QUADRO CLINICO DI INSUFFICIENZA RESPIRATORIA ACUTA INFLUENZA CORRELATA

FOCUS ON: INFLUENZA 2017-2018

Ezio Bonanomi

Anestesia e Rianimazione 5 – Pediatrica

Ospedale Papa Giovanni XXIII Bergamo

LA CONFERENZA PERMANENTE PER I RAPPORTI TRA LO STATO, LE REGIONI E LE PROVINCE AUTONOME DI TRENTO E BOLZANO

Nella odierna seduta del **5 novembre 2009**: […]
Considerata la diffusione al territorio italiano della influenza da nuovo virus pandemico A(H1N1), che rappresenta una minaccia per la salute pubblica, e per la quale l'Organizzazione Mondiale della Sanita' in data 11 giugno 2009 ha dichiarato il passaggio alla Fase 6 di allerta pandemico globale, con indicazione agli Stati membri per l'attuazione di quanto previsto dai rispettivi Piani pandemici nazionali; […]
Rilevato che nella presente pandemia da virus influenzale A(H1N1) si e' evidenziata, in altri Paesi, un'incidenza significativa di complicanze a carico dell'apparato respiratorio e, in particolare, di **polmoniti a rapida evoluzione in Acute Respiratory Distress Syndrome (ARDS);**
Rilevato, inoltre, che tale complicanza si manifesta prevalentemente in soggetti giovani adulti, anche privi di preesistente o concomitante comorbidita' o fattore di rischio;
Rilevato, infine, che il **tempestivo ed opportuno trattamento con ECMO therapy delle forme piu' severe di ARDS refrattaria alle terapie convenzionali ed alla ventilazione meccanica** puo' portare ad un contenimento del tasso di mortalita';
Considerato che, in previsione di un possibile picco epidemico e, dunque, di un potenziale aumento dei pazienti affetti da complicanze gravi della infezione da virus influenzale A(H1N1), **in Italia e' necessario predisporre un sistema che consenta la migliore gestione di tali casi gravi**;
Rilevata la necessita' di costituire, a livello regionale e nazionale, una rete di centri che disponendo dei requisiti per la corretta applicazione della terapia ECMO a fini respiratori, […]

Art. 1 1. Al fine di fronteggiare adeguatamente il corrente **evento pandemico da virus A(H1N1), e' istituita la Rete nazionale per la gestione della sindrome da insufficienza respiratoria acuta grave da polmoniti da virus A(H1N1) e l'eventuale utilizzo della terapia ECMO.**

2. La Rete di cui al comma 1 e' costituita dalle **strutture specialistiche** dei seguenti Centri:

- Azienda ospedaliera universitaria San Giovanni Battista di Torino - Molinette; Azienda ospedaliera San Gerardo di Monza;
- IRCCS Ospedale Maggiore-Policlinico di Milano;
- IRCCS San Raffaele di Milano; IRCCS Policlinico San Matteo di Pavia;
- Azienda ospedaliera Bergamo;
- Azienda ospedaliera di Padova;
- Policlinico S. Orsola Malpighi di Bologna;
- Azienda ospedaliera universitaria Careggi di Firenze;
- Policlinico Gemelli di Roma;
- Policlinico Umberto I di Roma;
- Azienda ospedaliera universitaria Federico II di Napoli;
- Azienda ospedaliera universitaria Policlinico di Bari;
- ISMETT di Palermo.

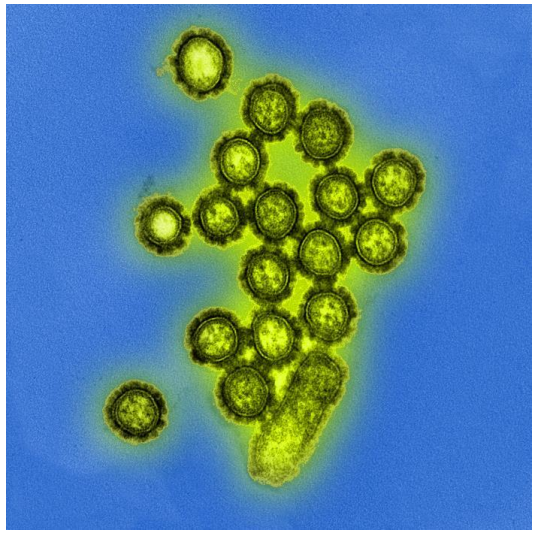
3. Ulteriori Centri, dotati della specifica competenza, potranno essere inseriti nell'elenco di cui al comma 2, su proposta delle regioni.

La **Rete Specializzata nell'Insufficienza Respiratoria Acuta è nata nel 2009 su iniziativa del Ministero della Sanità** per centralizzare i pazienti con **ARDS** e dare supporto alle terapie intensive italiane nella gestione di questi pazienti.
Vengono riconosciuti 17 centri **ECMO** localizzati su tutto il territorio nazionale.
Centri pediatrici di riferimento sono Bergamo (Ospedale Papa Giovanni XXIII) per il Nord e Roma (Ospedale Bambino Gesù) per il Centro e Sud Italia.

Respiratory failure is the most common cause of death in severe cases

CLINICAL RESPIRATORY MANIFESTATIONS:

- Upper respiratory tract infections
- Desquamative bronchiolitis
- Primary viral pneumonia
- Secondary bacteria pneumonia:
  - ✓ Streptococcus pneumoniae,
  - ✓ Streptococcus pyogenes
  - ✓ Staphylococcus aureus
  - ✓ Haemophius influenzae
- Hemorrhagic bronchitis
- Necrotizing pneumonia (Panton-Valentine leukocidin (PVL)-producing Staphylococcus aureus)



- **ARDS**

HIGH-RISK GROUPS:

- Young children (< 5 years)
- Elderly (> 60 years)
- Immunocompromised
- Pregnant female (third trimester)
- Comorbidities (bronchial ashma, chronic lung diseases, heart diseases, diabetes mellitus, obesity or neuromuscolar disease)

ARDS definition

RDS : Respiratory Distress Sindrome

VALI : ventilator associated lung injury

ILI : Influenza like illness

ALI : Acute Lung Injury

RS Respiratory distress

PARDS : Pediatric Acute Respiratory Sindrome

VARI : viral acute respiratory infection

ARDS : Acute Respiratory Distress Sindrome

ARDS : Adult Respiratory Distress Syndrome

ARI : Acute Respiratory Infection

ARI : Acute Respiratory illness

CAP Community-Acquired Pneumonia

ARDS – History

- **«Acute Respiratory Distress in Adult»** by Ashbaugh in Lancet in**1967**
  - 12 adult patients with clinical and pathological symptoms similar to infant respiratory distress syndrome (**RDS**) → **Adult respiratory distress syndrome (ARDS)**
  - Dyspnea, cyanosis resistant to supplemental oxygen and **bilateral chest infiltrates on chest radiography**.
  - ***«Positive end-expiratory pressure (PEEP)*** *was most helpful in combating atelectasis»*

Lancet 1967 Aug 12; 2 (7511):319-323

- **American – European Consensus Conference on ARDS** in **1994**
  - **Acute Respiratory Distress Syndrome**
  - Formal definition
  - **ALI** (acute lung injury)

Intensive Care Med. 1994 20(3):225-32

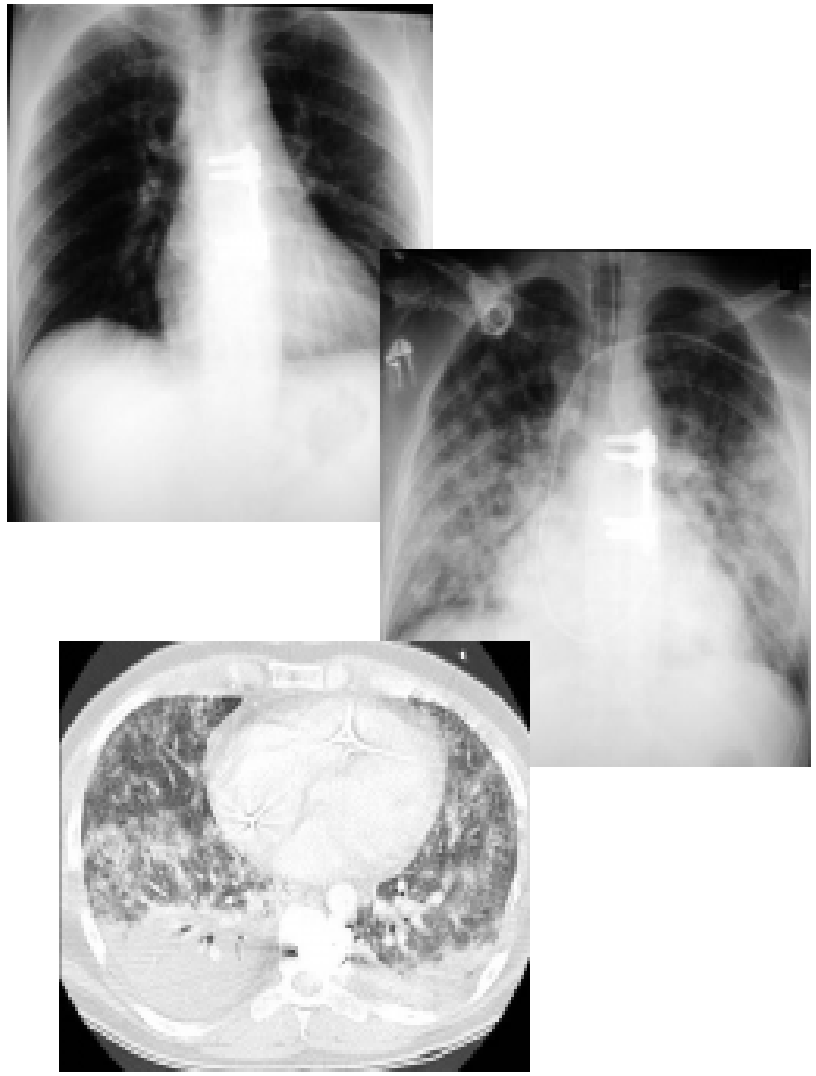
ARDS definition

ARDS – AECC Definition 1994

The American European Consensus Conference Definitions of ALI and ARDS

SYNDROME

- **Acute onset**
- **PaO2/FiO2** (regardless PEEP level)
  - **< 300** mmHg: **Acute Lung Injury (ALI)**
  - **<200** mmHg: **Acute Respiratory distress Syndrome (ARDS)**
- **Bilateral infiltrates** seen on frontal chest radiograph
- Pulmonary artery **wedge < 18 mmHg** or no clinical evidence of left atrial hypertension



Intensive Care Med. 1994 20(3):225-32

ARDS definition

ARDS – BERLIN Definition 2012

- **acute**, meaning onset over 1 week or less
- **bilateral opacities** consistent with pulmonary edema must be present and may be detected on CT or chest radiograph
- **PaO2/FiO2 <300mmHg with a minimum of 5 cmH20 PEEP** (or CPAP)
- **"must not be fully explained by cardiac failure or fluid overload,"** in the physician's best estimation using available information — an "objective assessment" (e.g. echocardiogram) should be performed in most cases if there is no clear cause such as trauma or sepsis.

ARDS definition

ARDS – BERLIN Definition 2012

JAMA The Journal of the American Medical Association

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	Bilateral opacities—not fully explained by effusions, lobar/lung collapse, or nodules
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg < Pa_{O_2}/F_{IO_2} ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H_2O[c]
Moderate	100 mm Hg < Pa_{O_2}/F_{IO_2} ≤ 200 mm Hg with PEEP ≥5 cm H_2O
Severe	Pa_{O_2}/F_{IO_2} ≤ 100 mm Hg with PEEP ≥5 cm H_2O

Abbreviations: CPAP, continuous positive airway pressure; F_{IO_2}, fraction of inspired oxygen; Pa_{O_2}, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.
[a] Chest radiograph or computed tomography scan.
[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [Pa_{O_2}/F_{IO_2} × (barometric pressure/760)].
[c] This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

JAMA 2012;307(23)2526-2533

- Patient-level meta-analysis of 4188 patients with ARDS from 4 multicenter clinical data sets and 269 patients with ARDS from 3 single-center data
- Stages **of mild, moderate, and severe ARDS** were associated with increased mortality
- Better predictive of **mortality**

ARDS definition

ARDS – BERLIN Definition 2012

ARDS Severity	PaO2/FiO2*	Mortality**
Mild	200 – 300	27%
Moderate	100 – 200	32%
Severe	< 100	45%
*on PEEP 5+; **observed in cohort		

ARDS definition

PaO2/FiO2

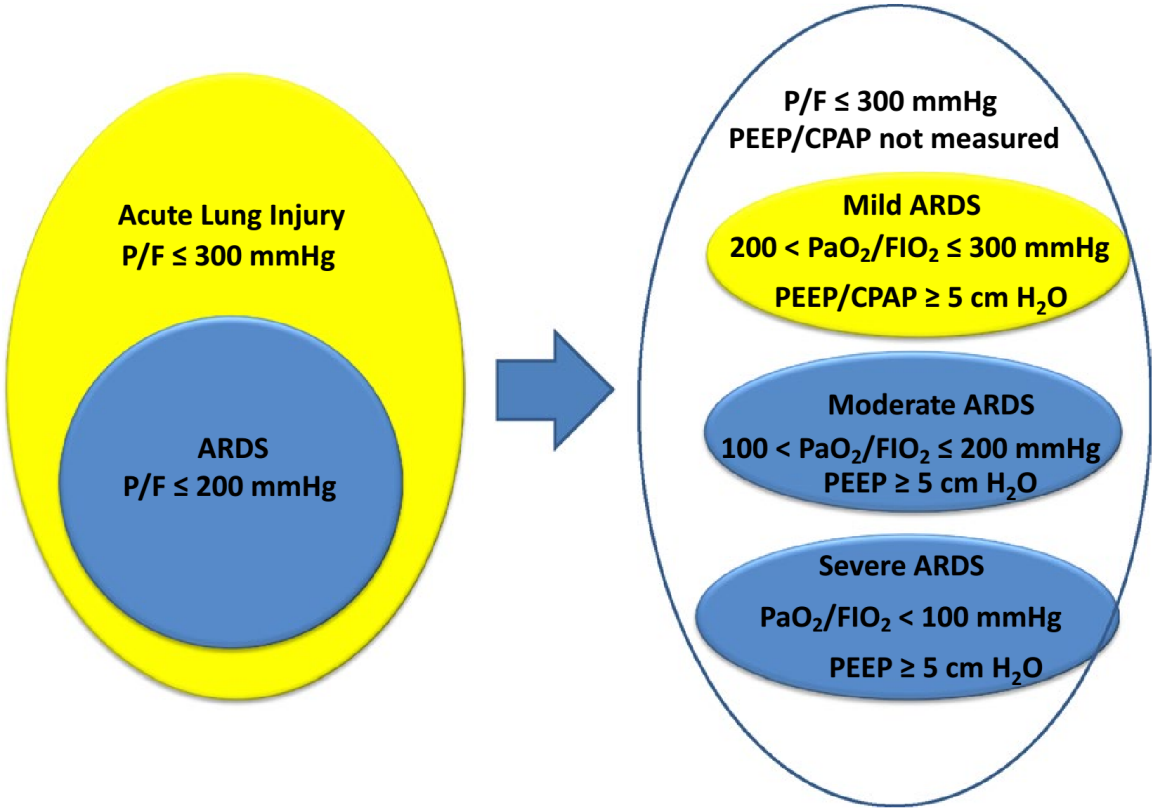


Fig. 1 Illustration of changes in ARDS definition moving from the AECC definition to the Berlin definition. For purposes of this figure all patients must have acute changes in chest radiograph consistent with pulmonary edema

ARDS definition

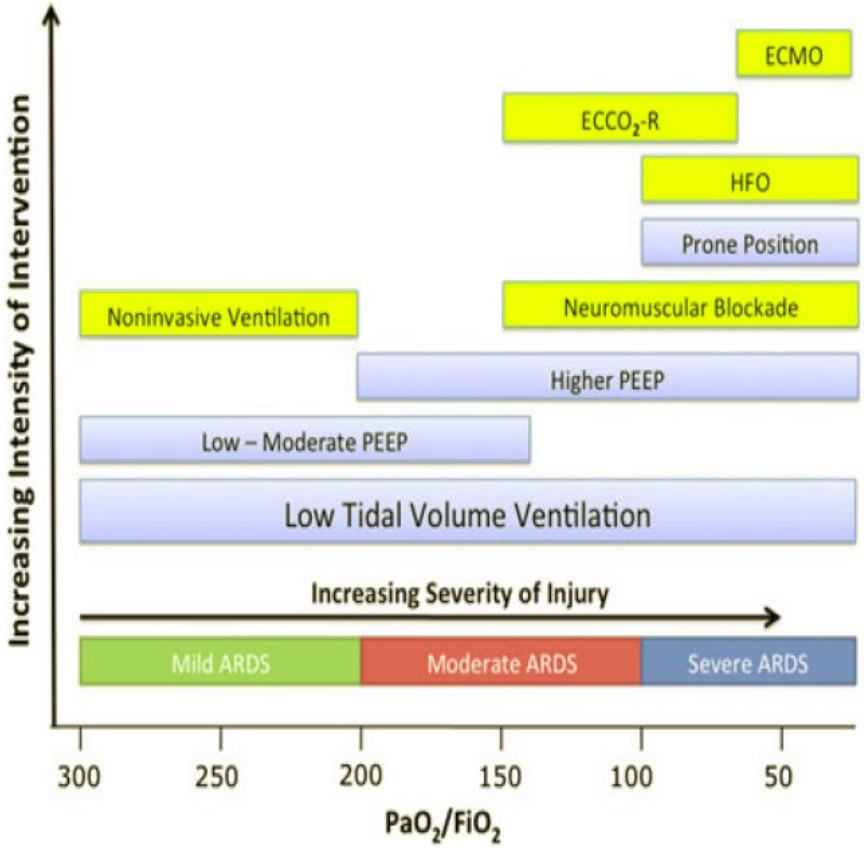
ARDS – BERLIN Definition 2012

Intensive Care Med (2012) 38:1573–1582
DOI 10.1007/s00134-012-2682-1

SPECIAL ARTICLE

Niall D. Ferguson
Eddy Fan
Luigi Camporota
Massimo Antonelli
Antonio Anzueto
Richard Beale
Laurent Brochard
Roy Brower
Andrés Esteban
Luciano Gattinoni
Andrew Rhodes
Arthur S. Slutsky
Jean-Louis Vincent
Gordon D. Rubenfeld
B. Taylor Thompson
V. Marco Ranieri

The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material



ARDS definition

ARDS - Adult or Acute Respiratory Distress Syndrome?

