Pharmacologic Treatment of ARDS: It's not all about the ventilator

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Objectives

- Discuss common pharmacotherapeutic options for the treatment of acute respiratory distress syndrome (ARDS)

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Conflicts of Interest

- None

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Think & Share

- You have just intubated a patient with acute respiratory distress syndrome (ARDS), P:F ratio is 108, PEEP 15, FiO2 1 and O2 sat remains at 86% regardless of optimizing ventilator recruitment strategies. The team is planning to prone the patient within the next hour.
- What options for pharmacotherapy would you consider starting on this patient and why?

Take 30 seconds to think then share it!

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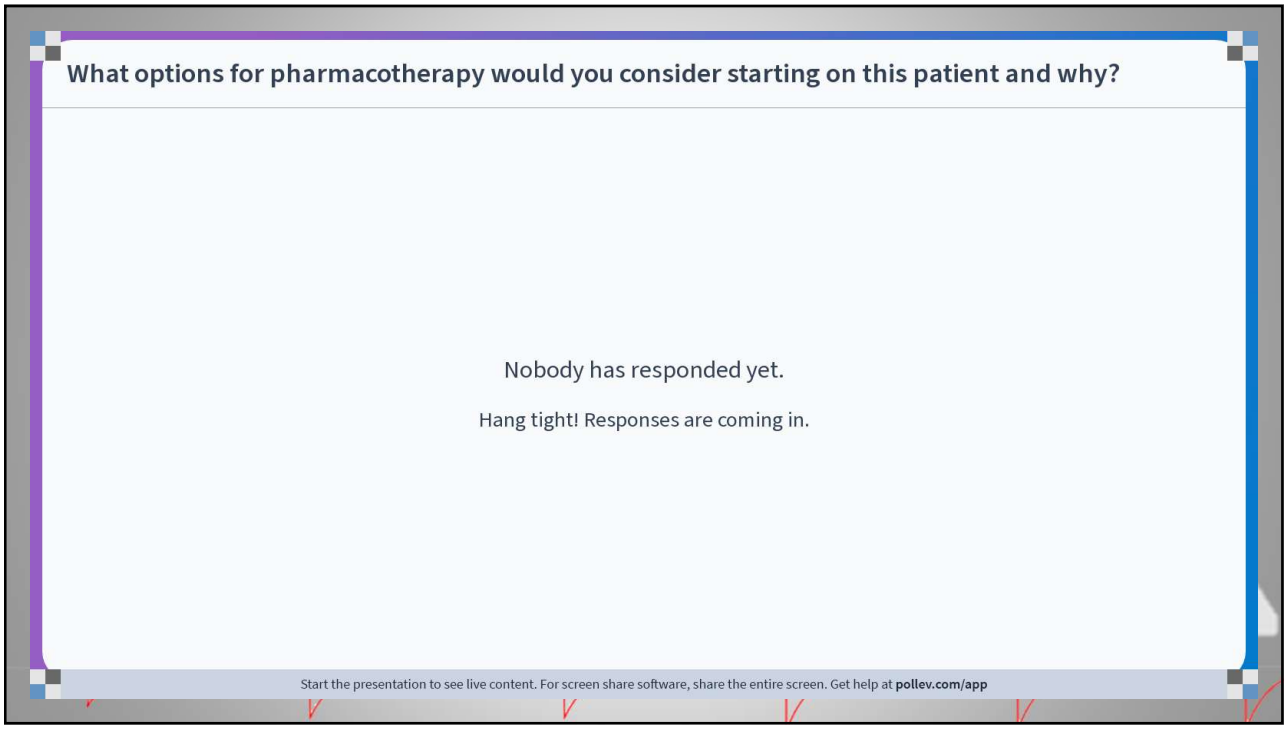
What options for pharmacotherapy would you consider starting on this patient and why?
Nobody has responded yet.
Hang tight! Responses are coming in.
Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

