

Reply to: ECCO2R and the Alveolar Gas Equation

Darryl Abrams, MD^{1,2} Antonio Pesenti, MD^{3,4} Laurent Brochard, MD^{5,6,*} Daniel Brodie, MD^{1,2}

¹Columbia University College of Physicians & Surgeons/New York-Presbyterian Hospital, New York, NY, USA

²Center for Acute Respiratory Failure, Columbia University Medical Center, New York, NY, USA

³Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy.

⁴Department of Anesthesia, Critical Care and Emergency Medicine, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milan, Milan, Italy

⁵Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, ON, Canada

⁶Keenan Research Center, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada

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Corresponding author:

Daniel Brodie

622 W168th St

PH 8E, Rm 101

New York, NY 10032

Phone: 212-305-9817

Fax: 212-305-8464

hdb5@cumc.columbia.edu

To the Editor:

We appreciate Dr. Dickstein's physiologically nuanced point in calling attention to the complete alveolar gas equation (AGE) in West's Respiratory Physiology primer (1) in response to our review "Mechanical Ventilation for Acute Respiratory Distress Syndrome During Extracorporeal Life Support"(2). The extra term in the complete AGE does, in fact, account for a portion of the decrease in oxygenation that would be anticipated with the introduction of extracorporeal carbon dioxide removal (ECCO₂R). Indeed, at high levels of FIO₂, the difference between the calculated PAO₂ based on the abbreviated and complete versions of the AGE is more pronounced but of less clinical significance, with PAO₂ well above 200 mmHg at an FIO₂ at or above 0.5. However, at lower FIO₂, which may be more relevant when ECCO₂R is used for patients with hypercapnia with relatively preserved oxygenation, the difference between the PAO₂ in the abbreviated and complete AGE is less pronounced. This results in more clinically significant decreases in PAO₂ when the respiratory exchange ratio is decreased in the context of ECCO₂R, regardless of which formula is used. For example, at FIO₂ of 0.3, PACO₂ 40 mmHg and respiratory exchange ratio (RER) of 0.8, the PAO₂ in the abbreviated AGE would be 164 mmHg and with the complete AGE is nearly identical at 166 mmHg; when RER is decreased to 0.4, the PAO₂ would be 114 mmHg with the abbreviated AGE and 131 mmHg with the complete AGE, so the PAO₂ does still decrease, just to a lesser degree than would be expected from the abbreviated AGE (Figure 1). There remains a notable decrease in PAO₂ regardless of which AGE is used, which poses a real risk of leading to hypoxemia. This decrease in PAO₂ due to reductions in RER could be overcome with an increase in FIO₂, as the author demonstrates in his figure.

Also, the concept of passive movement of fresh gas into the alveolus, as a consequence of the difference between inspired volume and expired volume, must be put into context. The extreme example is zero expired gas flow, which amounts to apneic oxygenation and, in principle, no change in PAO_2 . However this passive flow requires specific conditions to be maintained. Under normal conditions it might take place at low RER, but under pathological conditions (e.g. chronic obstructive pulmonary disease or the acute respiratory distress syndrome), with low RER usually associated with a low ventilation-perfusion ratio (VA/Q), the risk of alveolar collapse will be much higher, depending on mixed venous gas content and the presence of nonhomogeneous distribution of VA/Q (3), also potentially contributing to hypoxemia. The portion of hypoxemia due to shunt physiology will, notably, not be overcome by increasing FIO_2 .

References

1. West JB. Respiratory Physiology: The Essentials, 6th edn. Baltimore: Lippincott Williams and Wilkins; 2000.
2. Abrams D, Schmidt M, Pham T, Beitler JR, Fan E, Goligher EC, McNamee JJ, Patroniti N, Wilcox ME, Combes A, Ferguson ND, McAuley DF, Pesenti A, Quintel M, Fraser J, Hodgson CL, Hough CL, Mercat A, Mueller T, Pellegrino V, Ranieri VM, Rowan K, Shekar K, Brochard L, Brodie D. Mechanical Ventilation for Acute Respiratory Distress Syndrome during Extracorporeal Life Support. Research and Practice. *Am J Respir Crit Care Med* 2020; 201: 514-525.
3. West JB. State of the art: ventilation-perfusion relationships. *Am Rev Respir Dis* 1977; 116: 919-943.

Legend:

Figure 1. The PAO₂ was calculated using the simplified alveolar gas equation (dashed lines) and the complete equation (solid lines) at 3 different levels of FIO₂ (0.7 [green lines], 0.5 [red lines], and 0.3 [black lines]) and across a range (from 0 to 100 ml) of CO₂ elimination via ECCO₂R. Baseline RER=0.8. Note that at lower FIO₂, the PAO₂ curves from the simplified and complete equations become closer in approximation, with a substantial reduction in PAO₂ as CO₂ elimination via ECCO₂R increases.