- AECC and Berlin Definition focused on ADULT lung Injury

- Limitations when applied to **children**
  - Necessary of invasive measurement of **arterial oxygen**
  - Use of PaO2/FiO2 ratio: this ratio is greatly influenced by ventilator pressure. PICU ventilation managment is different realtive to adult ICUs
  - Difference in risk factor, etiologies , pathophysiology and outcomes

PARDS definition

Pediatric
Acute
Respiratory
Syndrome

Pediatric Acute Respiratory Distress Syndrome: Consensus Recommendations From the Pediatric Acute Lung Injury Consensus Conference*

The Pediatric Acute Lung Injury Consensus Conference Group

Objective: To describe the final recommendations of the Pediatric Acute Lung Injury Consensus Conference.

Design: Consensus conference of experts in pediatric acute lung injury.

Setting: Not applicable.

Subjects: PICU patients with evidence of acute lung injury or acute respiratory distress syndrome.

Interventions: None.

Methods: A panel of 27 experts met over the course of 2 years to develop a taxonomy to define pediatric acute respiratory distress syndrome and to make recommendations regarding treatment and research priorities. When published, data were lacking a modified Delphi approach emphasizing strong professional agreement was used.

Measurements and Main Results: A panel of 27 experts met over the course of 2 years to develop a taxonomy to define pediatric acute respiratory distress syndrome and to make recommendations regarding treatment and research priorities. When published data were lacking a modified Delphi approach emphasizing strong professional agreement was used. The Pediatric Acute Lung Injury Consensus Conference experts developed and voted on a total of 151 recommendations addressing the following topics related to pediatric acute respiratory distress syndrome: 1) Definition, prevalence, and epidemiology; 2) Pathophysiology, comorbidities, and severity; 3) Ventilatory support; 4) Pulmonary-specific ancillary treatment; 5) Nonpulmonary treatment; 6) Monitoring; 7) Noninvasive support and ventilation; 8) Extracorporeal support; and 9) Morbidity and long-term outcomes. There were 132 recommendations with strong agreement and 19 recommendations with weak agreement. Once restated, the final iteration of the recommendations had none with equipoise or disagreement.

***See also p. 483.**

Supported, in part, by the Department of Pediatrics, The Pennsylvania State University College of Medicine; Health Outcome Axis–Ste Justine Research Center, Montreal, Canada; Respiratory Research Network of Fonds de Recherche du Québec-Santé, QC, Canada; Mother and Children French-Speaking Network; French-Speaking Group in Pediatric Emergency and Intensive Care, French-Speaking Intensive Care Society (SRLF); European Society for Pediatric and Neonatal Intensive Care Society (travel support for European experts); Australian and New Zealand Intensive Care Society (travel support for Australian expert); Children's Hospital of Richmond of Virginia Commonwealth University; Division of Critical Care Medicine, CS Mott Children's Hospital at the University of Michigan; and Department of Anesthesia and Critical Care, Children's Hospital of Philadelphia.

Listen to the iCritical Care podcasts for an in-depth interview on this article. Visit www.sccm.org/iCriticalCare or search "SCCM" at iTunes.

Dr. Jouvet received grants from the respiratory research network of Fonds de Recherche du Québec-Santé, Réseau mère enfant de la francophonie, and Research Center of Ste-Justine Hospital related to the submitted work; and received equipment on loan from Philips and Maquet outside the submitted work. Dr. Thomas served on the Advisory Board for Discovery Laboratories and Ikaria outside the submitted work; received a grant from United States Food and Drug Administration Office of Orphan Product Development outside the submitted work. Dr. Willson served on the Advisory Board for Discovery Laboratories outside the submitted work. Drs. Khemani, Smith, Dahmer, and Watson received grants from the National Institutes of Health (NIH) outside the submitted work. Dr. Zimmerman received research grants

PARDS definition

Pediatric Acute Respiratory Distress Syndrome: Consensus Recommendations From the Pediatric Acute Lung Injury Consensus Conference*

The Pediatric Acute Lung Injury Consensus Conference Group

- Section 1: Definition, Prevalence and Epidemiology
- Section 2: Pathophysiology, Comorbidities and Severity
- Section 3: Ventilatory support
- Section 4: Pulmonary- Specific Ancillary Treatment
- Section 5: Nonpulmonary Treatment
- Section 6: Monitoring
- Section 7: Noninvasive Support and Ventilation
- Section 8: Extracorporeal Support
- Section 9: Morbidity and Long Term Outcomes

PARDS definition

Age	Exclude patients with peri-natal related lung disease			
Timing	Within 7 days of known clinical insult			
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload			
Chest Imaging	Chest imaging findings of new infiltrate(s) consistent with acute pulmonary parenchymal disease			
Oxygenation	**Non Invasive mechanical ventilation**	**Invasive mechanical ventilation**		
	PARDS (No severity stratification)	Mild	Moderate	Severe
	Full face-mask bi-level ventilation or CPAP ≥5 cm H_20 [2] PF ratio ≤ 300 SF ratio ≤ 264 [1]	4 ≤ OI < 8 5 ≤ OSI < 7.5[1]	8 ≤ OI < 16 7.5 ≤ OSI < 12.3[1]	OI ≥ 16 OSI ≥ 12.3[1]
Special Populations				
Cyanotic Heart Disease	Standard Criteria above for age, timing, origin of edema and chest imaging with an acute deterioration in oxygenation not explained by underlying cardiac disease. [3]			
Chronic Lung Disease	Standard Criteria above for age, timing, and origin of edema with chest imaging consistent with new infiltrate and acute deterioration in oxygenation from baseline which meet oxygenation criteria above.[3]			
Left Ventricular dysfunction	Standard Criteria for age, timing and origin of edema with chest imaging changes consistent with new infiltrate and acute deterioration in oxygenation which meet criteria above not explained by left ventricular dysfunction.			

Figure 1. Pediatric acute respiratory distress syndrome (PARDS) definition. [1]Use Pao_2-based metric when available. If Pao_2 is not available, wean Fio_2 to maintain $Spo_2 \leq 97\%$ to calculate oxygen saturation index (OSI; [Fio_2 × mean airway pressure × 100]/Spo_2) or Spo_2:Fio_2 (SF) ratio. [2]For nonintubated patients treated with supplemental oxygen or nasal modes of noninvasive ventilation, see **Figure 2** for "at-risk" criteria. [3]Acute respiratory distress syndrome severity groups stratified by oxygenation index (OI; [Fio_2 × mean airway pressure × 100]/Pao_2) or OSI should not be applied to children with chronic lung disease who normally receive invasive mechanical ventilation or children with cyanotic congenital heart disease. CPAP = continuous positive airway pressure, PF = Pao_2:Fio_2.

PARDS definition

Age	Exclude patients with peri-natal related lung disease

- **Prematurity** related lung disease
- **Perinatal lung injury** (i.e. Meconium Aspiration and Pneumonia and sepsis acquired during delivery)
- **Congenital abnormalities** (e.g. congenital diaphragmatic hernia or alveolar capillary displasia)

NO AGE CRITERIA

PARDS definition

Age	Exclude patients with peri-natal related lung disease
Timing	Within 7 days of known clinical insult
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload

Both ARDS and PARDS are associated with many different underlying clinical conditions

Direct Lung Injury

Pneumonia
Aspiration
Lung Contusion
Smoke Inalation
Hydrocarbon ingestion
Sickle Cell Disease

Indirect Lung Injury

Sepsis
Multiple Emergent Transfusion
Burns
Pancreatitis
Submersion Injury

→ the most common underlying condition is **respiratory infection** rather than sepsis as observed for ARDS
→ **viral infections** are a much more common cause of ARDS in children than in adults

PARD definition - etiology

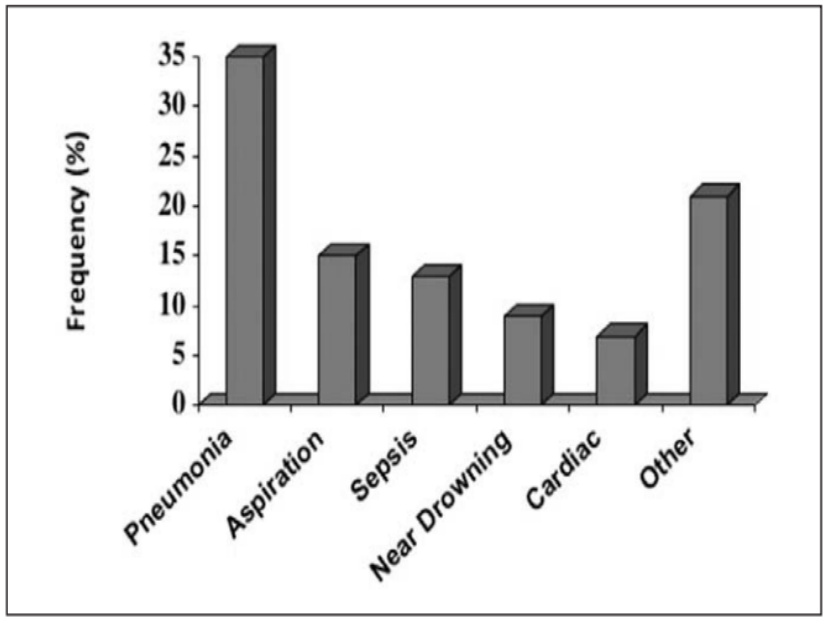


Figure 2. Clinical disorders associated with pediatric acute lung injury. Reprinted with permission from Flori et al (9). Copyright 2014 American Thoracic Society.

TABLE 1. Center for Disease Control and Prevention Age-Adjusted Mortality per 100,000 Persons From Sepsis and Influenza and Pneumonia in the United States in 2009

Age (Yr)	Sepsis	Influenza and Pneumonia
< 1	5.2	5.9
1–4	0.4	0.9
5–14	0.2	0.6
15–24	0.3	1
25–34	0.9	1.9
35–44	2.2	3.2
45–54	5.5	6.5
55–64	13.3	11.9
65–74	32	30.1
75–84	78.4	105.9
≥ 85	173.8	413.5

PARDS definition

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PF ratio
(PaO_2 / FiO_2)

SF ratio
(SpO_2/FiO_2)
wean FiO_2 to mantain SpO_2 < 97%

PARDS definition

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OI (Oxigenation Index) = (FiO_2 x Mean Airway Pressure x 100) / PaO_2

OSI (Oxygen Saturation Index) = (FiO_2 x Mean Airway Pressure x 100) / SpO_2

(SpO_2: wean FiO_2 2 to mantain SpO_2 < 97%)

Prevalence and epidemiology

TABLE 2. Distribution of Patients and Mortality Based on Oxygenation Index Cut Points Drawn From the Literature

Studies	Oxygenation Index				Total
	> 20	13–20	6–13	< 6	
Khemani et al (6) (%)					
No. of patients	76 (19.1)	51 (12.8)	138 (34.7)	132 (33.2)	397
Mortality	33 (43.4)	12 (23.5)	23 (16.7)	12 (9.1)	80 (20.2)
Erickson et al (5) (%)					
No. of patients	32 (28.1)	16 (14.0)	31 (27.2)	35 (30.7)	114
Mortality	18 (56.3)	7 (43.8)	5 (16.1)	5 (14.3)	35 (30.7)

Data from two published studies on pediatric lung injury.

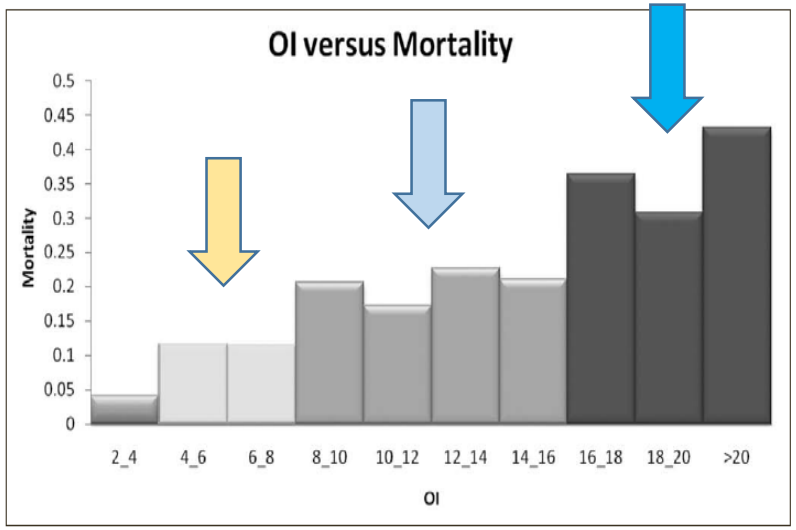

Figure 3. Distribution of initial oxygenation index (OI) and mortality from Children's Hospital of Los Angeles dataset (Khemani et al [6]) ($n = 397$). Mortality increases as OI increases, but there appear to be clear groups where mortality steps up (OI, < 4, 4–8, 8–16, and > 16).

