The CO₂ content in blood ([CO₂]) depends not only on PₐCO₂, but also on the O₂ saturation ([SO₂]). Since SO₂ changes in parallel with [CO₂] in capillary blood ([CO₂]*) at steady state, the slope of [CO₂]* against PₐCO₂ becomes steeper than that of [CO₂] measured in oxygenated or deoxygenated blood. In the preceding paper it was made clear that the change in [CO₂] due to that in SO₂ (i.e., the Haldane effect, [CO₂]HE) became proportional to the respiratory quotient (RQ). Since the ratio of the arterial-venous (a-v) difference in [SO₂] to that in [CO₂]* was in inverse proportion to the RQ, the ratio of the a-v difference in [CO₂]HE (AV[CO₂]HE) to AV[CO₂]* became constant irrespective of the RQ. Designating the PCO₂ dependent component of [CO₂] except for [CO₂]HE by [CO₂]P, the ratio [CO₂]P/AV[CO₂]* also became constant. Thus, using [CO₂]P measured in oxygenated blood in vitro, [CO₂]* could be expressed by an exponential function of PₐCO₂.

Key words: Carbonic anhydrase, O₂ saturation, Haldane effect, Respiratory quotient, Va/Q ratio

INTRODUCTION

The change in CO₂ content [CO₂] in blood occurs mainly on the active site of carbonic anhydrase, which is present not only in the red blood cell, but also in the capillary endothelium. When [CO₂] and [H⁺] change at the active site due to the changes in PCO₂ and O₂ saturation ([SO₂]), respectively, changes in carbamate and bicarbonate concentration take place. Designating the change in [CO₂] resulting from the change in SO₂ (i.e., the Haldane effect) by [CO₂]HE and that resulting from the change in PCO₂ by [CO₂]P, the change in [CO₂] in capillary blood ([CO₂]*) is given by...
the sum of changes in \([\text{CO}_2]\) and \([\text{CO}_2]_p\).

Basically, \([\text{CO}_2]\) is the difference in \([\text{CO}_2]\) between oxygenated and deoxygenated blood\(^{3,4}\) and the arterial-venous (a-v) difference in \([\text{CO}_2]\) (\(\text{av}[\text{CO}_2]\)) is given by multiplying \([\text{CO}_2]\) by the a-v difference in \(\text{SO}_2\) (\(\text{av}[\text{SO}_2]\)). \(\text{av}[\text{SO}_2]\) is given by dividing the a-v difference in \(\text{O}_2\) content (\(\text{av}[\text{O}_2]\)) by the \(\text{O}_2\) capacity (\(\text{CapO}_2\)). The a-v difference in \([\text{CO}_2]^*\) (\(\text{av}[\text{CO}_2]^*\)) is derived by multiplying \(\text{av}[\text{O}_2]\) by the respiratory quotient (RQ). Hence, the ratio \(\text{av}[\text{SO}_2]/\text{av}[\text{CO}_2]^*\) is given by \(1/(\text{RQ} \cdot \text{CapO}_2)\).

In the preceding paper it was clarified that \([\text{CO}_2]\) at the steady state became constant irrespective of RQ, \(\text{P}_\text{CO}_2\) and \(\text{SO}_2\). \([\text{CO}_2]_p\) had been measured in oxygenated blood and expressed by an exponential function of \(\text{P}_\text{CO}_2\). Thus, \([\text{CO}_2]^*\) could be approximated from the ratio \(\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^*\) by a definite exponential function of \(\text{P}_\text{CO}_2\). The change in carbamate concentration in the red cell is included in \([\text{CO}_2]\), and therefore, the ratio \(\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^*\) becomes higher than that of the a-v difference in Haldane effect component of \([\text{HCO}_3^-]\) in plasma (\([\text{HCO}_3^-]\)) to that in \([\text{HCO}_3^-]\) measured (\([\text{HCO}_3^-]^*\)) (see Eq. 19 in the preceding paper)\(^5\). Thus, it is imperative to apply \([\text{CO}_2]^*\) to analyze the gas exchange rate at the steady state.