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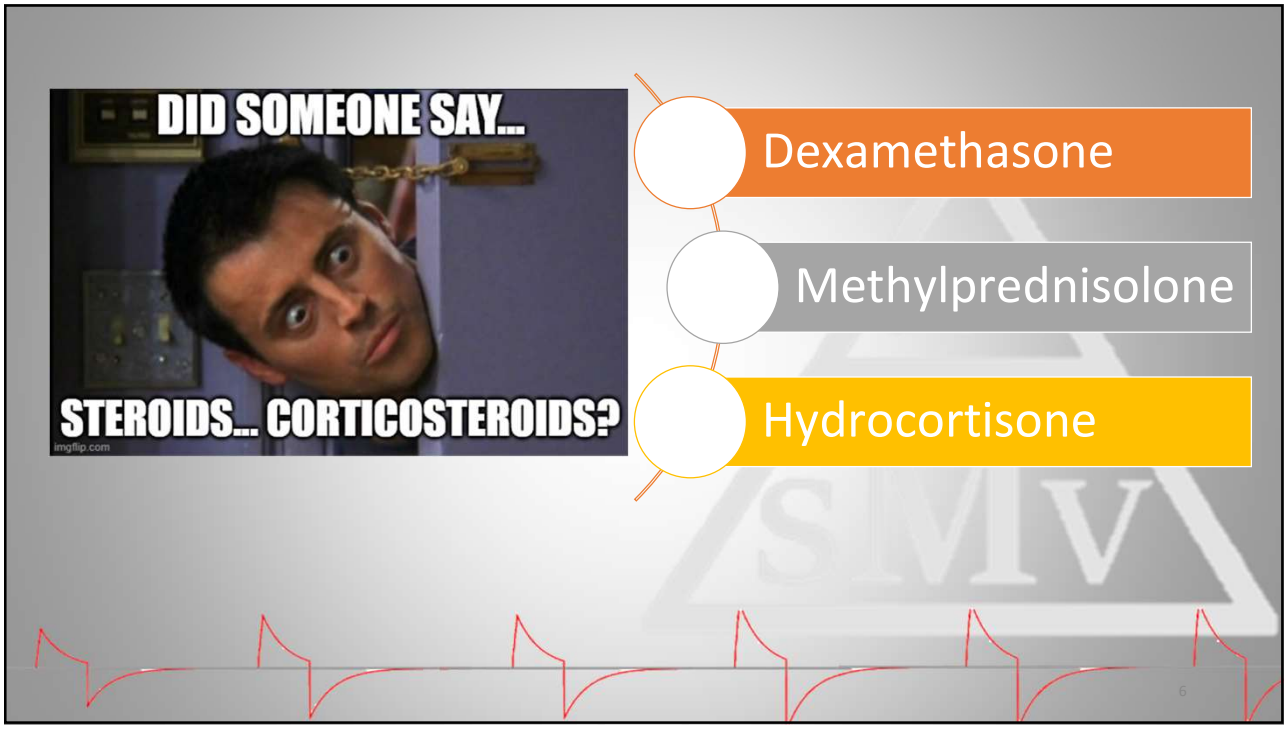
DID SOMEONE SAY...
STEROIDS... CORTICOSTEROIDS?
imgflip.com
Dexamethasone
Methylprednisolone
Hydrocortisone