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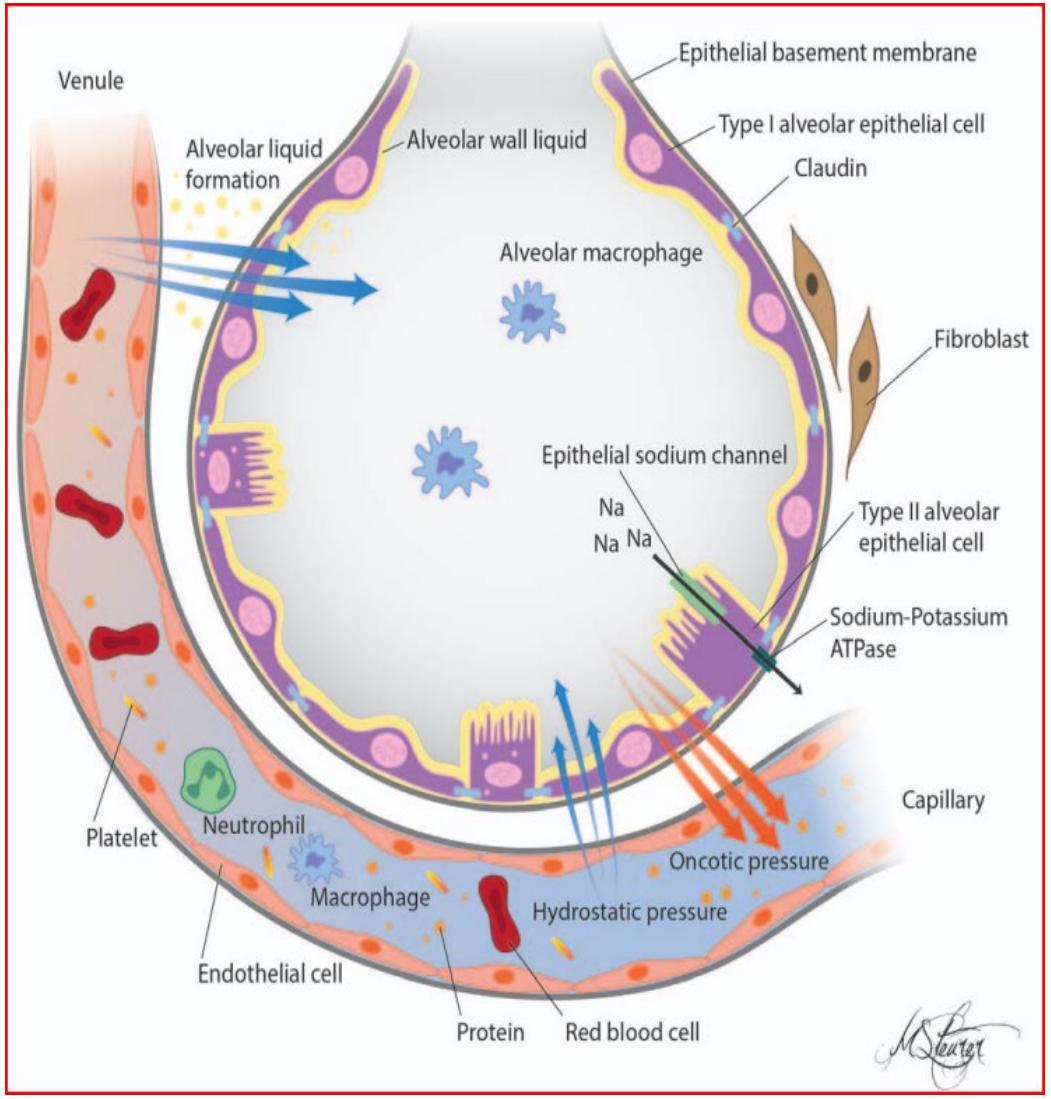
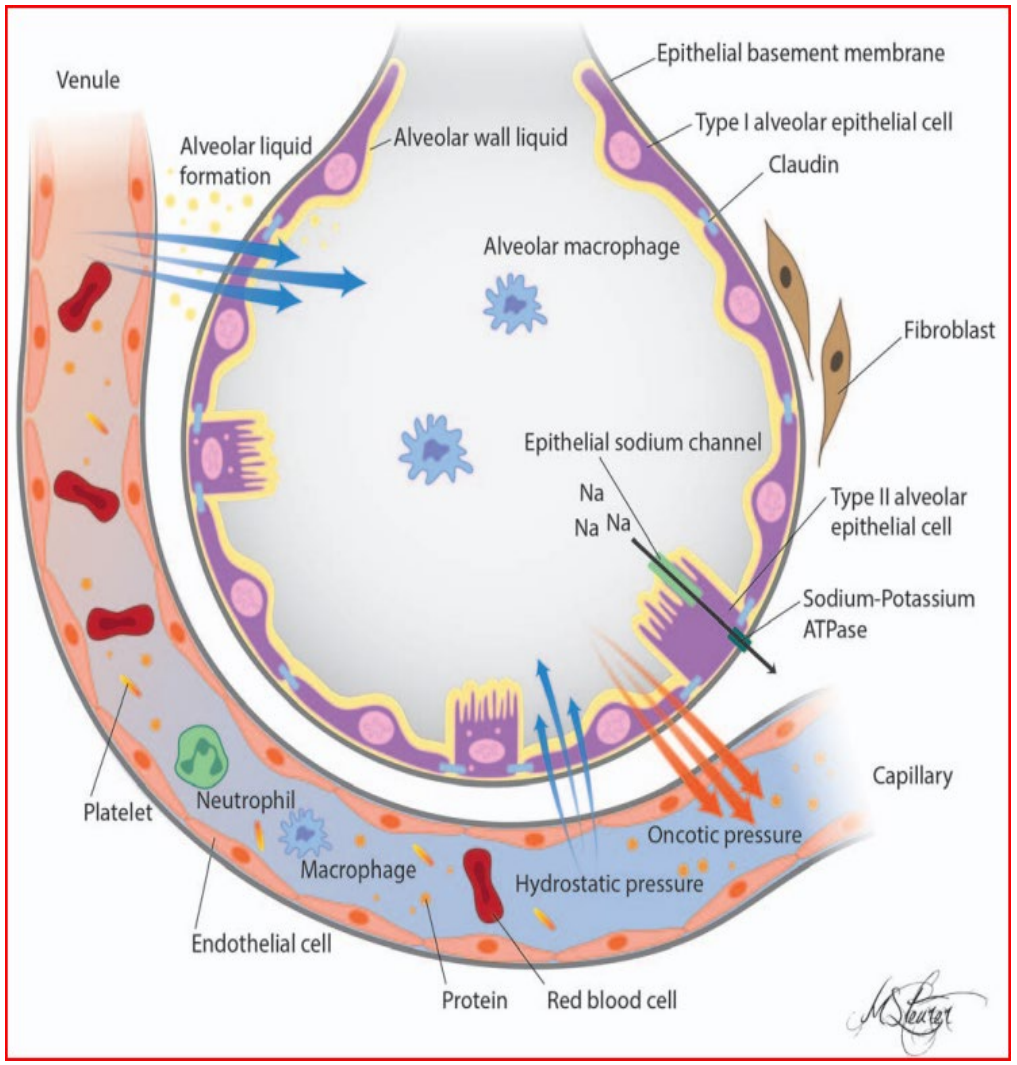
Pathobiology



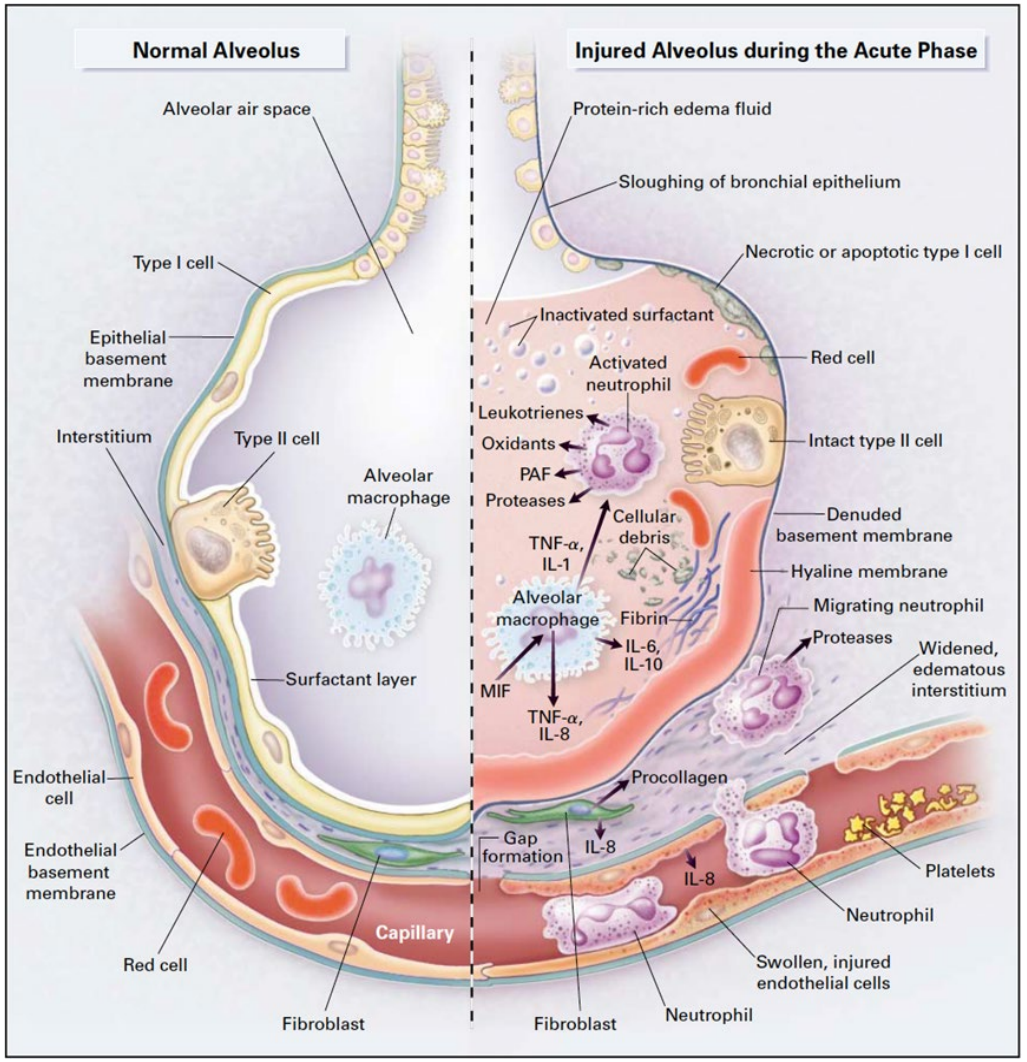
Schematic of a healthy alveolus

The **alveolar epithelium and capillary endothelium are intact**.
The characteristics of the pulmonary circulation and **intact epithelial endothelial barrier** allow for formation of the **alveolar wall liquid (AWL)** while maintaining the air-filled, fluid-free, status of the alveoli.
The AWL facilitates **gas exchange** and is a medium for **dispersal of surfactant** and **alveolar macrophages**, which is essential for maintaining alveolar stability and host defenses.
The intact sodium-dependent vectorial transport across type II alveolar epithelial cells regulates the removal of excess alveolar fluid.

