人工肺經驗有關，本港私家醫院至今進行的兩宗病例，均無出現人工肺引致的併發症。接受人工肺治療的病人，必須未有嚴重休克及多重器官衰竭，以及心肺衰竭有逆轉可能，「如果個肺已壞晒，用人工肺都唔會好得番，就唔值得做。」



■曾華德（左）及鍾世文（右）指人工肺可為嚴重肺功能疾病患者「買時間」，讓心肺爭取休息及復原。（袁志豪攝）

肺功能衰竭令其他器官壞死

人工肺吊命 存活率七成



■俗稱人工肺的體外膜氧合器可為體內輸出的血液帶入氧氣，再注入體內。

【本報訊】呼吸系統疾病可導致急性肺功能衰竭，身體器官可能因缺氧和衰竭，甚至致命。本港多間公立和私營醫院近年引入俗稱人工肺的體外膜氧合器（ECMO），仿照呼吸循環系統，代替肺部把氧氣帶入血液，為肺衰竭的病人「買時間」避免器官衰竭，減低死亡率。　　記者：林家華

目前本港有七間醫院應用人工肺治療，包括威爾斯親王醫院、聯合醫院、東區醫院、屯門醫院、伊利沙伯醫院、港安醫院和養和醫院，港安醫院呼吸系統專科曾華德醫生指，肺炎、肺纖維化、禽流感和沙士等呼吸系統疾病，嚴重影響肺功能，令血液含氧量下降，導致身體其他器官衰竭，甚至死亡。

