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Reply to Dorrington et al. and to Swenson

From the Authors:

We want to thank Dr. Dorrington and colleagues and Dr. Swenson for their interest in our paper (1). We agree that hypercapnic pulmonary vasoconstriction is underappreciated as an independent component of the vascular response. However, our estimates suggest that CO₂ fails as a singular explanation for the nonhypoxic component of perfusion redistribution during bronchoconstriction, and that other possible mechanisms, such as those we propose in the article, should be considered.

For a quantitative estimate of the contribution of hypercapnia to the decrease in regional perfusion during bronchoconstriction in our study, we rely on results from animal studies reporting relative reductions in regional perfusion per mm Hg hypercapnia (%/mm Hg) of 0.35 in cats (2), 0.97 (2) and 0.64 (3) in dogs, and 1.9 (4) in sheep. In addition, it is known that human subjects during mild bronchoconstriction do not develop hypercapnia (5–7) and would be expected to have an arteriovenous difference in PCO₂ of ~6 mm Hg (8). Thus, assuming, based on the animal data, a reduction in perfusion of ~1%/mm Hg in humans, the upper limit for hypercapnia with an increase of 6 mm Hg in severely constricted hypoventilated regions would explain a relative reduction in perfusion of only 6%. For comparison with our study, we chose a representative data point of average values in our subregion analysis that included a narrow range of V/Q, a low PO₂ breathing air, and a degree of hypoventilation allowing for regional PO₂ greater than 100 mm Hg breathing 100% O₂, but a CO₂ as close as possible to the mixed venous level. A change in alveolar PO₂ from 61 mm Hg at room air to 291 mm Hg at 100% O₂ resulted in a relative change in perfusion after methacholine treatment from –31.2% to –16.5%, respectively. Thus, the estimated 6% reduction in perfusion in response to hypercapnia is indeed a relevant contribution but accounts for only a small fraction of the remaining nonhypoxic decrease of –16.5% and falls well short as a singular explanation.

Contributions of other factors to vasoconstriction are known for lobar collapse (9), which likely involves the loss of parenchymal tethering forces that counterbalance vascular smooth muscle constriction. In contrast, bronchoconstriction may affect the vascular tree by distorting vessels adjacent to the constricted airway or by stimulating vascular smooth muscle. Dr. Swenson suggests the use of a correlation analysis to determine the contribution of PCO₂ to the perfusion redistribution, but the regional bronchoconstriction in ventilation defects would affect

both PCO₂ and any other component of the vascular response, resulting in correlated inputs.

In conclusion, hypercapnia in ventilation defects certainly contributes to vasoconstriction and changes in regional perfusion during bronchoconstriction, but the magnitude of the nonhypoxic reduction in regional blood flow compared with the estimated effect of hypercapnia is many-fold higher. This suggests that other mechanisms, such as parenchymal forces or a vascular smooth muscle agonist, have a substantial effect on the regional change in vascular resistance during bronchoconstriction. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Erratum: FIFTY YEARS OF RESEARCH IN ARDS. Setting Positive End-Expiratory Pressure in Acute Respiratory Distress Syndrome

There is an error in the article by Sahetya and colleagues (1), published in the June 1, 2017, issue of the *Journal*. On page 1433, one of the sentences in the second paragraph under the heading DRIVING PRESSURE should read: “With constant tidal volume, if PEEP is raised and driving pressure decreases, the C_{RS} has **increased**, suggesting that the higher PEEP caused lung recruitment.” The sentence incorrectly stated that the C_{RS} would have decreased. ■

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