Pathobiology

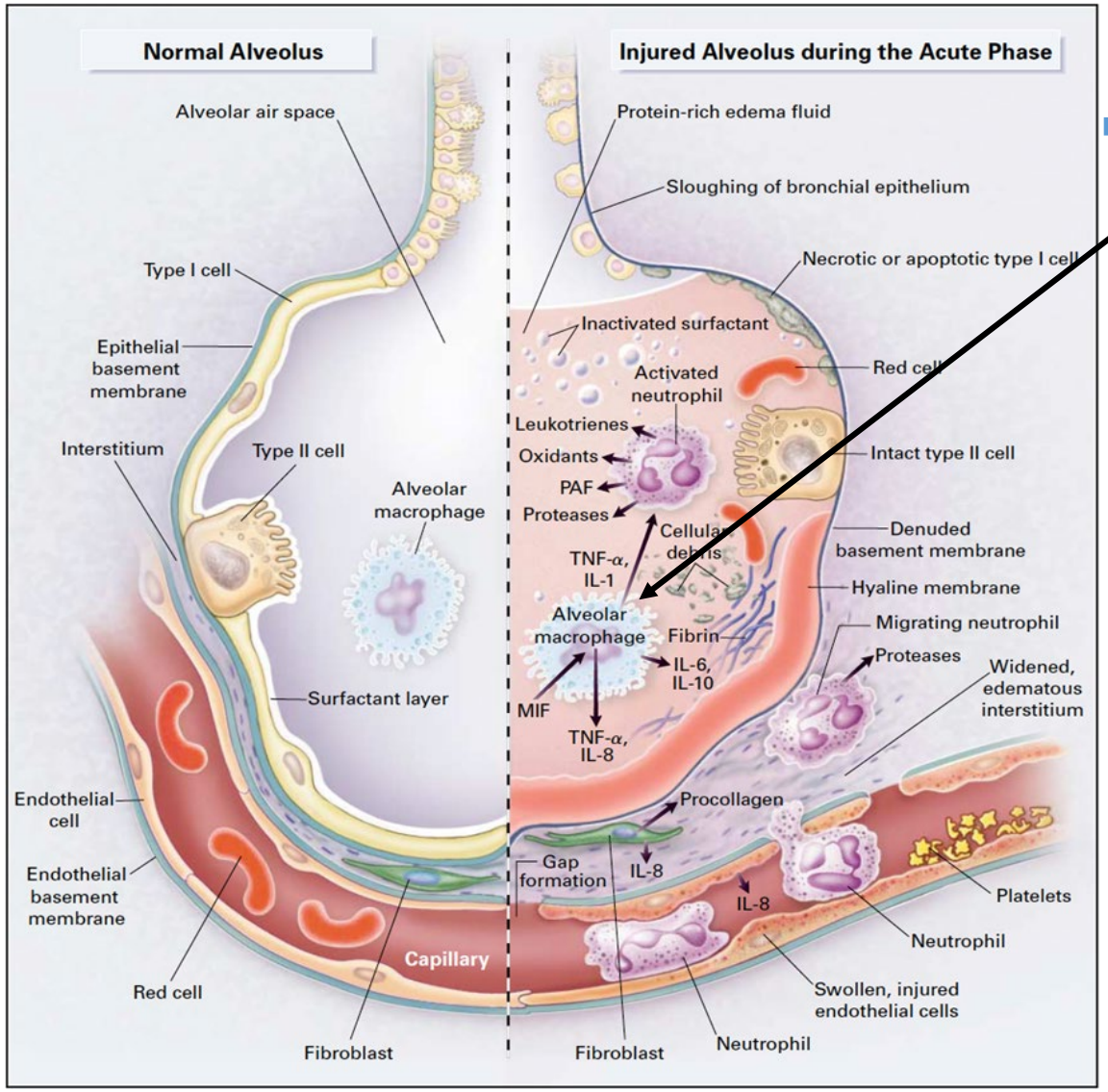


healthy alveolus



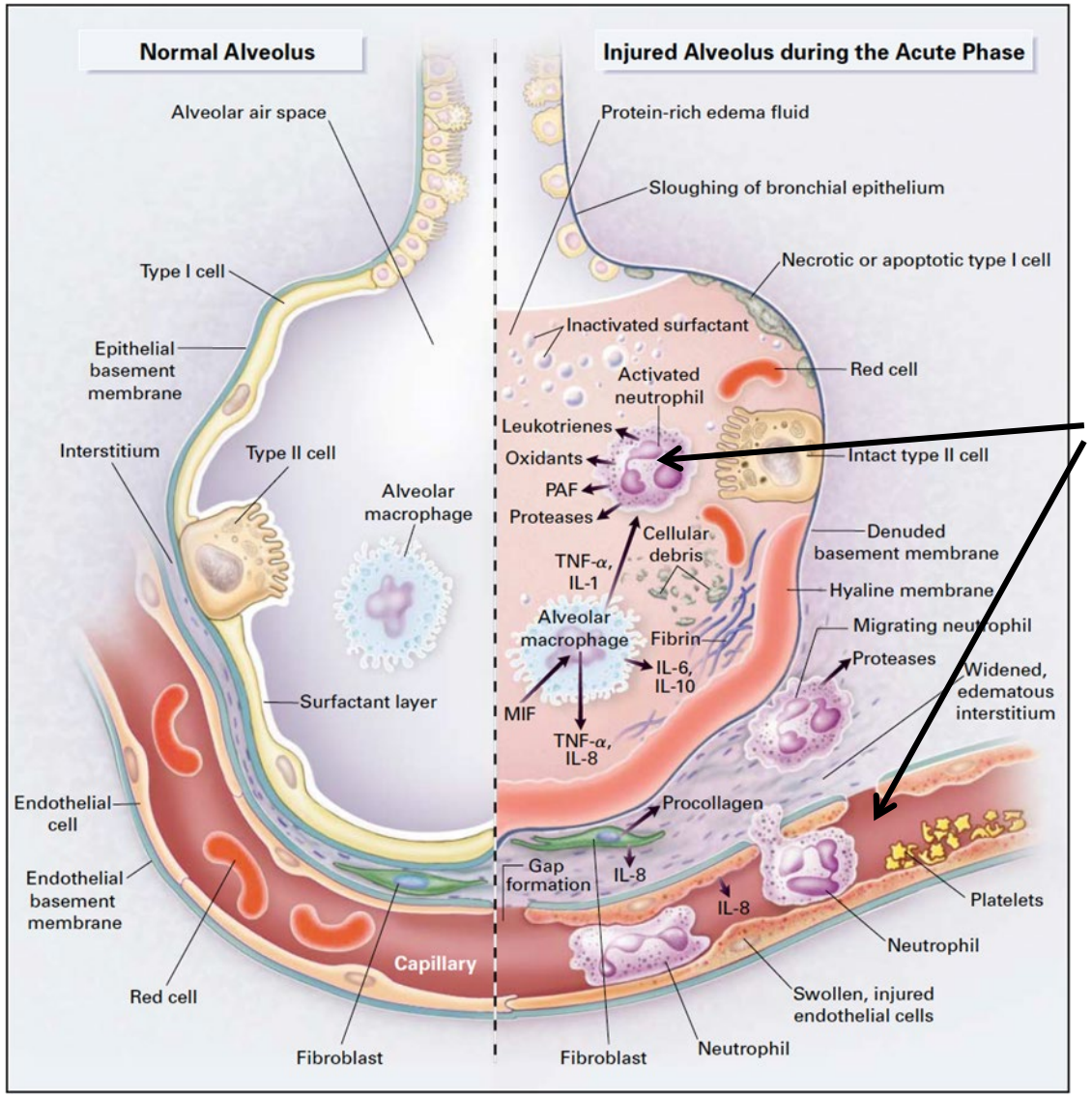
ARDS

Pathobiology



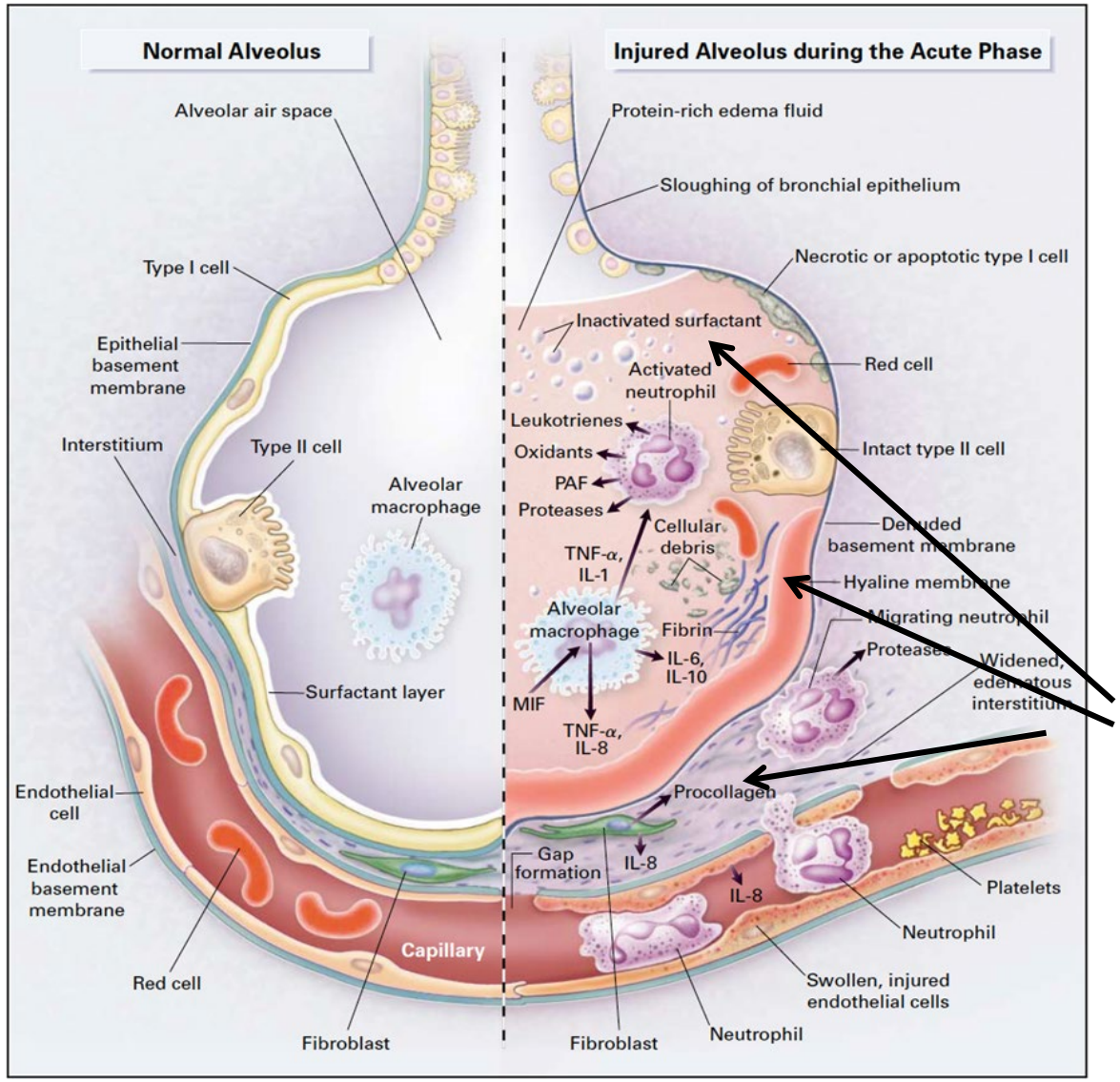
- 1. Direct or indirect injury to the alveolus causes alveolar **macrophages** to release **pro-inflammatory cytokines**

Pathobiology



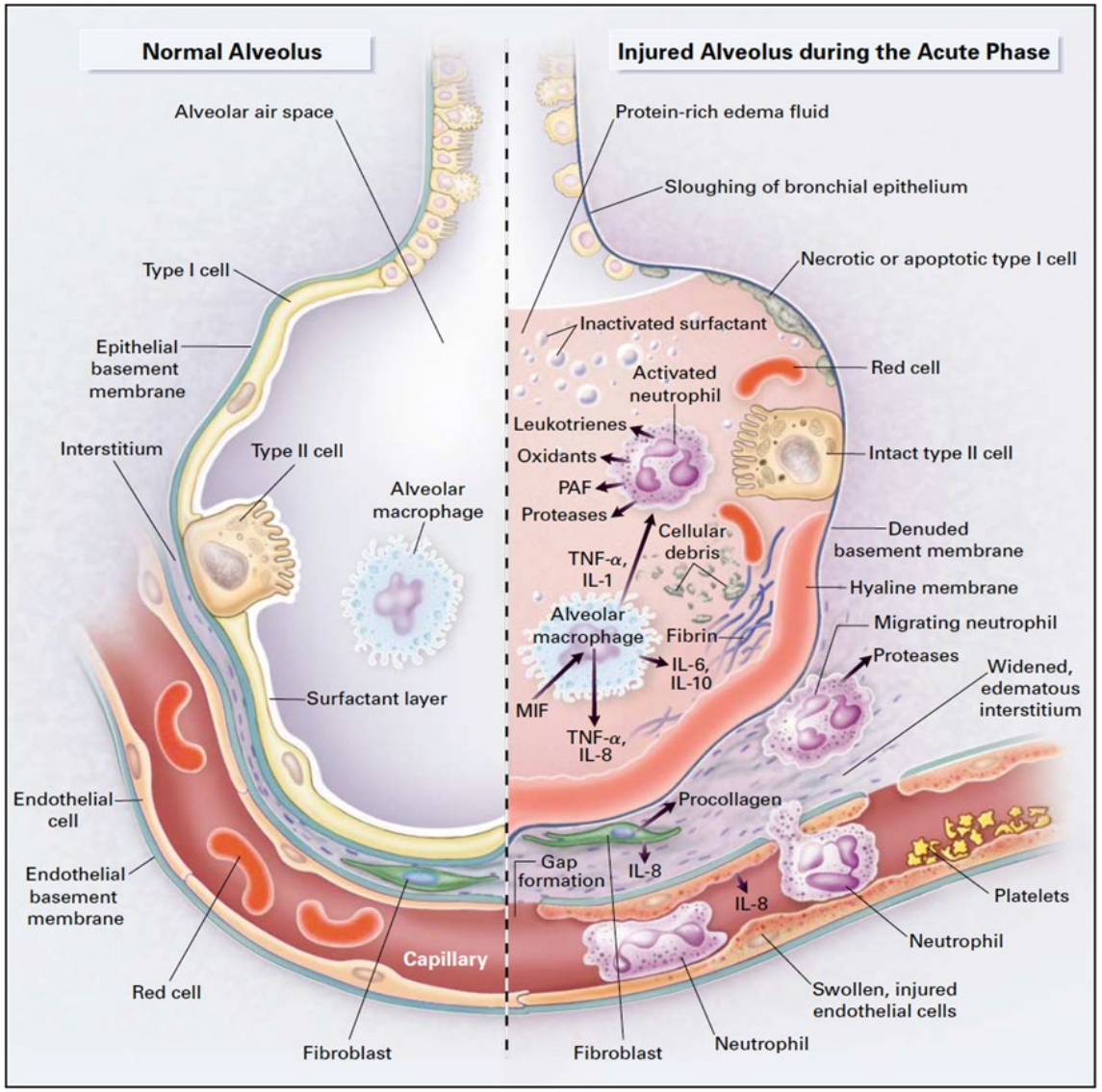
- 1. Direct or indirect injury to the alveolus causes alveolar macrophages to release **pro-inflammatory cytokines**
- 2. Cytokines attract **neutrophils** into the alveolus and interstitium, where they **damage the alveolar-capillary membrane (ACM).**

Pathobiology



- 1. Direct or indirect injury to the alveolus causes alveolar macrophages to release **pro-inflammatory cytokines**
- 2. Cytokines attract neutrophils into the alveolus and interstitum, where they **damage the alveolar-capillary membrane (ACM).**
- 3. ACM integrity is lost, interstitial and **alveolus fills with proteinaceous fluid,** surfactant can no longer support alveolus

Pathobiology



CONSEQUENCE OF LUNG INJURY INCLUDE:

IMPAIRED GAS EXCHANGE

✓ V/Q mismatch

✓ Increased dead space

DECREASED COMPLIANCE (Vol /P)

✓ increased pressure to deliver Tidal Volume (TV)

INCREASED PULMONARY ARTERIAL PRESSURE

✓occurs in up to 25% of ARDS patients

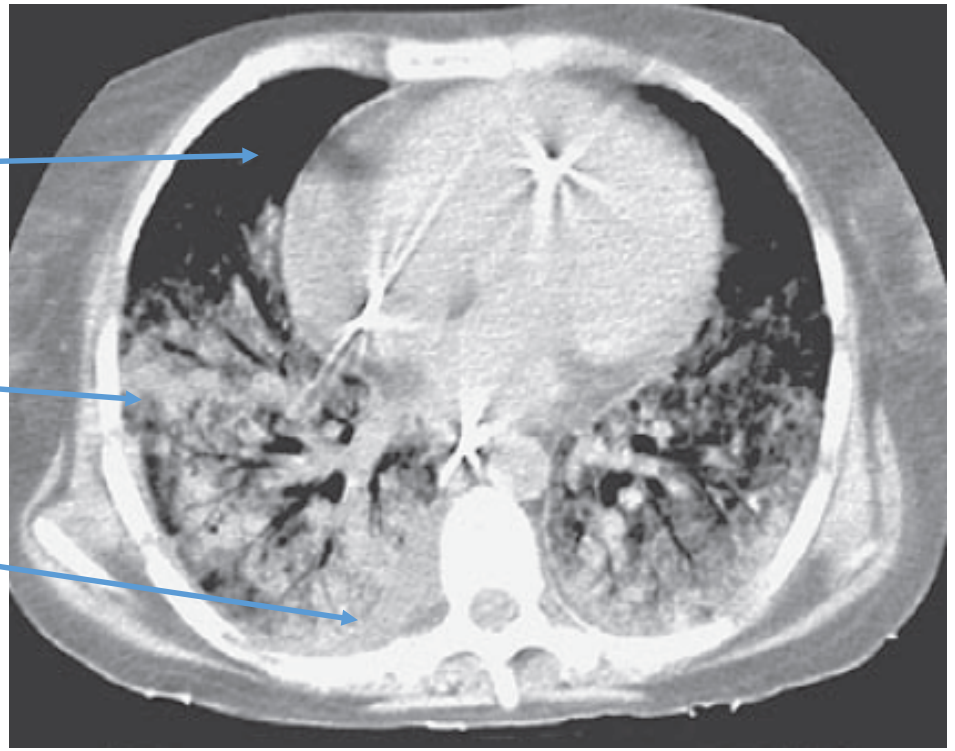
✓ results from hypoxic vasoconstriction

✓ positive airway pressure causing vascular compression can result in right ventricular failure

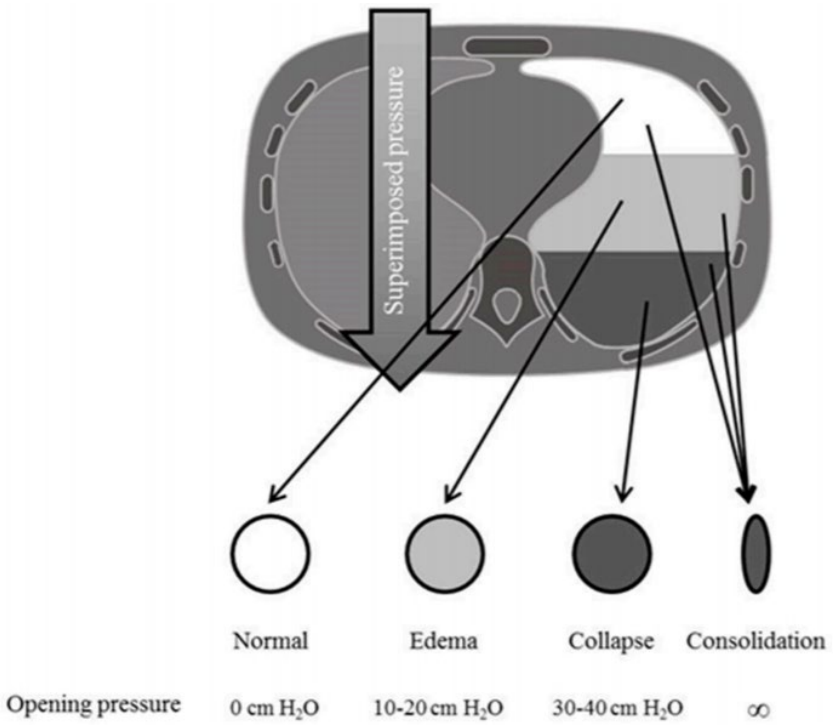
Pathobiology

ARDS affects the lung in a **heterogeneous** fashion

- Normal alveoli
- Injured alveoli can potentially participate in gas exchange, susceptible to damage from opening and closing
- Damaged alveoli filled with fluid, do not participate in gas exchange



Pathobiology



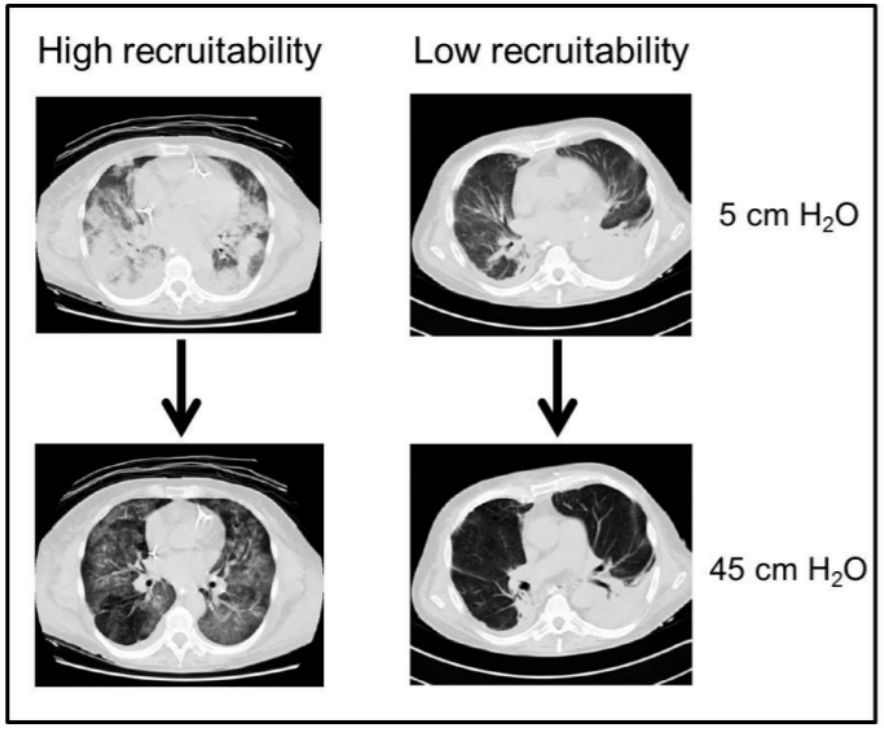


Figure 3. Example of lung CT scan of patients with high (**upper** panel) or low (**lower** panel) potential of lung recruitment. Arrows depict the morphologic change from a condition of low airway pressure (i.e., 5 cm H_2O), to one of high airway pressure (i.e., 45 cm H_2O).