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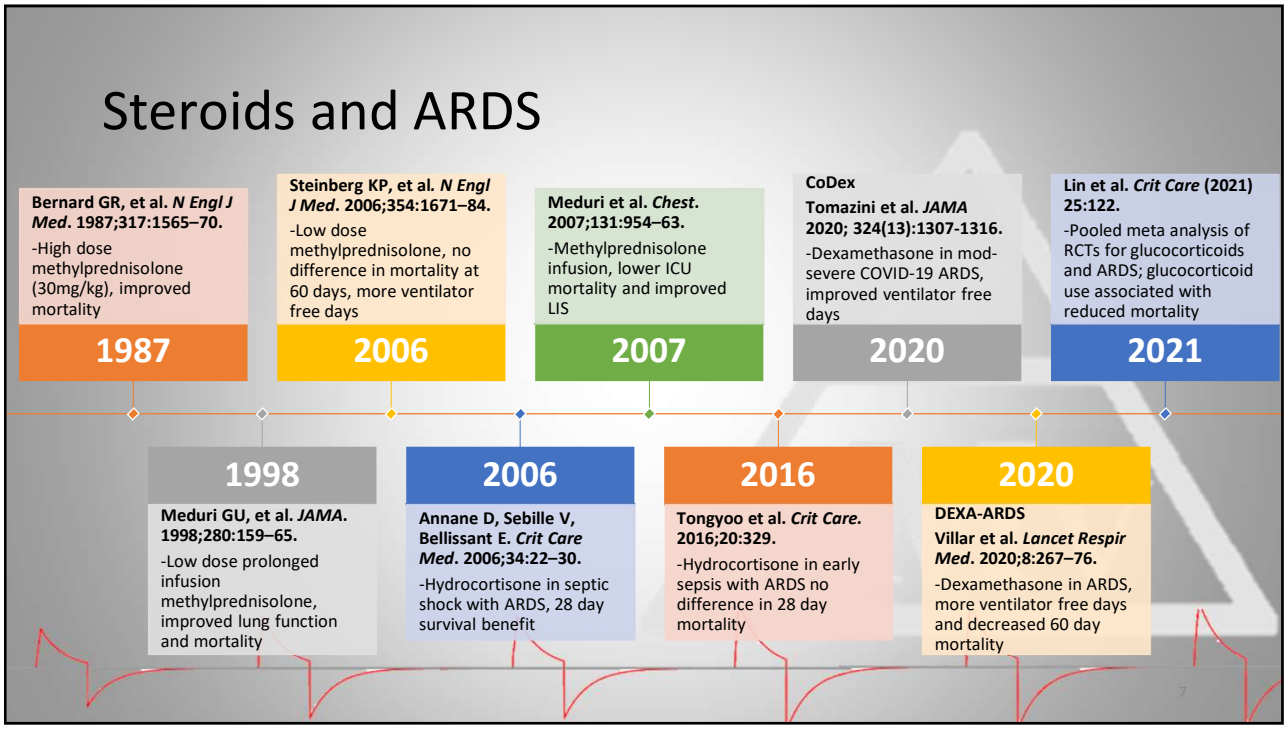
Steroids and ARDS



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What we know…

- ✓ Mortality benefit
- ✓ More ventilator free days
- ✓ Improved oxygenation
- ✓ Use low dose systemic corticosteroids
- ✓ Start early (< 14 days)
- ✓ Questionable impact on viral pneumonias except COVID-19

Lin et al. *Crit Care* (2021) 25:122
Qadir N, Chang S. *Crit Care Clin* 37 (2021) 877–893
Tasaka S, et al. *Journal of Intensive Care* (2022) 10:32

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Corticosteroids used in ARDS

- Methylprednisolone 1-2 mg/kg/day for 21 to 28 days
- Dexamethasone 20 mg IV once daily for five days, tapering to 10 mg once daily for five days
- COVID-19 ARDS: Dexamethasone 6-10 mg daily for 10 days
- Hydrocortisone 50 mg IV q6h or 100 mg IV q8h

Prescott, HC, Rice, TW. *JAMA*, *324*(13), 1292–1295.
Villar J, et al. *Lancet Respir Med* 2020; 8(3):267-276.
Qadir N, Chang S. *Crit Care Clin* 37 (2021) 877–893

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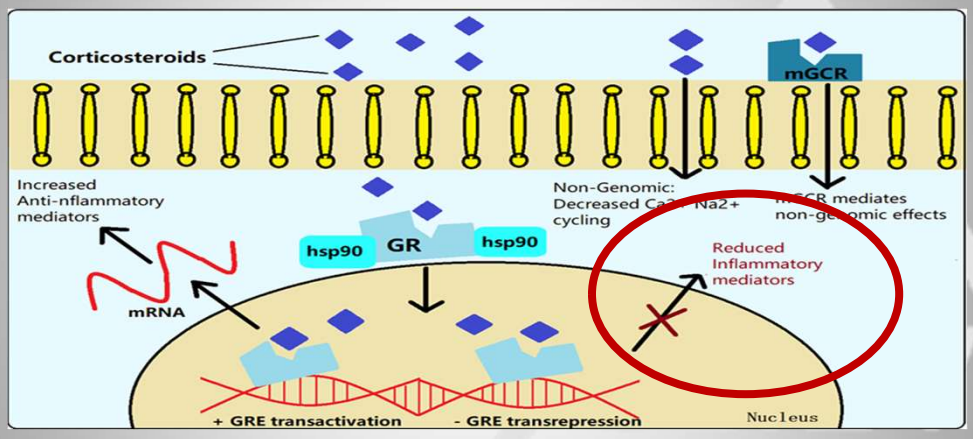
Mechanism of corticosteroids



