Intracapillary CO₂ Gradients

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The appearance of a number of reports that CO₂ tensions in the alveoli may exceed those in the pulmonary artery and vein have led to several hypotheses which are intended to explain such a gradient [17, 11, 18, 8]. Much attention has been given to the proposal of Gurtner et al. that this phenomenon could be explained on the basis of a charged membrane hypothesis [11, 13]: Hydrogen ions are dissociated from serum protein molecules under the influence of the negative charge on the endothelial cell surfaces and they are attracted to the capillary wall. Bicarbonate ions are repelled from the endothelium but at a slower rate. Consequently carbonic acid concentrations are elevated and CO₂ is formed in the region near the capillary wall and diffuses into the alveoli, raising alveolar P_CO₂.

Our original objection to this hypothesis was based on the amount of energy which would be required to maintain a gradient of CO₂ in the pulmonary capillaries [1]. Any increase in CO₂ tensions near the capillary wall should be rapidly dissipated in the plasma phase. Gurtner proposed that diffusion of CO₂ away from the endothelium could be slowed by red cells passing through the vessels [12]. Work by Roughton, Forster, and Silverman seems to show that the red cell membranes are less permeable to CO₂ than might be expected in aqueous or lipid solutions [20, 7, 23]. However, even if the red cells provide a barrier to diffusion, numerous problems remain:

1. Red cells flowing through the capillaries appear to remain about one μ away from the capillary wall and could not maintain a P_CO₂ gradient in the intervening plasma [10, 19]. CO₂ diffusion across this layer of plasma would quickly eliminate the proposed gradient [2].

2. If, on the contrary, it were assumed that the red cell membrane very closely approached the endothelial cell, the amount of HCO₃⁻ in the volume between these surfaces could become a limiting factor [2]. Since the hypothesis assumes that CO₂ does not readily escape from this region, it would not be appropriate to assume that additional bicarbonate would be transferred from between red cells to this same volume.

3. Convection near the capillary wall and between and around red cells may be sufficient to eliminate local H⁺, HCO₃⁻, or CO₂ gradients.

4. It is by no means clear that the charge on the endothelium is any greater than that on red cells [21, 22]. Since convection near the red cell surface may be as great as that near the endothelial surface, CO₂ generation by the proposed mechanism might be equal at both surfaces.

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5. If red cell membranes were sufficiently impermeable to impede CO₂ movement, then CO₂ generated within red cells should be released to the plasma slowly and a rise in $P_{CO_2}$ might therefore occur in the pulmonary veins.

6. There is no evidence that CO₂ diffusion across the alveolar capillary wall is more rapid than diffusion back into the center of the vessel. Consequently, even if $P_{CO_2}$ is greater near the endothelial surface, this would not necessarily elevate alveolar $P_{CO_2}$ above capillary $P_{CO_2}$.

7. Calculations by Forster suggest that although the movement of $HCO_3^-$ away from the wall is only one-eighth as rapid as the movement of $H^+$ toward the wall, an equilibrium distribution of $H^+$ and $HCO_3^-$ near the wall would be obtained within $10^{-9}$ s and excess CO₂ generation at the periphery of the capillary would not be significant [8].

Forster also argued that there was no evidence for carbonic anhydrase near the endothelial surface to accelerate the production of CO₂ and the uncatalyzed rate of conversion would be too slow to produce an elevated $P_{CO_2}$ in this region [8]. In addition, Forster and Crandall and several other investigators have suggested that the absence of carbonic anhydrase on red cell surfaces, plasma and endothelium should result in a slow equilibration of hydrogen ion in concentrations between red cells and plasma following gas exchange [6, 9, 14, 15, 24]. One consequence of this disequilibrium would be a slow rise in the $P_{CO_2}$ of venous blood draining the peripheral tissues. In those experimental preparations in which gas exchange was avoided, this gradual increase in $P_{CO_2}$ could continue in the blood traversing the pulmonary vasculature and the arterial $P_{CO_2}$ could, therefore, exceed alveolar $P_{CO_2}$.

This mechanism would not explain those experiments in which gas exchange was permitted and alveolar $P_{CO_2}$ appeared to exceed pulmonary arterial or venous $P_{CO_2}$ since a decline in $P_{CO_2}$ would be predicted in blood leaving the lungs after CO₂ exchange had occurred. Furthermore, recent studies suggest that carbonic anhydrase is readily accessible to plasma in both the lungs and legs and may be associated with the external surface of the endothelial cells [3a, 3b, 4, 5]. However, the location of this enzyme suggests an alternative manner in which CO₂ tensions might be elevated at the endothelial wall. If the conversion of plasma $HCO_3^-$ arriving in the pulmonary capillaries to CO₂ is specifically catalyzed by the endothelial enzyme, $P_{CO_2}$ would increase near the wall. This could only occur if gas exchange were permitted and would not explain the gradients reported in which exchange was avoided. Furthermore, the considerations outlined above make it unlikely that a significant difference between alveolar and capillary $P_{CO_2}$ would be created in this fashion. Further speculation in this regard would only be justified if a consensus could be reached that such gradients do exist in some experimental situation.

References