Pathobiology

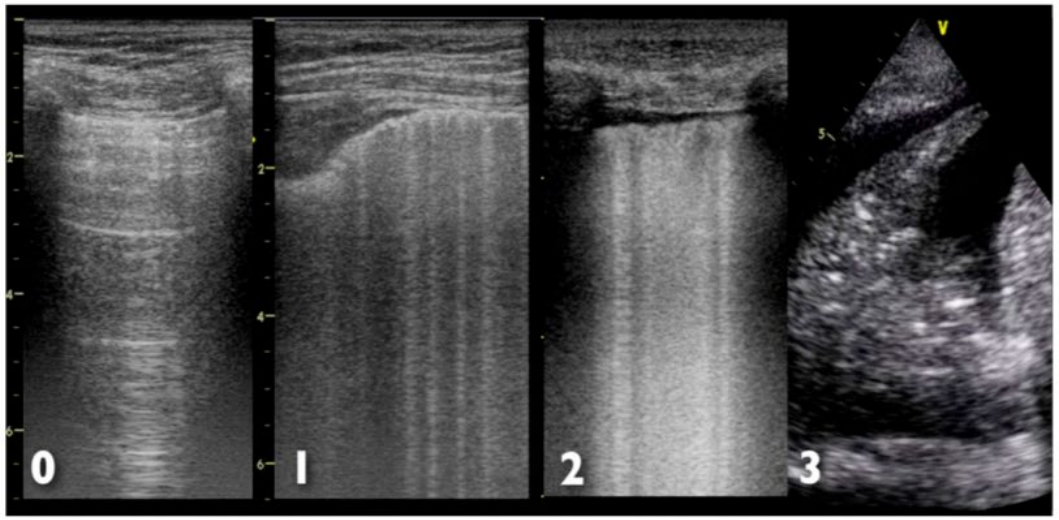


Figure 4. Possible ultrasonographic findings at lung examination. **0**: Normal aeration with normal sliding, with A-lines pattern; **1**: Multiple B-lines but separated by at least 5 mm; **2**: Multiple, coalescent, not well-separated B-lines; **3**: Lung consolidation, hyperechoic area with air bronchogram. Numbers on the left side of each ultrasound image represent the depth (in cm).

Diagnostic testing

Table 3 Diagnostic procedures for infection management in patients with severe ARDS (c/o Standard Operating Procedure, Charitè Berlin). All these diagnostic measures are subject to individual patient assessments and indications

General lab to detect focus of infection, host defense, and organ dysfunction
Blood
Blood count[a], differential hemogram[a]; C-reactive protein, procalcitonin
Severe immunosuppression: immune status (lymphocyte subpopulation as B cells, T cells, natural killer cells, T cell subpopulation (CD3, CD4, CD8), HLA-DR expression on monocytes
In ECMO patients: free hemoglobin, haptoglobin
Urine
Leucocytes, nitrites
Bacterial infections
Blood
Blood cultures; atypical pneumonia: *Mycoplasma pneumoniae* AB, *Legionella pneumophila* AB/nonpneumophila AB, *Chlamydia pneumoniae* AB, *Chlamydia psittaci* AB; interferon gamma release assay (tuberculosis)
TBS/BAL
Culturing bacteria on pathogen level and resistance; direct preparation and number of granulocytes/number of epithelium cells; direct immune fluorescence (DIF) for legionella; PCR for tuberculosis and acid-resistant rod, Giemsa staining for *Pneumocystis jirovecii*
Urine
Culturing bacteria on pathogen level and resistance; *Legionella pneumophila* antigen/nonpneumophila antigen; *Streptococcus pneumoniae* antigen
Viral infections[b]
Blood
Influenza A/B IgA, parainfluenza IgA, RSV IgA, CMV-DNA quantitative[c], CMV-AG (pp65)[c], CMV IgM[c], EBV-IgM[d], EBV-DNA[d]; VZV-IgM[e], adenovirus IgM[f]; HSV1/2-IgM[g]
TBS/BAL
Influenza A/B virus RNA, influenza virus Ag, parainfluenza virus RNA, influenza H1N1 (2009) RNA RSV-Ag; CMV-DNA[c]q/q; EBV-DNAq/q[d]; VZV-DNA[e]; adenovirus-DNA[f]; HSV Typ1/2-DNA[g]
Laryngo-pharyngeal scrape test
H1N1-RNA
Mycoses
Blood
Aspergillus -AG (galactomannan), candida AG/AB (manna-anti-mannan); biopsies for invasive mycosis, e.g., intra-abdominal mycoses; β-D-glucan[h]
TBS/BAL
Aspergillus AG (galactomannan)
Autoimmune disease to detect vasculitis, M. Wegener/sarcoidosis, Goodpasture syndrome, Hamman–Rich syndrome
Blood
Rheumatoid factor; IgA/M, antinuclear antibody (ANA/HEp2), anti-dsDNS-Ak/ELISA, glomerular basal membrane Ab, anti-mitochondrial-Ab (AMA), cANCA-ELISA (PR3), pANCA-ELISA (MPO)
TBS/BAL
Differential hemogram; cytology
Urine
Protein

Intensive Care Med (2016) 42:699–711
DOI 10.1007/s00134-016-4325-4

REVIEW

The standard of care of patients with ARDS: ventilatory settings and rescue therapies for refractory hypoxemia

Thomas Bein[1*], Salvatore Grasso[2], Onnen Moerer[3], Michael Quintel[3], Claude Guerin[4,5], Maria Deja[6], Anita Brondani[7] and Sangeeta Mehta[7]

Diagnostic testing

Table 2. Most common pathogens responsible for ARDS genesis.

Bacteria	Virus	Fungi	Parasites
Streptococcus pneumoniae	Influenza A and B		
Haemophilus influenzae	Rhinoviruses		
Enterobacteriaceae	RSV	*Pneumocystis Jirovecii*	
Staphylococcus aureus	Parainfluenza viruses		
Legionella pneumophila	Coronavirus		*Toxoplasma gondii*
Clamydia pneumoniae	Enterovirus		
Mycoplasma pneumoniae	HSV		
Pseudomonas aeruginosa	CMV	*Aspergillus fumigatus*	
Acinetobacter baumannii	–		
Stenotrophompnas maltophilia	–		

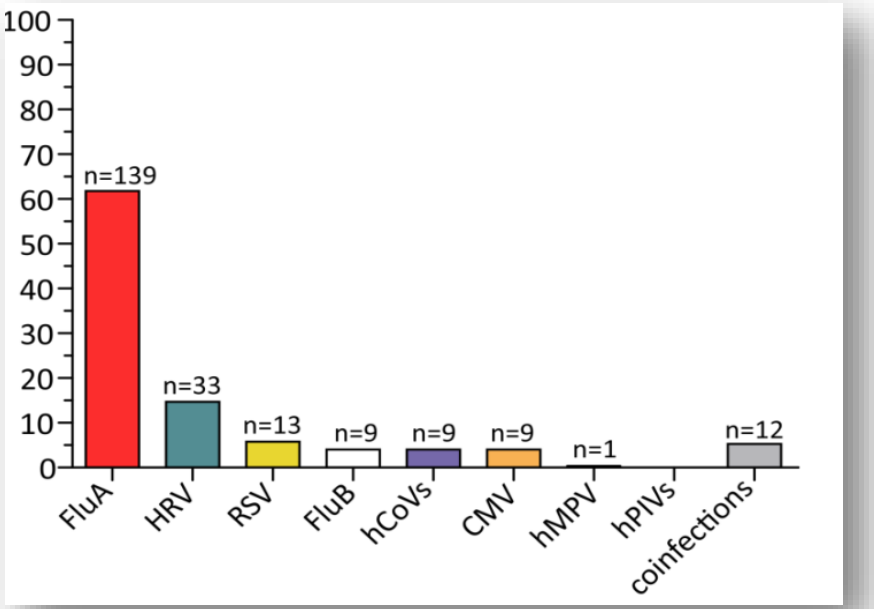
Journal of Clinical Virology
Volume 92, July 2017, Pages 48-51

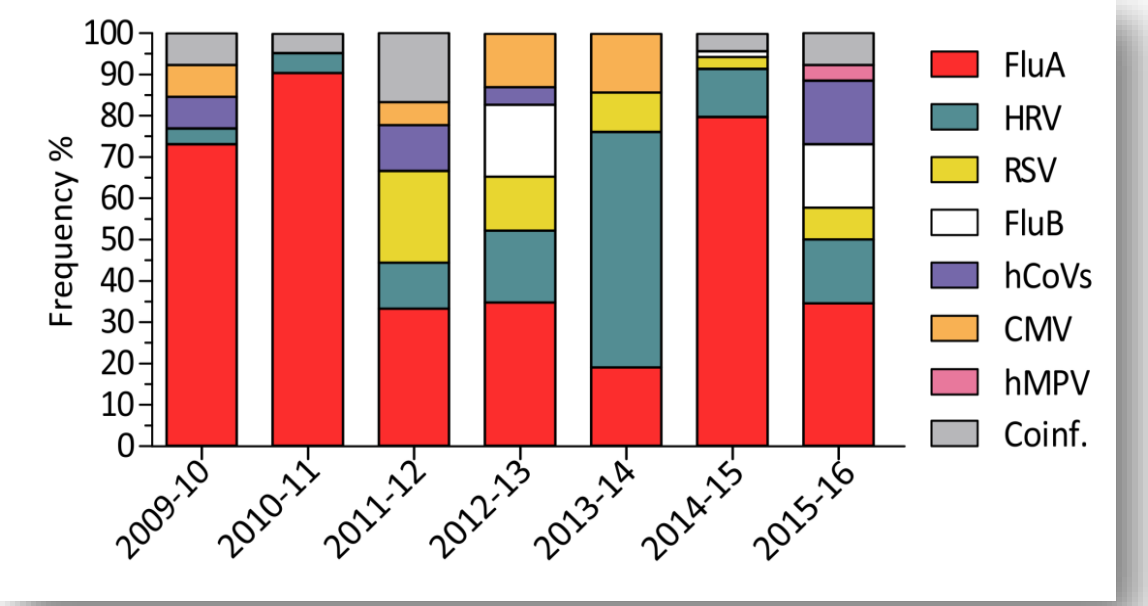
Frequency of respiratory viruses among patients admitted to 26 Intensive Care Units in seven consecutive winter-spring seasons (2009–2016) in Northern Italy

Antonio Piralla [a, 1], Bianca Mariani [a, 1], Francesca Rovida [a], Fausto Baldanti [a, b]

Show more

https://doi.org/10.1016/j.jcv.2017.05.004



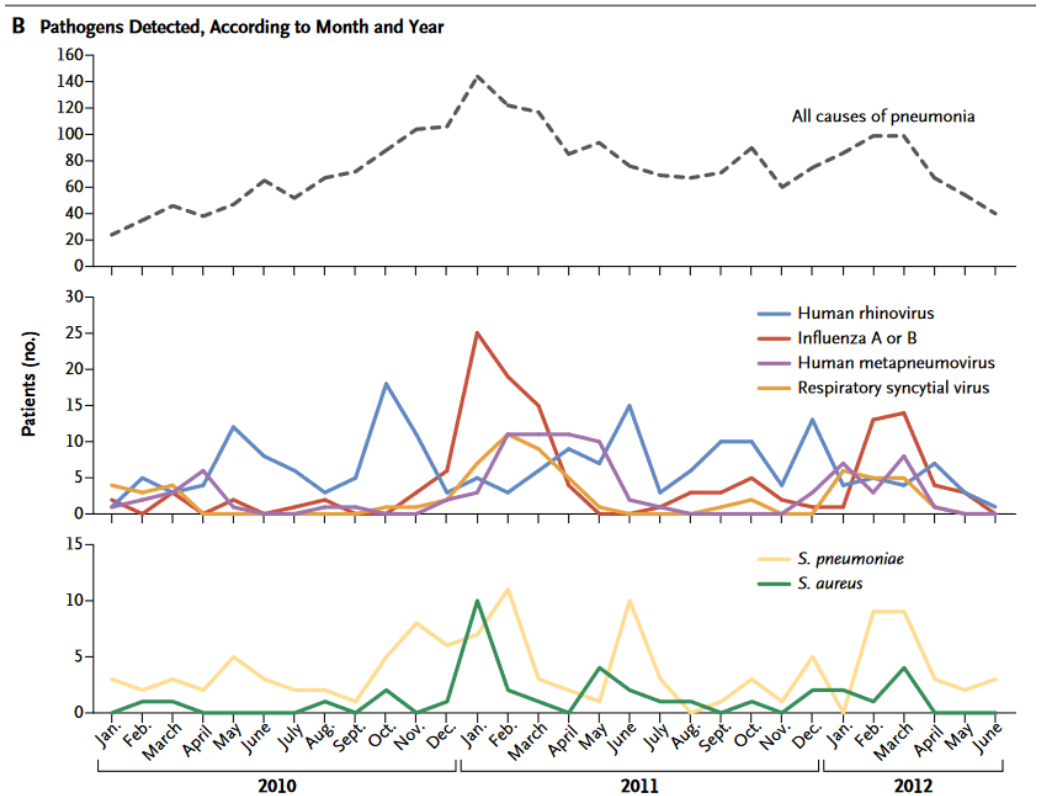


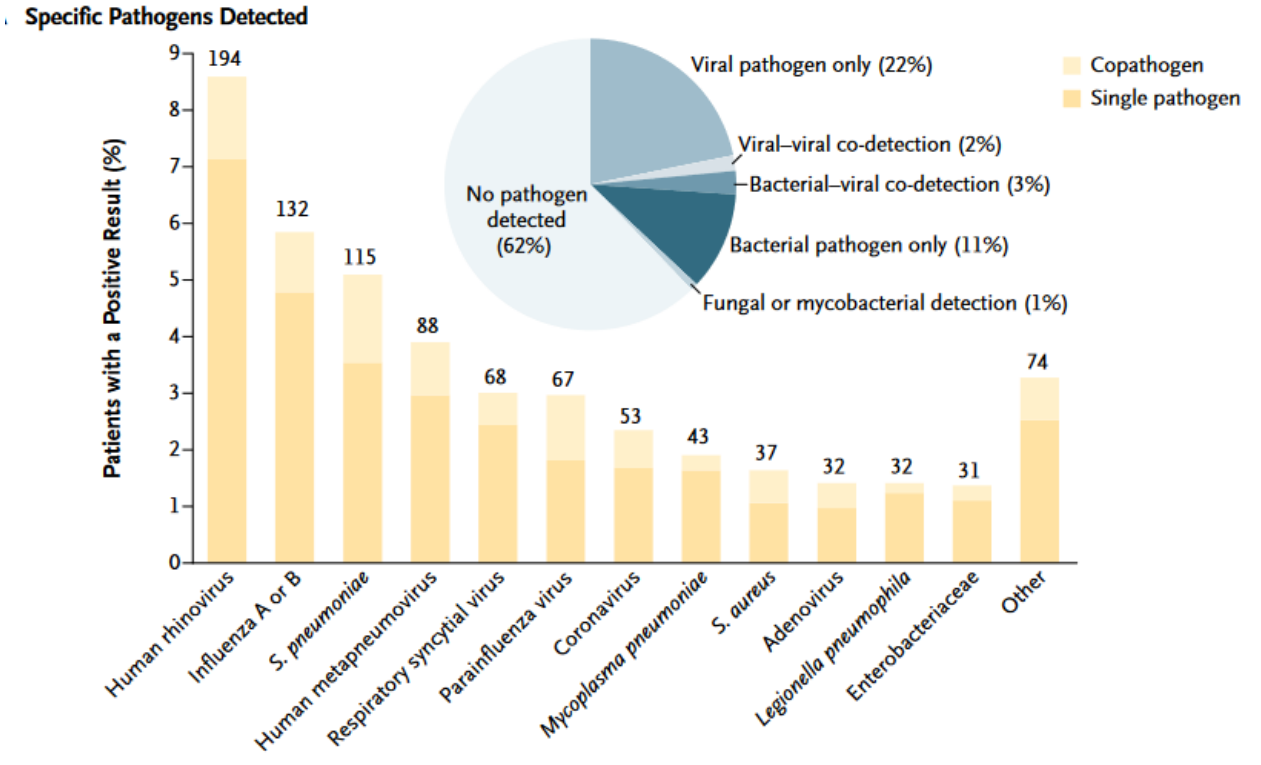
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

S. Jain, W.H. Self, R.G. Wunderink, S. Fakhran, R. Balk, A.M. Bramley, C. Reed, C.G. Grijalva, E.J. Anderson, D.M. Courtney, J.D. Chappell, C. Qi, E.M. Hart, F. Carroll, C. Trabue, H.K. Donnelly, D.J. Williams, Y. Zhu, S.R. Arnold, K. Ampofo, G.W. Waterer, M. Levine, S. Lindstrom, J.M. Winchell, J.M. Katz, D. Erdman, E. Schneider, L.A. Hicks, J.A. McCullers, A.T. Pavia, K.M. Edwards, and L. Finelli, for the CDC EPIC Study Team*





Diagnostic testing

Journal of Clinical Virology 108 (2018) 72–76

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Using a novel rapid viral test to improve triage of emergency department patients with acute respiratory illness during flu season

Courtney J. Pedersen[a,*], Daniel T. Rogan[b], Samuel Yang[b,1], James V. Quinn[b,1]

[a] Stanford School of Medicine, Stanford University, 291 Campus Dr, Stanford, CA, 94305, USA
[b] Department of Emergency Medicine, Stanford University, Alway Building, M023, 300 Pasteur Drive - MC: 5768, Stanford, CA, 94305, USA

Study Design: A **prospective cohort study of consecutive ED patients with ARI (acute respiratory illnesses) symptoms** during peak flu season was conducted. Patient **nasopharyngeal swabs** were collected and tested using a **POC-PCR device**; **physicians and patients were blinded to results**

Results: Of 119 participants, **52.9% were POC-PCR positive** - Influenza A (42.9%), RSV (41.3%), influenza B (15.9%). Nearly **70% of virus positive patients were placed rooms shared with non-ARI patients**. **Antibiotics were prescribed for 27.3% of virus positive patients**, and **77.8% of oseltamivir-eligible patients did not receive therapy.**
POC-PCR was 100% sensitive (95% CI, 80.5–100.0%) and 95.2% specific (95% CI, 76.2–99.9%).