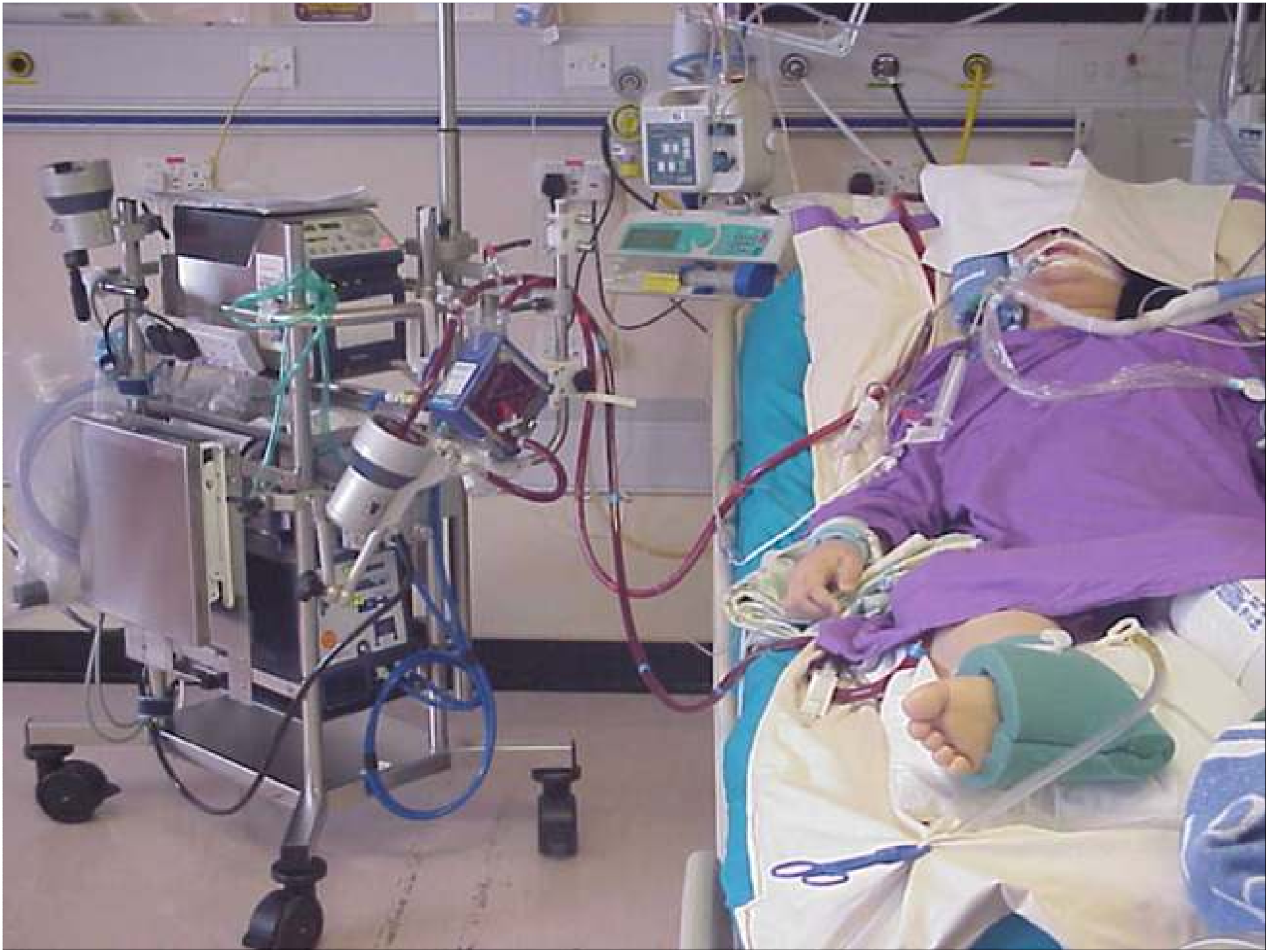
每日收費約三萬元

曾華德指往往需以注射藥物用於病情治療，現應用於急性肺功能衰竭疾病，是在病人體的靜脈流出血液，經人工肺將氧氣帶入血液中，同時帶走血液中的二氧化碳，再將血液帶回大動脈，其好處在於可讓病人「買時間」，令肺部恢復健康，然後可移除儀器，病人需同時使用呼吸機，維持肺部正常運作，但如患者已出現多重器官衰竭，晚期惡性腫瘤，腦部缺氧等則不適用。病人於該院使用人工肺每日收費約3萬元，較使用呼吸機昂貴近3倍。

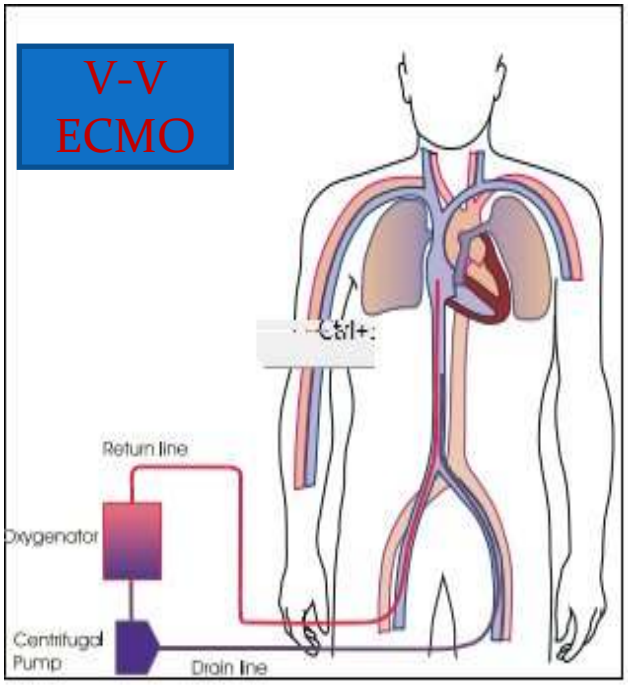
他指傳統使用呼吸機輔助病人呼吸，為功能受損的肺部提供氧份，讓今肺部得以獲充分充足休息，有機會引致肺炎加劇或肺水腫等併發症，如肺功能嚴重受損，醫生注入高濃度氧氣，會增加病人氧氣中毒的風險。