Dinh T, Chu C. *J Mech Vent* 2021; 2(4)

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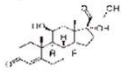
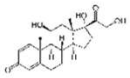
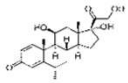
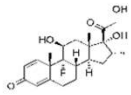
Medication	MC : GC* Activity**	Duration of action (Hours)	Half-Life (Hours)	Equivalent GC dose (mg)
Hydrocortisone 	1 : 1	8-12	IV: 2 ± 0.3 Oral: 1.8 ± 0.5	20
Prednisone 	0.8 : 4	12-36	2.1-3.5	5
Methylprednisolone 	0.5 : 5	12-36	Oral: 2.5 ± 1.2 IV: 0.25 ± 0.1	4
Dexamethasone 	0 : 30	36-54	Oral: 4 ± 0.9 IV: ~1 to 5	0.75

*MC = Mineralocorticoid activity; GC = Glucocorticoid (anti-inflammatory) activity
**Potency relative to hydrocortisone

Adapted from Dinh T, Chu C. *J Mech Vent* 2021; 2(4)

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Considerations from a pharmacist perspective

- Gradual taper if used more than 48 hrs
- Myopathy or post-paralytic quadriparesis
- Psychological derangements
- Hyperglycemia
- Stress ulcer prophylaxis

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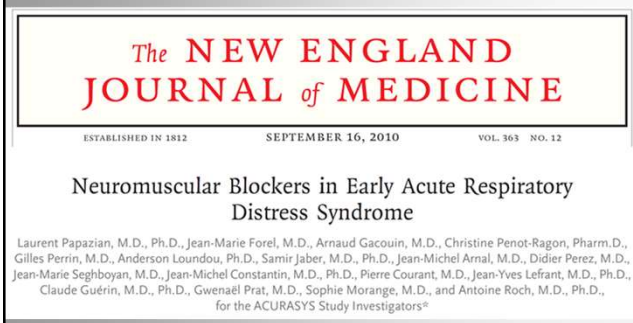
Lung Protective Ventilation and Paralytics

ACURASYS



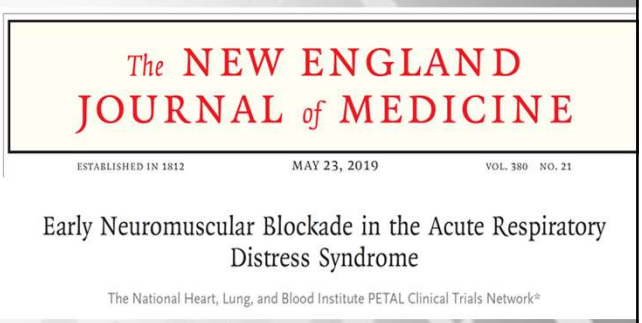
The NEW ENGLAND JOURNAL of MEDICINE

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

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*

ROSE



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 23, 2019 VOL. 380 NO. 21

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

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

Papazian L, et al. *N Engl J Med* 2010;363:1107-16.
The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, et al. *N Engl J Med* 2019;380:1997-2008.

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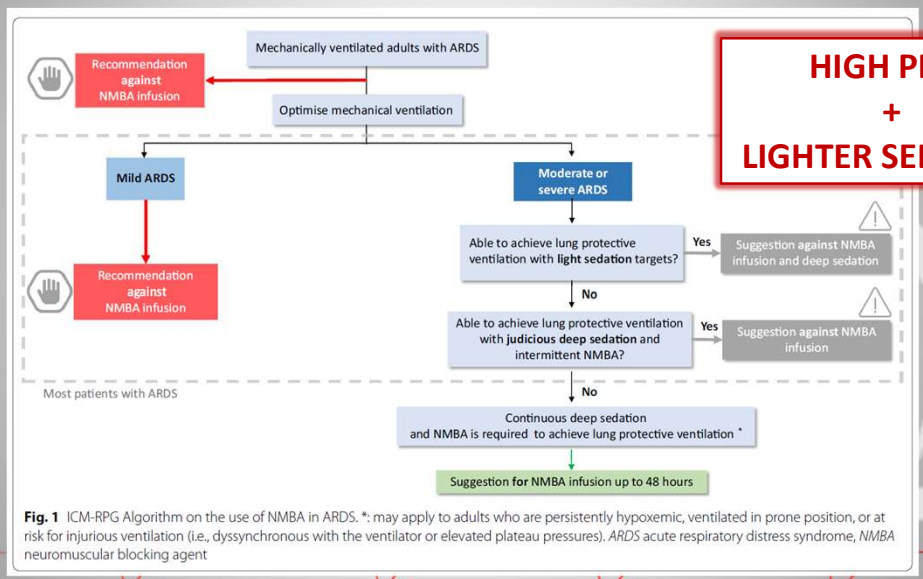
Lung Protective Ventilation and Paralytics