Conclusions: Rapid **POC-PCR for influenza and RSV in ED triage has excellent sensitivity and specificity and the potential to improve social distancing practices through better triage and increase appropriate prescription of antimicrobials**

Diagnostic testing

MULTIPEX
- Influenza A virus (Flu A)
- Influenza B virus (Flu B)
- Respiratory syncytial virus A (RSV A)
- Respiratory syncytial virus B (RSV B)
- Adenovirus (AdV)
- Enterovirus (HEV)
- Parainfluenza virus
- Metapneumovirus (MPV)
- Bocavirus (HBoV)
- Rhinovirus (HRV)
- Coronavirus

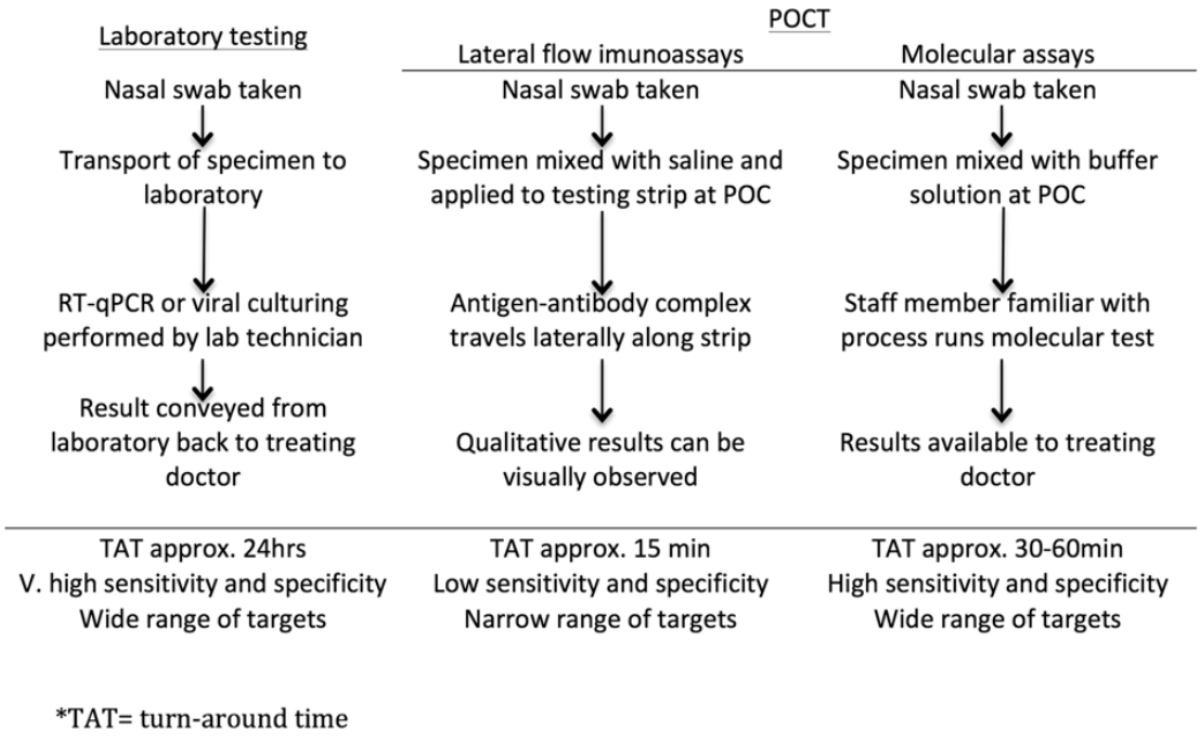


FIGURE 1 Generalised steps in different methods of diagnostic testing for influenza. POC, point of care; POCT, point of care tests; RT-qPCR quantitative reverse transcription PCR

Received: 20 March 2018 | Revised: 11 June 2018 | Accepted: 14 June 2018
DOI: 10.1002/rmv.1995

REVIEW

WILEY

Systematic review of the impact of point-of-care testing for influenza on the outcomes of patients with acute respiratory tract infection

Ece Egilmezer[1] | Gregory J. Walker[1] | Padmavathy Bakthavathsalam[2] | Joshua R. Peterson[2] | J. Justin Gooding[2] | William Rawlinson[1,3] | Sacha Stelzer-Braid[1,3]

Diagnostic testing

Multiplex Tests in Critically Ill Children With Severe Lower Respiratory Tract Infections.

Colombo J, Bonanomi E.

Pediatr Crit Care Med. 2016 Jun;17(6):586-7. doi: 10.1097/PCC.0000000000000749.

To the Editor:

- **Viral agents are the leading cause of lower respiratory tract infection in infants and children**
- **Reverse transcription-polymerase chain reaction (RT-PCR)–based testing for influenza has the highest diagnostic accuracy**, whereas rapid antigen influenza diagnostic testing has low sensitivity and should not be routinely used for guiding use of influenza antiviral therapy.
- **We would like to underline** the **importance of early and correct diagnosis of influenza** infection because these viruses are **potentially life treating and have a therapy** that is effective only if started in the early phase of infection.
- **Multiplex tests** allow the **rapid and accurate identification of most common human respiratory virus**, but at the moment, they do not guide therapy because viruses they detect, except for influenza virus, have no therapy.
- These multiplex tests **may reduce empirical antimicrobial treatment enhancing antibiotic stewardship** and may help to describe better the etiology and epidemiology of severe infection.

Ventilatory support

GAS EXCHANGE

OXYGENATION

- We recommend that oxygenation and ventilation goals be titrated on the «perceived» risks of the toxicity of the ventilatory support required
- We recommend that, for **mild PARDS with PEEP less than 10 cmH20, SpO2 should generally be maintained between 92 – 97%**
- We recommend that, **after optimising PEEP, lower SpO2 levels (in the range of 88 -92%) should be considered for those with PARDS with PEEP greater or equal to 10 cmH20**
- When **SpO_2 is less than 92%,** monitoring of **central venous saturation** and markers of oxygen delivery is recommended

VENTILATION

- We recommend that **permissive hypercapnia should be considered** for moderate – to – severe PARDS to minimize VILI (ventiator induced lung injury)
- We recommend **maintaning Ph 7,15 – 7,30** within lung protective strategy guidelines. **Exceptions** to permissive hypercapnia should include **intracranial hypertension, select congenital heart disease, hemodinamic instability and significant ventricular dysfunction**

Non invasive Support and Ventilation

- **Noninvasive Support Ventilation (NPPV)**

- We recommend that **NPPV is considered early in disease in children** at risks for PARDS to improve gas exchange, decrease work of breathing and potentially avoid complications of invasive vetilation
- We recommend that selected populations of children, such as children with **immunodeficiency** who are at greater risk of complications from invasive mechanical ventilation, may benefit more from **earlier noninvasive support** ventilation to avoid invasive mechanical ventilation.
- We recommend the use of an **oronasal or full facial mask** to provide the most efficient patient-ventilator synchronization for children with PARDS

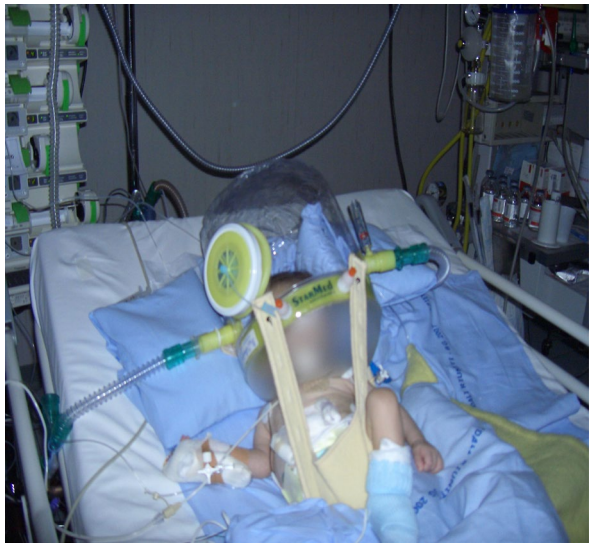
Non invasive Support and Ventilation

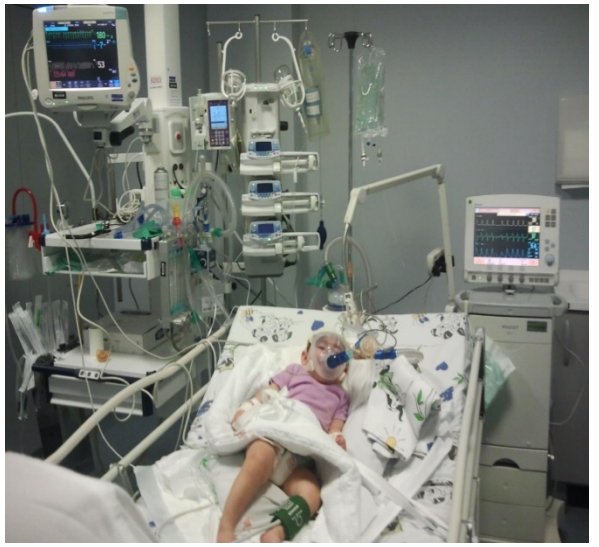
- **Noninvasive Support Ventilation (NPPV)**

TABLE 1. Studies of Noninvasive Positive Pressure Ventilation for the Treatment of Acute Lung Injury or Acute Respiratory Distress Syndrome in Children

Study	Study Design	Total Sample Size	ARDS/ALI Sample Size	ARDS Sample Size	Results	
					ALI: Progressed to Intubation (%)	ARDS: Progressed to Intubation (%)
Fortenberry et al (16)	Retrospective descriptive	28	28		11	
Padman et al (20)	Prospective descriptive	34	17		17	
Bernet et al (12)	Prospective descriptive	42	23		43	
Essouri et al (15)	Retrospective descriptive	114	53	9	21	78
Joshi and Tobias (17)	Retrospective descriptive	45	29		38	
Ottonello et al (30)	Retrospective cohort	20	4	4	0	
Yañez et al (23)	Prospective randomized	50	25		28	
Mayordomo-Colunga et al (18)	Prospective descriptive	116	38	3	16	
Piastra et al (28)	Prospective descriptive	23	23	23		43
Munoz-Bonet et al (19)	Prospective descriptive	32	22	7	18	57
Chidini et al (13)	Prospective pilot	40	40		28	
Dohna-Schwake et al (14)	Retrospective descriptive	74	54		28	
Piastra et al (29)	Retrospective descriptive	61	61		38	

ARDS = acute respiratory distress syndrome, ALI = acute lung injury.



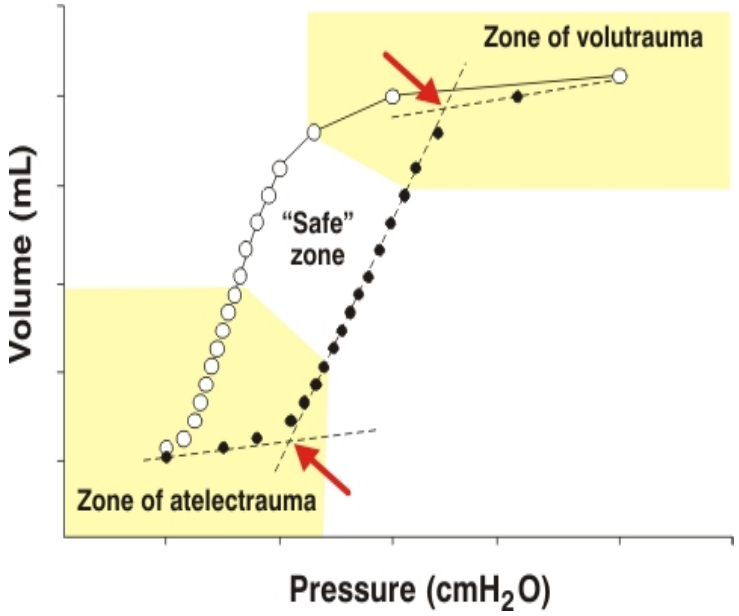


Ventilatory support

CONVENTIONAL VENTILATION

- **MODES OF CONVENTIONAL VENTILATION**: no outcome data on the influence of mode (**controlled or assist**). No recommendation. *STRONG AGREEMENT*
- **TIDAL VOLUME:** use of TV in or below physiologic tidal volume for predicted body weight (5 – 8 ml/kg) according to lung pathology and Cpl Rs
  - **3-6 ml/kg** for poor Cpl Rs
  - **5 – 8 ml/kg** for preserved Cpl Rs

  WEAK AGREEMENT (84% AGREEMENT)



- **PLATEAU PRESSURE:** **plateau pressure limit of 28 cmH20**, allowing for slightly higher plateau pressures (29 – 32 cmH20) for patients with increased chest wall elastance (WEAK AGREEMENT 72%)

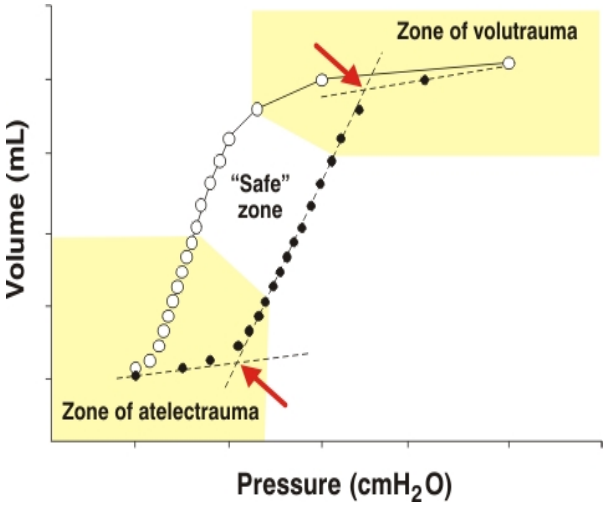
Ventilatory support

CONVENTIONAL VENTILATION

- **<u>PEEP/Lung Recruitment</u>**:

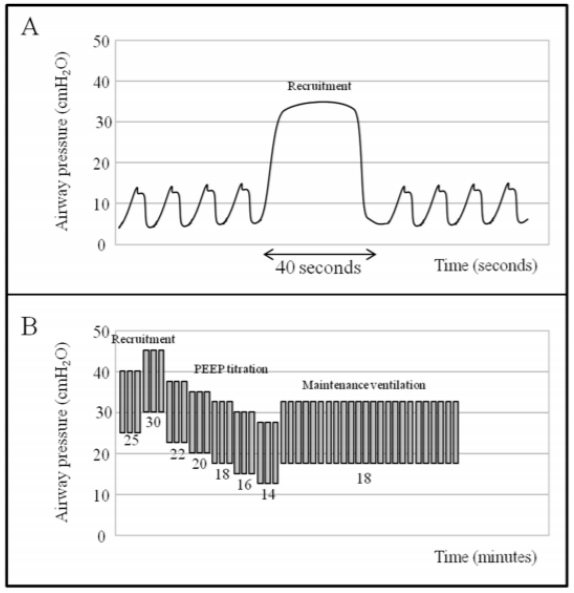
- **moderately elevated levels of PEEP** (10-15 cmH2O) titrated to the observed oxygenation and heamodinamic response in pts with severe PARDS. *(WEAK AGREEMENT 88%*)

- **PEEP levels greater than 15** cmH20 may be needed for severe PARDS, although attention should be paid to limiting the Plateau Pressure (STRONG AGREEMENT)



- **<u>Lung Recruitment</u>**:

- Careful recruitment maneuvers in the attempt to improve severe oxigenation failure by slow incremental and decremental PEEP. Sustained inflation maneuvers cannot be recommended due to lack of available data. (WEAK AGREEMENT 88%)



Ventilatory support

- **NON CONVENTIONAL VENTILATION - HFOV**

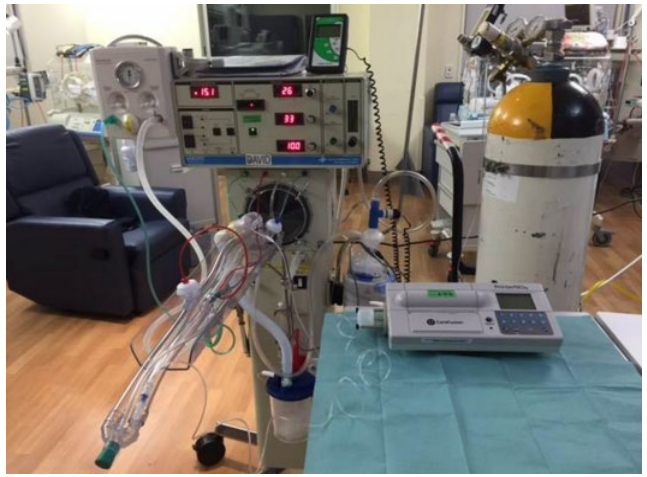
- HFOV should be considered as an **alternative ventilatory mode** in hypoxic respiratory failure in patients in whom **plateau pressures exceed 28 cmH20** in the absence of clinical evidence of reduced chest wall compliance. Such an approach should be considered for those **patient with moderate to severe PARDS**