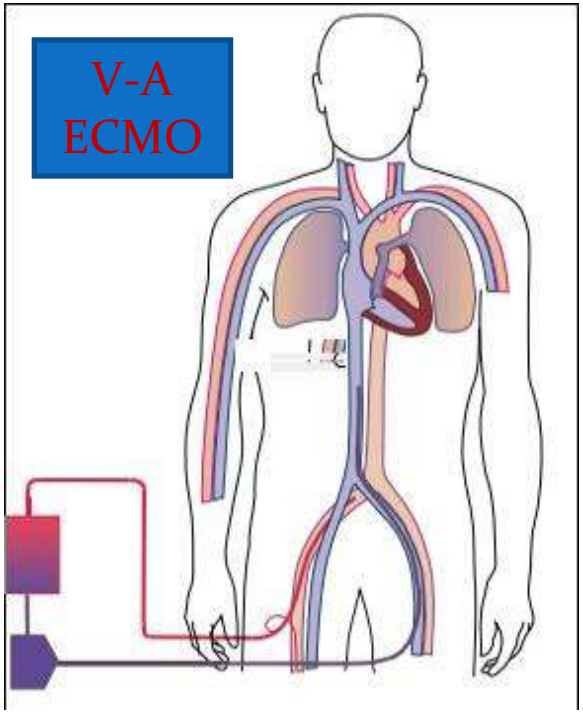
根據去年澳洲和新西蘭一份研究，在H1N1甲型流感爆發期間，64名因流感併發急性呼吸衰竭症候群，發現使用人工肺存活率達七成，較傳統治療五成高，但逾五成人有出血性併發症，包括出血、凝血、血小板減少症等，六成人出現感染性併發症。

07年一名20歲老翁因肺纖維化呼吸困難入院，是首宗使用人工肺用作治療急性肺炎個案，他使用人工肺兩星期後治療，後因心臟病病死亡。去年一名38歲印度男子，患嚴性瘧疾引致急性呼吸窘迫症，使用人工肺後康復出院。



Types of ECMO





Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

Inclusion criteria

- Age 18-65 years
- Reasonable long term outlook
- IPPV < 7 days
- Reversible pathology
- Optimal conventional treatment tried
- Murray score 3.0 or higher
- Uncompensated hyperpnoea with pH < 7.2

Exclusion criteria

- Had been on high peak inspiratory pressure > 30 cmH_2O or high FiO_2 > 0.8 for more than 7 days

- Contraindication for anticoagulation
- Contraindication for active treatment

Management

- Conventional group:
  - Specific management protocol not mandatory
  - Advised to ventilate at tidal volume of 4-8ml/kg BW
  - Keep plateau pressure less than 30cm H2O
- ECMO group
  - 12 hours standard ARDS treatment protocol
  - If FiO2 > 90% to achieve SaO2 > 90% or respiratory acidosis with pH < 7.2, ECMO will be started
- 90 patients in each group

  → 68 (75%) actually put on ECMO

Outcomes in CESAR

- Among 90 patients in ECMO group, 63% survived to 6 months compared to 47% in conventional group (RR 0.69; p=0.03).

- Number needed to treat for one extra survival is 6

Cost estimation

- Median length of stay of adult ECMO patients is 14 days (range 0-41days). Ideally specialist to patient ration 2:1

- Daily cost for conventional care for severe respiratory failure is £1500 -£2300 (Sheffield Health care costing system)

- Total cost per case £27000 - £63000

Future direction

- ECMO
  - Best population and longterm outlook
- Immunonutrition
  - Fish oil enriched formula
- Exogenous surfactants
  - Extrapolate benefit from newborn/ infant
- Gene therapy
  - Target Na/K/ATPase, anti-inflammatory cytokines
- Mesenchymal stem cells
  - Ex vivo human lung models: improved alveolar fluid clearance

Conclusion

- ARDS is still evolving in definition and case finding
- Lung protective strategy improves survival
- Significant controversy in optimal PEEP
- Specific agent to halt the process is unknown
- Adjunct appears important, including fluid management optimization
- ECMO provides another option which however requires closed follow of the long term outlook
- Future studies for innovative treatment is needed