HIGH PEEP
+
LIGHTER SEDATION

Fig. 1 ICM-RPG Algorithm on the use of NMBA in ARDS. *: may apply to adults who are persistently hypoxemic, ventilated in prone position, or at risk for injurious ventilation (i.e., dyssynchronous with the ventilator or elevated plateau pressures). *ARDS* acute respiratory distress syndrome, *NMBA* neuromuscular blocking agent

Alhazzani, W et al. *Intensive Care Med* (2020) 46:1977–1986

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Key Takeaways…

- High PEEP and lighter sedation!
- Use paralytics sparingly and start early
  - Prevent ventilator associated lung injury (VALI)
- Intermittent IV bolus > continuous infusion
  - Keep continuous infusions to < 48 hrs
- Cisatracurium only?
- What about proning?

Alhazzani, W et al. *Intensive Care Med* (2020) 46:1977–1986
Papazian L, et al. *N Engl J Med* 2010;363:1107-16.
The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, et al. *N Engl J Med* 2019;380:1997-2008.

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Considerations from a pharmacist perspective

- How's your sedation?
- Concurrent steroids
- Bowel regimen
- Venous thromboembolism prophylaxis
- Eye care

Haywood, S. (2021) https://i0.wp.com/criticalcarenow.com/wp-content/uploads/2021/06/Screen-Shot-2021-06-27-at-10.13.21-PM.png?w=690&ssl=1

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To use, or NOT to use in severe ARDS…

Polling Question- Do you currently use inhaled vasodilators (nitrous oxide or prostacyclin's) in your ARDS patients?

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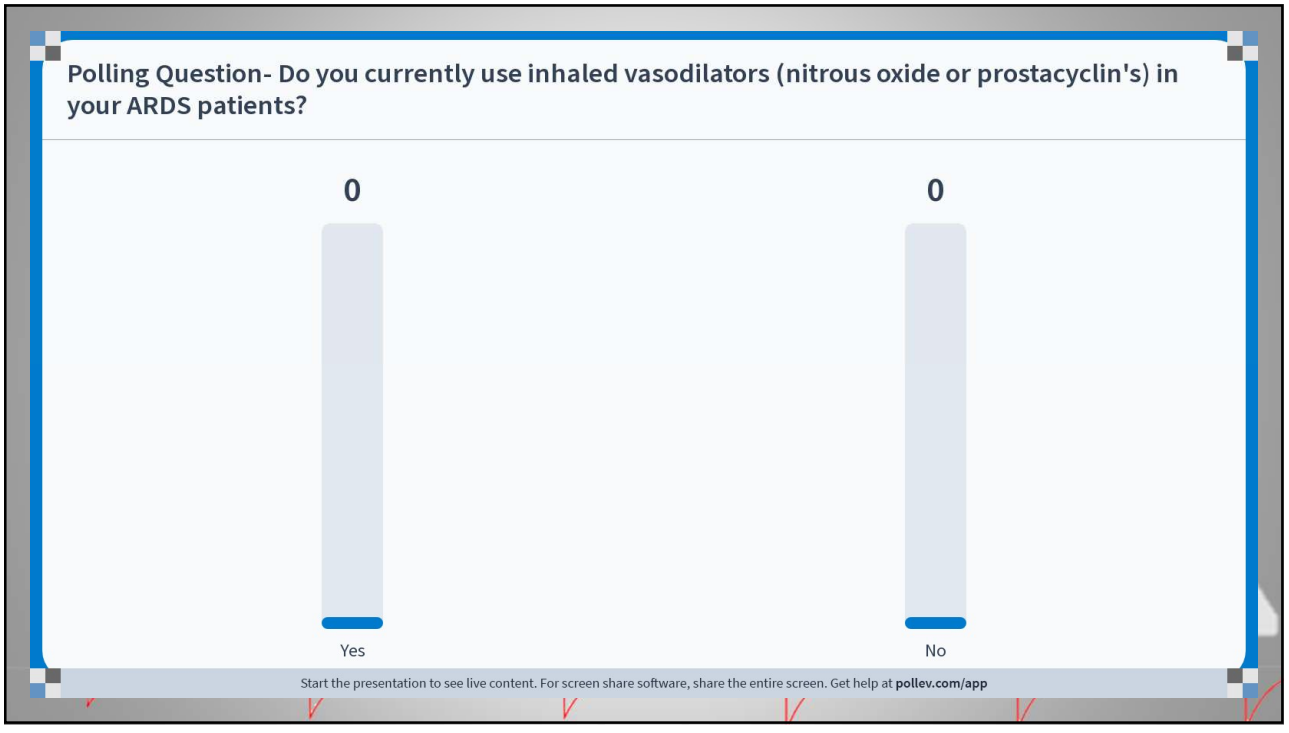