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., Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D., for the OSCAR Study Group*



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

Niall D. Ferguson, M.D., Deborah J. Cook, M.D., Gordon H. Guyatt, M.D., Sangeeta Mehta, M.D., Lori Hand, R.R.T., Peggy Austin, C.C.R.A., Qi Zhou, Ph.D., Andrea Matte, R.R.T., Stephen D. Walter, Ph.D., Francois Lamontagne, M.D., John T. Granton, M.D., Yaseen M. Arabi, M.D., Alejandro C. Arroliga, M.D., Thomas E. Stewart, M.D., Arthur S. Slutsky, M.D., and Maureen O. Meade, M.D., for the OSCILLATE Trial Investigators and the Canadian Critical Care Trials Group*

Until more definitive data are obtained, it would seem reasonable to continue to incude HFOV in the ventilatory armamentarium for the managment of pediatric ARDS

Pulmonary specific ancillary treatment

- **Inhaled Nitric Oxyde**
- **Exogenous Surfactant**
- **Prone Positioning**
- **Suctioning**
- **Corticosteroids**

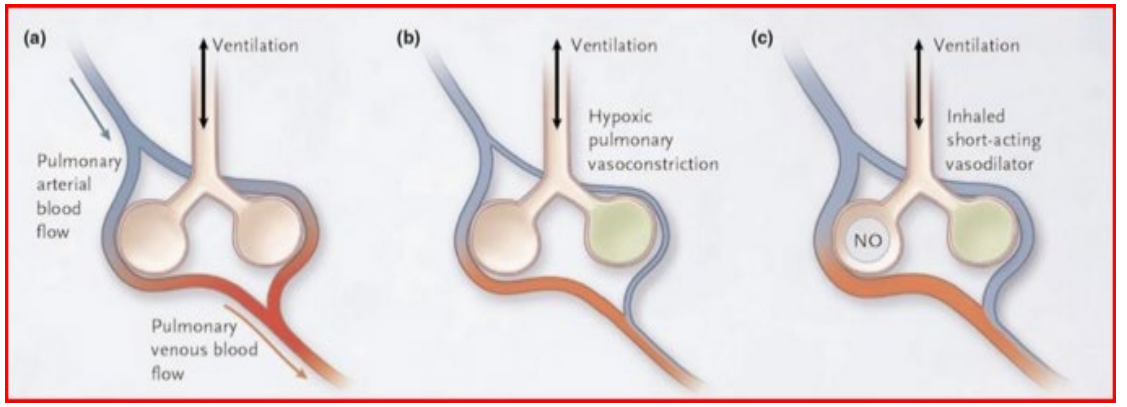
Pulmonary specific ancillary treatment

- **Inhaled Nitric Oxyde**
- Exogenous Surfactant
- Prone Positioning
- Suctioning
- Corticosteroids

Pulmonary specific ancillary treatment

- **Inhaled Nitric Oxyde**

Potent selective vasodilator: goal is to improve V/Q matching by directing blood toward the more open alveoli



Pulmonary specific ancillary treatment

- Inhaled Nitric Oxyde

A Randomized, Controlled Study of the 1-hour and 24-hour Effects of Inhaled Nitric Oxide Therapy in Children With Acute Hypoxemic Respiratory Failure*

Ronald W. Day, MD; Elizabeth M. Allen, MD; and Madolin K. Witte, MD

Inhaled Nitric Oxide and Prone Position: How Far They Can Improve Oxygenation in Pediatric Patients with Acute Respiratory Distress Syndrome?

[1]Tarek Salah Ibrahim and [2]Hala Samir El-Mohamady

ORIGINAL ARTICLES

Multicenter randomized controlled trial of the effects of inhaled nitric oxide therapy on gas exchange in children with acute hypoxemic respiratory failure

Emily L. Dobyns, MD, David N. Cornfield, MD, Nick G. Anas, MD, James D. Fortenberry, MD, Robert C. Tasker, MD, Amy Lynch, MD, Paul Liu, MD, Patricia L. Eells, CPNP, Jeff Griebel, RRT, Monika Baier, MS, John P. Kinsella, MD, and Steven H. Abman, MD

Documented improvement in oxygenation, no improvement in mortality

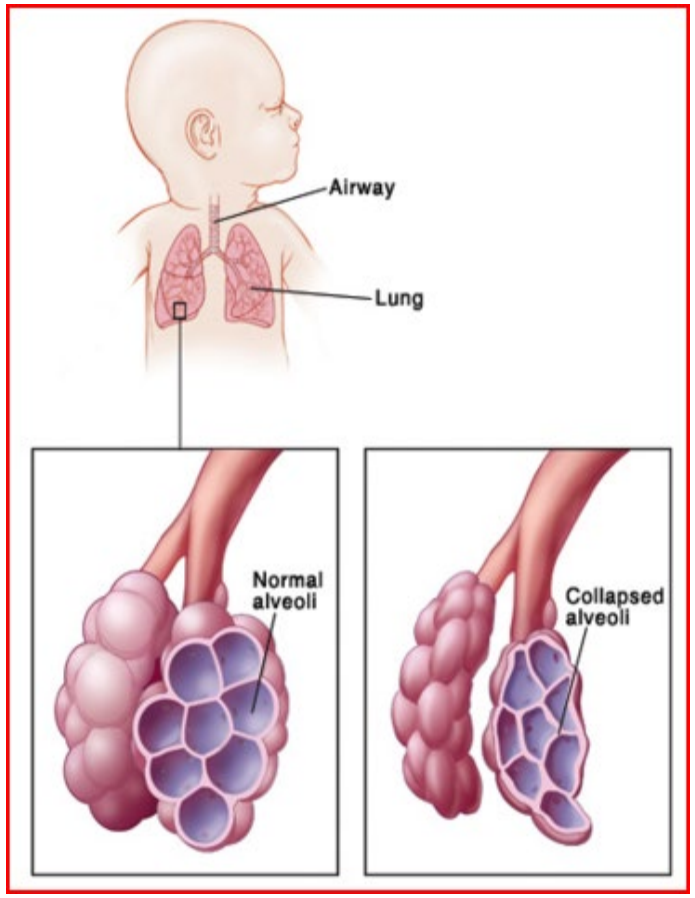
- **Not recommended for routine use**
- May be considered:
  - In patients with documented **pulmonary hypertension** or severe right ventricular dysfunction
  - In severe cases of PARDS as a rescue from or **bridge to extracorporeal life support**

Pulmonary specific ancillary treatment

- Inhaled Nitric Oxyde
- **Exogenous Surfactant**
- Prone Positioning
- Suctioning
- Corticosteroids

Pulmonary specific ancillary treatment

- Exogenous Surfactant



Pulmonary specific ancillary treatment

- **Exogenous Surfactant**

Exogenous surfactant				
Luchetti et al (33)	N = 20 Severe bronchiolitis	Porcine surfactant vs no surfactant in mechanically ventilated children	Surfactant use was associated with improved oxygenation, decreased inspiratory pressures, and shorter ventilation courses and PICU stays.	Single center No deaths
Luchetti et al (34)	N = 40 Severe respiratory syncytial virus bronchiolitis	Porcine surfactant vs no surfactant in mechanically ventilated children	Surfactant use was associated with improved oxygenation, increased compliance, and shorter courses of ventilation and PICU admission.	Multicenter No deaths Earlier treatment associated with a more robust effect. Surfactant well tolerated
Willson et al (35)	N = 42 Acute hypoxemic respiratory failure (OI > 7)	Bovine surfactant vs air placebo	Surfactant use was associated with improved oxygenation, decreased ventilation time, and shorter PICU stays.	Prospective multicenter unmasked RCT No difference in mortality; however, overall mortality only 12%.
Möller et al (36)	N = 35 (20 surfactant) Severe ARDS (Pao_2/Fio_2 < 100 mm Hg)	Surfactant vs standard therapy	Surfactant use was associated with improved oxygenation 2 hr after therapy. However, that difference in oxygenation was only maintained in those with Pao_2/Fio_2 ratio > 65 mm Hg and those without pneumonia.	Single/multicenter statistically insignificant trend toward lower mortality (44% vs 60%) and a lesser need for rescue therapies in the surfactant group

Multiple smaller studies

- improved oxygenation
- increased compliance
- shorter PICU stays

Willson et al (37)	N = 153 Infants, children, and adolescents with respiratory failure from acute lung injury (OI > 7)	Bovine surfactant vs air placebo	Surfactant use associated with improved oxygenation and decreased mortality. No difference in ventilator-free days (primary study outcome)	Prospective multicenter masked RCT Controlling for unequal distribution of immunocompromised rendered mortality difference insignificant

Multicentre randomized placebo controlled trial (2005)

- improved oxygenation
- no difference in ventilator free days
- no difference in mortality

Pulmonary specific ancillary treatment

- **Exogenous Surfactant**

Willson et al (38)	N = 109 Direct lung injury only Pediatric arm (≤ 18 yr) of concurrent pediatric and adult trial	Pneumosurf vs air placebo	Surfactant had no effect on oxygenation or mortality	Study closed prematurely secondary to futility
Thomas et al (39)	N = 165 Infants < 2 yr old Acute hypoxemic respiratory failure	Lucinactant (synthetic surfactant) vs air placebo	Lucinactant improved oxygenation; no effect on mortality, length of ventilation, or length of stay	Multinational prospective masked phase II RCT Low mortality

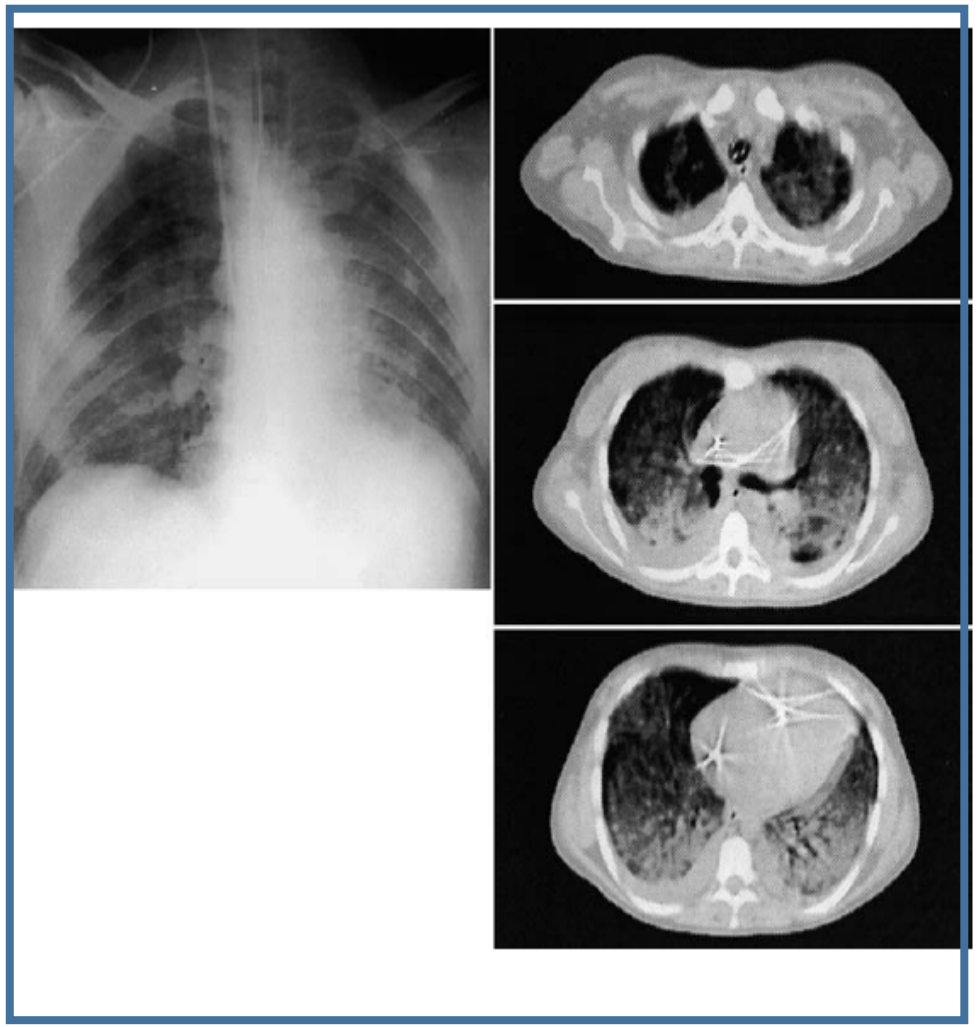
At this time, surfactant therapy cannot be recommended as routine therapy in PARDS. Further study should focus on specific patient populations that may be likely to benefit and specific dosing and delivery regimens strong agreement

Pulmonary specific ancillary treatment

- Inhaled Nitric Oxyde
- Exogenous Surfactant
- **Prone Positioning**
- Suctioning
- Corticosteroids

Pulmonary specific ancillary treatment

- **Prone Positioning**



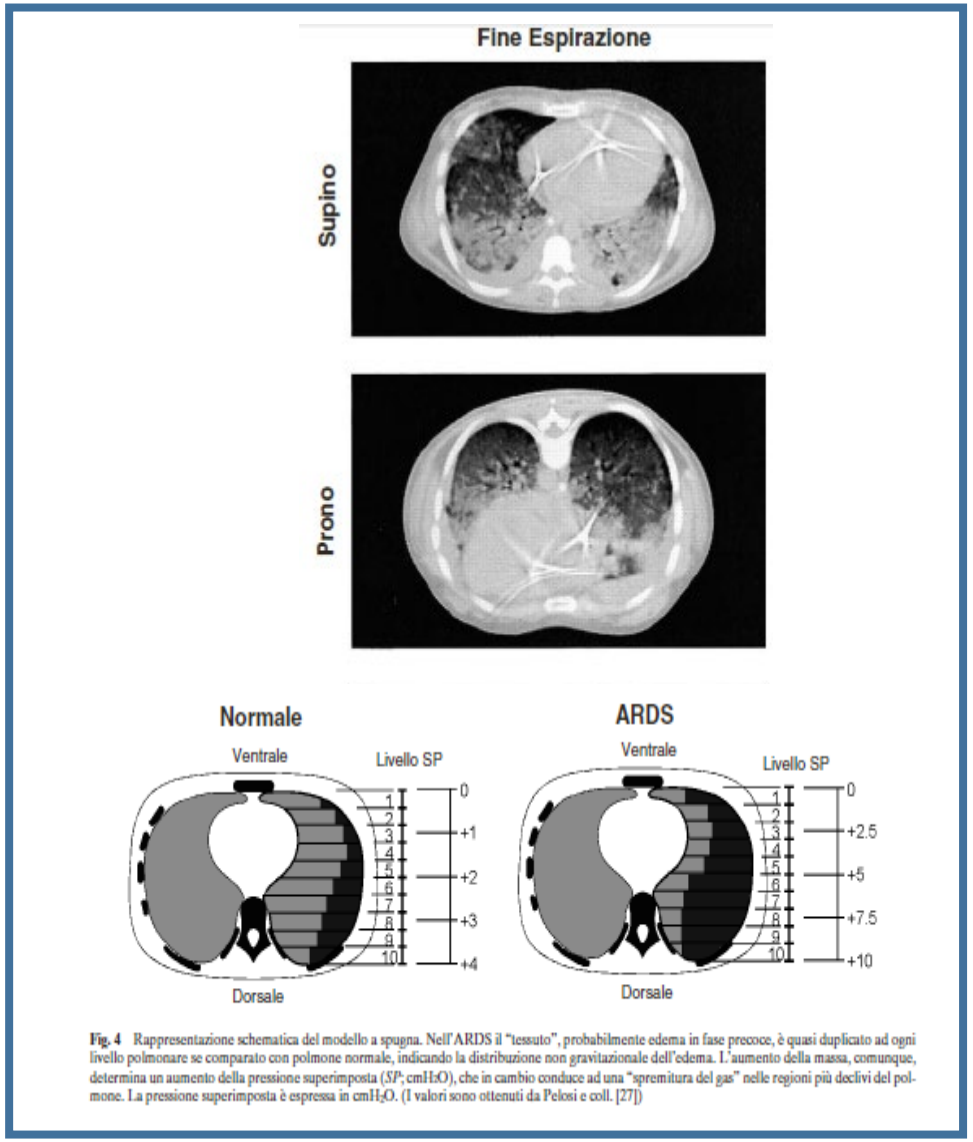


Fig. 4 Rappresentazione schematica del modello a spugna. Nell'ARDS il "tessuto", probabilmente edema in fase precoce, è quasi duplicato ad ogni livello polmonare se comparato con polmone normale, indicando la distribuzione non gravitazionale dell'edema. L'aumento della massa, comunque, determina un aumento della pressione superimposta (*SP*; cmH_2O), che in cambio conduce ad una "spremitura del gas" nelle regioni più declivi del polmone. La pressione superimposta è espressa in cmH_2O. (I valori sono ottenuti da Pelosi e coll. [27])

Pulmonary specific ancillary treatment

- **Prone Positioning**

ARDS

The NEW ENGLAND JOURNAL of MEDICINE

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

Prone Positioning in Severe Acute Respiratory Distress Syndrome

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PARDS

JAMA. 2005 July 13; 294(2): 229–237.