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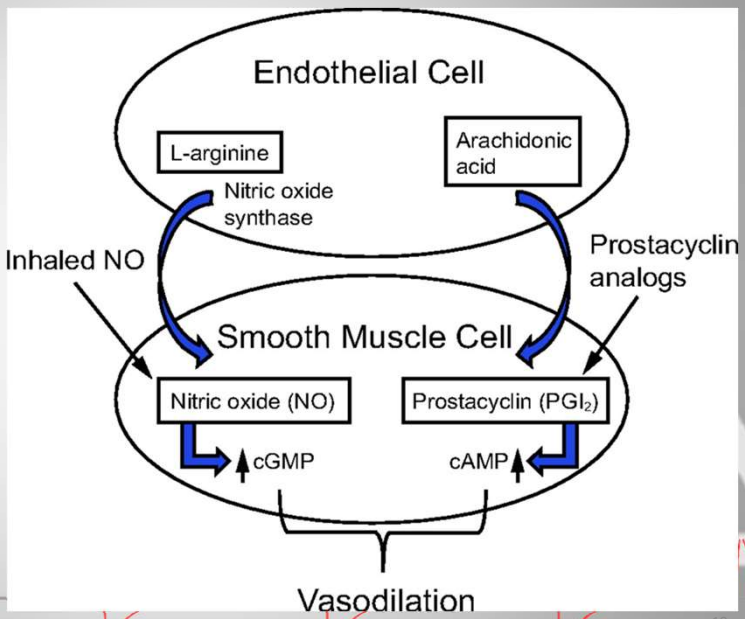
Vasodilators



Walsh B. K. *Respiratory care*, *65*(10), 1611–1623.

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Vasodilators for ARDS

Inhaled Nitric Oxide (iNO)

- No mortality benefit
- No benefit in length of mechanical ventilation
- Increased risk of acute kidney injury

Prostacyclines

- No mortality benefit

Tasaka S, et al. *Journal of Intensive Care* (2022) 10:32
Qadir N, Chang S. *Crit Care Clin* 37 (2021) 877–893

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To use, or NOT to use in severe ARDS…

Polling Question- Do you currently use inhaled b-agonists in your ARDS patients?