Effect of Prone Positioning on Clinical Outcomes in Children with Acute Lung Injury: A Randomized Controlled Trial

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Children's Hospital Boston (Drs Curley, Wypij, Shih, Mr Thompson, Dr Arnold); Tufts-New England Medical Center, Boston (Dr Hibberd); University of California, San Francisco (Ms Fineman, Dr Matthay); Primary Children's Medical Center (Dr Grant); Vanderbilt Children's Hospital (Dr Barr); Children's Hospital Oakland (Dr Cvijanovich); Children's Memorial Hospital, Chicago (Ms Sorce); Children's Medical Center of Dallas (Dr Luckett).

- **Prone positioning *cannot be recommended as routine therapy in PARDS*. However, it should be considered AN OPTION IN CASE OF SEVERE PARDS. Further pediatric study is warranted,particular study stratifying on the basis of severity of lung injury. Weak agreement**

Pulmonary specific ancillary treatment

- Inhaled Nitric Oxyde
- Exogenous Surfactant
- Prone Positioning
- **Suctioning**
- Corticosteroids

Pulmonary specific ancillary treatment

Suctioning

- Maintaining a clear airway is essential to the PARDS patient. However, endotracheal suctioning must be performed with caution to **minimize risk of derecruitment** (STRONG AGREEMENT)
- Insufficient data to support a recommendation on the use of either an **open or closed suctioning system.** However, in severe PARDS consideration should be given to the technique of suctioning with careful attention to minimize the potential of derecruitment (STRONG AGREEMENT)
- The routine **instillation** of isotonic saline prior to endotracheal suctioning **is not recommended**. However, the instillation of isotonic saline prior to endotracheal suctioning may be indicated at times for lavage to remove thick tenacious secretions (STRONG AGREEEMENT)

Pulmonary specific ancillary treatment

- Inhaled Nitric Oxyde
- Exogenous Surfactant
- Prone Positioning
- Suctioning
- Corticosteroids

Pulmonary specific ancillary treatment

Corticosteroid

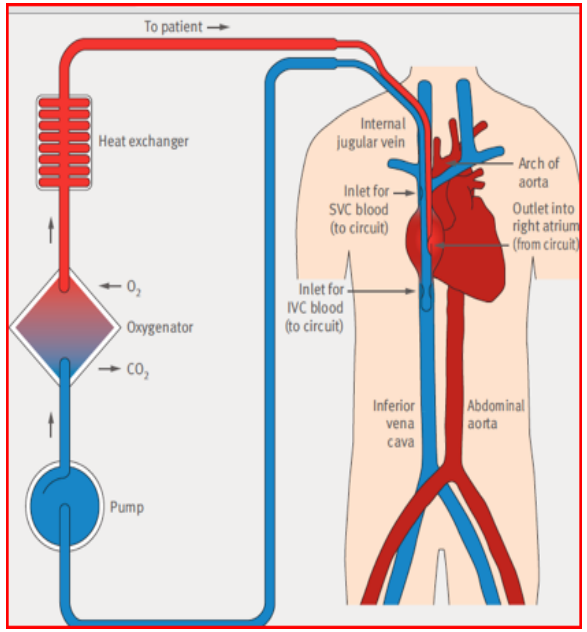
- ARDS is characterized by an overwhelming **inflammatory process**
- **Available pediatric data limited** to case series
- Corticosteroid **cannot be recommended** as routine therapy in PARDS. Further study should focus on specific patient populations that are likely to benefit from corticosteroid therapy and specific dosing and delivery regimens

Non Pulmonary treatment

- Sedation
- Neuromuscolar Blockade
- Nutrition
- Fluid Managment and Transfusion

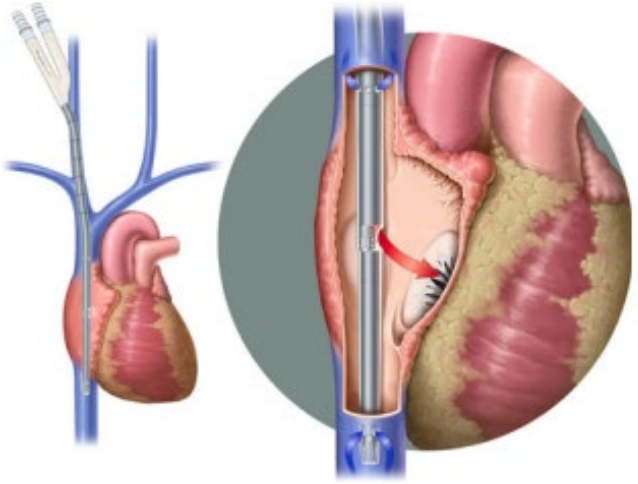
Extracorporeal Life Support (ECLS)

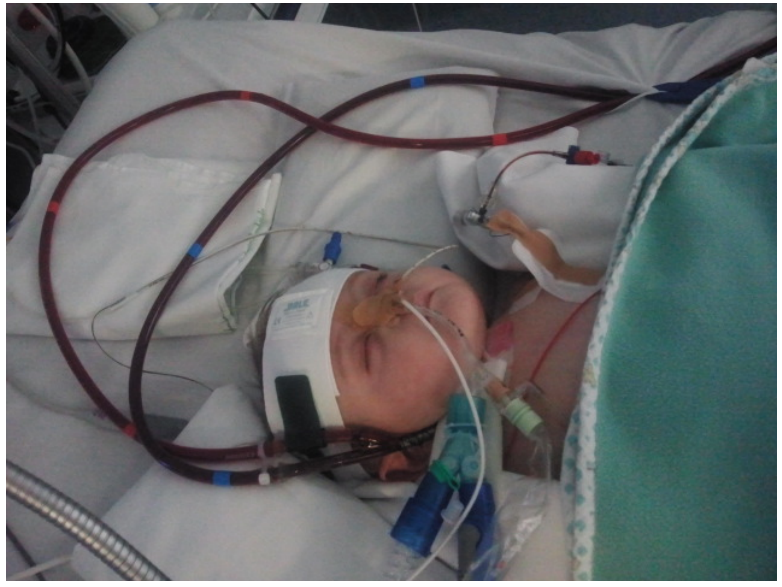
- **ECMO Extracorporeal membrane Oxigenation**



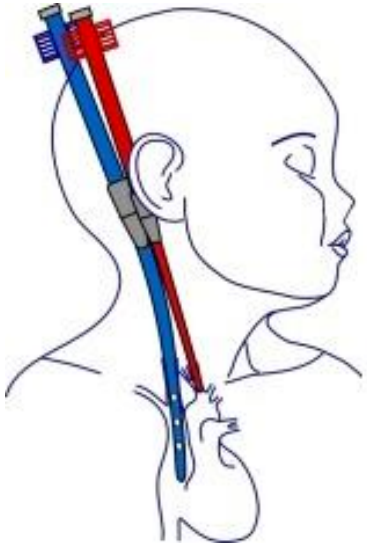
Extracorporeal Life Support (ECLS)

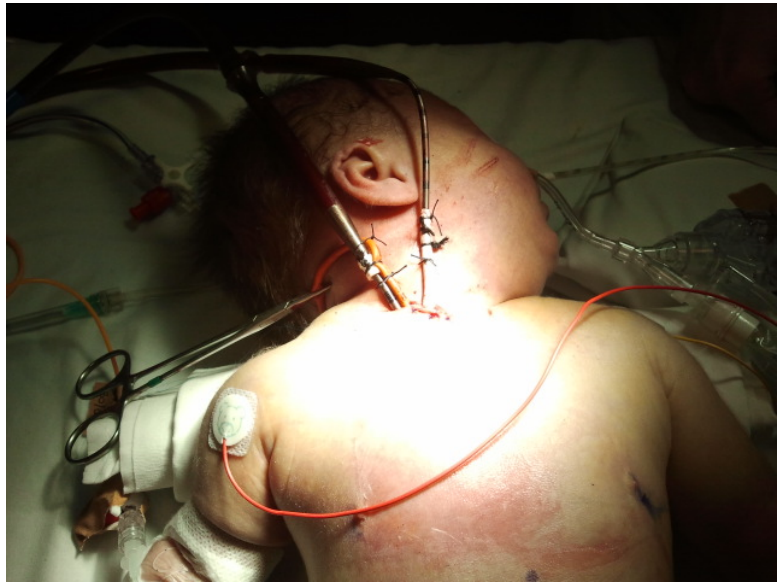
ECMO veno-venoso





ECMO veno-arterioso





Extracorporeal Life Support (ECLS)

- **ECMO**

- International Extracorporeal Life Support Organization Registry (ELSO)
- **www. ELSO.org**
- Data from 55.000 pts
- Respiratory, cardiac, multiorgan failure for NEONATES, CHILDREN and ADULTS

- HIGH QUALITY CLINICAL-TRIAL EXIST ONLY IN SUPPORT OF THE USE OF ECMO IN **NEONATES** AND **ADULT** SEVERE RESPIRATORY FAILURE
- Despite lack of evidence for superiority, however, **ECMO in pediatric patients is used throughout the world**

Extracorporeal Life Support (ECLS)

- ECMO

Outcome of Pediatric Patients Who Receive Extracorporeal Membrane Oxygenation: Pediatric Respiratory Runs by Diagnosis

Diagnosis	Total Runs	Average Run Time	Longest Run Time	Survived	% Survived
Viral pneumonia	1,371	320	2,968	884	64%
Bacterial pneumonia	651	282	1,411	379	58%
Pneumocystis pneumonia	33	359	1,144	17	52%
Aspiration pneumonia	293	247	2,437	201	69%
ARDS, postoperative/trauma	183	248	935	114	62%
ARDS, not postoperative/trauma	530	305	3,086	285	54%
Acute respiratory failure, not ARDS	1,101	255	2,429	594	54%
Other	2,108	217	2,465	1,073	51%

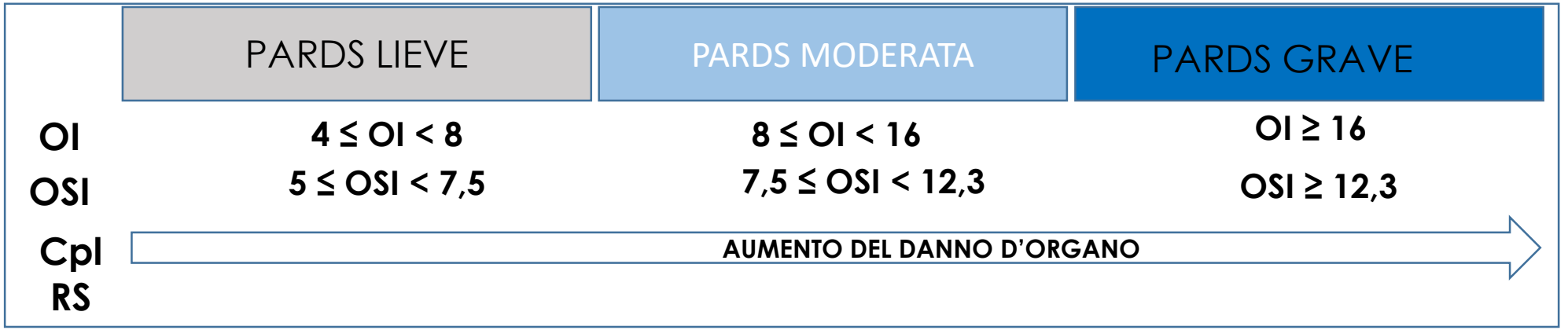
ARDS = acute respiratory distress syndrome.

Run time is represented in hours. Data adapted from the International Registry of Extracorporeal Life Support Organization, July 2013, with permission.

Extracorporeal Life Support (ECLS)

- We recommend that ECMO should be **considered to support children with severe PARDS where the cause of the respiratory failure is believed to be reversible** or the child is likely to be suitable for lung tansplantation
- It is **not possible to applly strict criteria** for the selection of children who will benefit from ECMO in PARDS. We recommend that **children with severe PARDS should be considered for ECMO when lung protective strategies results in inadequate gas exchange**
- We recommend that **serial evaluation of ECMO eligibility is more useful than single point assesment**
- We recommend that **careful consideration of quality of life and likelihood of benefit** should be assessed

Algoritmo ventilatorio



VENTILAZIONE

VENTILAZIONE PROTETTIVA

VENTILAZIONE NON INVASIVA

VENTILAZIONE INVASIVA

VENTILAZIONE ASSISTITA — VENTILAZIONE CONTROLLATA

5-8 ml/kg----------**TV**---------- 3 – 6 ml/kg

5 ----------**PEEP**---------- >15

P Pplat <28 cmH20

VENTILAZIONE

PARDS GRAVE

OI ≥ 16

OSI ≥ 12,3

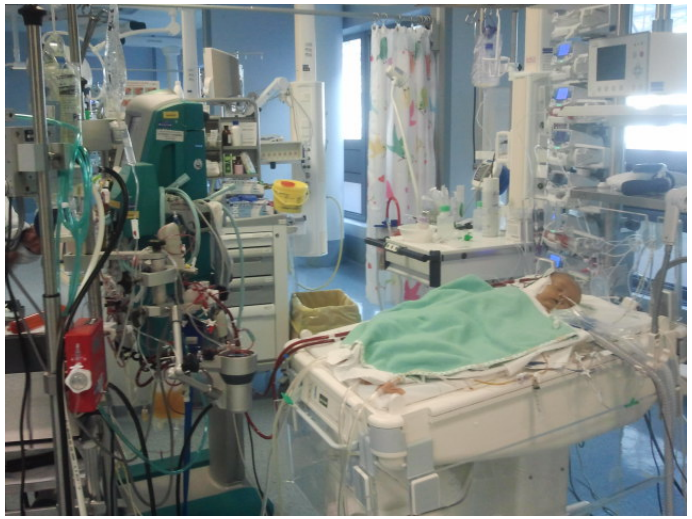
VENTILAZIONE CONTROLLATA
3 – 6 ml/kg
PEEP ≥ 15
P Plat ≤ 28 cmH20 (32*)

POSIZIONE PRONA ⇄ iNO

- **BLOCCO NEUROMUSCOLARE**
- **SURFACTANTE**
- **CORTICOSTEROIDI**

HFOV

ECMO



* ridotta cpl CW

Conclusion

- Acute respiratory distress syndrome (**ARDS**) is characterized by the acute onset of pulmonary edema of non-cardiogenic origin, along with bilateral pulmonary infiltrates and reduction in respiratory system compliance. The hallmark of the syndrome is **refractory hypoxemia.**

- **ARDS in children** is different from ARDS in adults, the PARDS Consensus Conference (2015) developed **pediatric specific definitions** and **recommendations regarding treatment** and future research priorities.

- **Pulse oximetry** is increasingly obviating the use of arterial blood gas measurement in pediatrics.

- **Protective mechanical ventilation** should be the standard of care, especially in patients who develop ARDS

Conclusion

- **infection by specific viruses** can lead to severe respiratory failure possibly because of an **exaggerate inflammatory reaction**, which is associated with severe pneumonitis and eventually acute respiratory distress syndrome (**ARDS**)

- **systemic steroid administration** for the treatment of severe viral pneumonia was suggested as a valid therapeutic option but **no data are available to support the generalized use of steroids**

- **The mainstream of the treatment for severe viral pneumonia is mostly supportive and few antiviral medications are available and effective in case of severe infection**

Conclusion

- If suspicion of viral pneumonia is present, **nasopharyngeal swab or bronchial sample** should be collected and **screened for virus infection**

- Laboratory testing is required to definitively distinguish infecting influenza virus from other pathogens, resulting in **unnecessary antibiotic use**.

- Recently available **rapid tests** may allow for appropriate **use of antiviral** (antivirals are of most clinical benefit if taken within 48 hours of symptom onset) and for **prevention** of **nosocomial spread of viral illness**.

- **Bacterial super-infection** is a common complication of severe viral pneumonia; **bacterial culture and empiric antibiotic treatment should be considered in case of clinical suspicion**.