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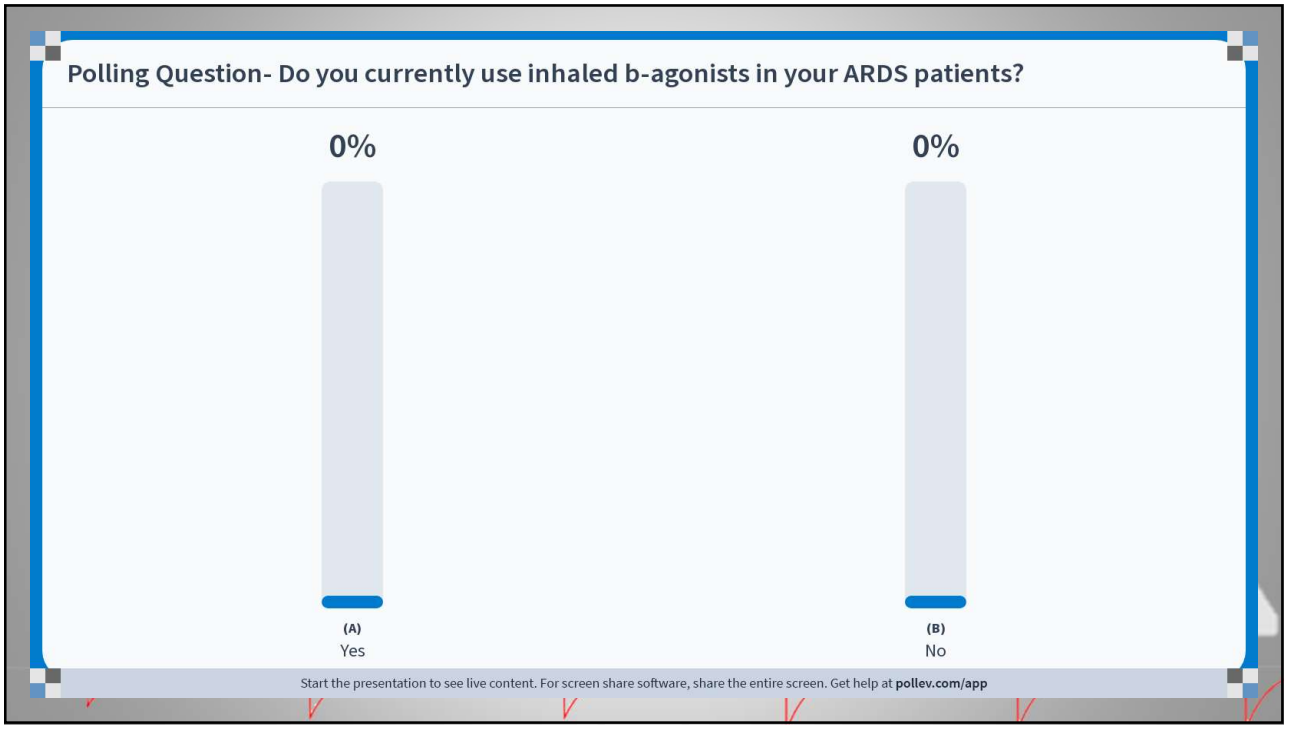

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Inhaled B-agonists for ARDS

- Stimulate alveolar fluid clearance may decrease lung vascular permeability
- Albuterol nebulized- rapid onset (< 5 min); short acting (3-6 hrs)
- Increased ICU days
- No mortality benefit
- No benefit in length of mechanical ventilation

Qadir N, Chang S. *Crit Care Clin* 37 (2021) 877–893

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B-agonists used for prevention???

Crit Care Med. 2017 May ; 45(5): 798–805. doi:10.1097/CCM.0000000000002284.

Randomized Clinical Trial of a Combination of an Inhaled Corticosteroid and Beta Agonist in Patients at Risk of Developing the Acute Respiratory Distress Syndrome

Emir Festic, MD[1], Gordon E Carr, MD[2], Rodrigo Cartin–Ceba, MD[3], Richard F Hinds, MS[4], Valerie Banner–Goodspeed, MPH[5], Vikas Bansal, MBBS[1], Adijat T Asuni, MPH[6], Daniel Talmor, MD[5], Govindarajan Rajagopalan, PhD[7], Ryan D Frank, MS[8], Ognjen Gajic, MD[4], Michael A Matthay, MD[9], and Joseph E Levitt, MD[6]

The ARREST Pneumonia Clinical Trial

Rationale and Design

Joseph E. Levitt[1]*, Emir Festic[2,3]*, Manisha Desai[4], Haley Hedlin[4], Kenneth W. Mahaffey[5], Angela J. Rogers[1], Ognjen Gajic[6,7], and Michael A. Matthay[8]; on behalf of ARREST Pneumonia Clinical Trial Investigators

Festic E, et al. *Crit Care Med*. 2017 May ; 45(5): 798–805.
Levitt JE, et al. *Ann Am Thorac Soc* Vol 18, No 4, pp 698–708, Apr 2021

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Pharmacologic Treatment of ARDS: It's ~~not~~ all about the ventilator… AND steroids

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