**THEORETICAL DERIVATION OF THE FUNCTION FOR \([\text{CO}_2]^*\)**

As written in the preceding paper \([\text{HCO}_3^-]\) was proportional to the RQ at steady state as given by \(2.09 \cdot \text{RQ}^3\). \([\text{HCO}_3^-]\) in plasma was expressed by the molar concentration. Taking the mean of plasma volume in blood (1 - Hct) to be 0.544 over the \(\text{P}_\text{CO}_2\) range of 30 to 70 mmHg, the molar unit in plasma is converted to vol% in blood by multiplying 0.544 \(\times\) 2.226. In addition, the ratio \([\text{HCO}_3^-]/[\text{CO}_2]_p\) was 0.386 over the physiological \(\text{P}_\text{CO}_2\) range. Hence, \([\text{CO}_2]\) was rewritten as follows:

\[
[\text{CO}_2]_p = 6.555 \cdot \text{RQ}, \text{ (vol%)}. \quad (1)
\]

\([\text{CO}_2]\) measured in tonometered blood was about 5.9 vol% and agreed well with \([\text{CO}_2]\) of Eq. (1) when \(\text{RQ} = 0.9^4,5\). As described in the Introduction, the ratio \(\text{av}[\text{SO}_2]/\text{av}[\text{CO}_2]^*\) was given by

\[
(\text{-})\text{av}[\text{SO}_2]/\text{av}[\text{CO}_2]^* = 1/(\text{RQ} \cdot \text{CapO}_2). \quad (2)
\]

Taking \(\text{CapO}_2\) to be 20 vol%, the ratio \(\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^*\) is written from Eqs. (1) and (2) as

\[
\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^* = 0.328. \quad (3)
\]

Since \(\text{av}[\text{CO}_2]_p = \text{av}[\text{CO}_2]^* \cdot \text{av}[\text{CO}_2]_p\), the ratio \(\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^*\) is expressed as follows:

\[
\text{av}[\text{CO}_2]_p/\text{av}[\text{CO}_2]^* = 0.672. \quad (4)
\]

The \(\text{CO}_2\) content obtained in oxygenated blood\(^5\) was given by

\[
[\text{CO}_2]_p = 8.748 \cdot \text{P}_\text{CO}_2^{0.435}, \text{ (vol%)}. \quad (5)
\]

Assuming \([\text{CO}_2]_p\) of Eq. (5) to be equal to \([\text{CO}_2]^*\) at 40 mmHg \(\text{P}_\text{CO}_2\), the difference in \([\text{CO}_2]^*\) between any \(\text{P}_\text{CO}_2\) and 40 mmHg can be
CO₂ Dissociation Curve at Steady State

Calculated from Eqs. (4) and (5). [CO₂]ₗ is then numerically plotted against P₂CO₂. The solid line in Fig. 1 shows [CO₂]ₗ and the broken line [CO₂] previously calculated from Eqs. (4) and (5). Furthermore, from the relationship between P₂CO₂ and [CO₂]ₗ, [CO₂]ₗ was approximated by the following equation:

$$[\text{CO}_2]^* = 4.208 \cdot \text{PCO}_2^{0.632}, \text{(vol%)}.$$  (6)

[CO₂]ₗ of Eq. (6) agreed with [CO₂]ₗ of Eq. (5) at 41.04 mmHg PCO₂, and the ratio aV[CO₂]ₗ/aV[CO₂]ₗ was 0.709 at 30 mmHg PCO₂ and decreased to 0.651 at 70 mmHg PCO₂. In the PCO₂ range of 30 to 70 mmHg, the mean ratio was 0.678 ± 0.018.

**DISCUSSION**

[CO₂]ₗ of Eq. (6) is very important to estimate aV[CO₂]ₗ from the a-v difference in PCO₂. The points a and v in Fig. 1 indicate the arterial and venous PCO₂ levels. The vertical segment at PaCO₂ shows the a-v difference in [CO₂]ₗ, [CO₂]ₗ and [CO₂]HE.

The relationship between aV[CO₂]ₗ and aV[O₂] was further calculated, using the relationship of alveolar ventilation to pulmonary blood flow (Vv/Q) as follows:

$$\dot{V}_v/\dot{Q} = 8.63 \cdot \text{RQ} \cdot aV[\text{O}_2]/\text{PaCO}_2$$  (7)

Calculated data are shown in Fig. 2, where PaCO₂ was taken to be 41 mmHg and [O₂] (vol%) in arterial blood was derived from the alveolar air equation, assuming [O₂] was fully saturated with alveolar PO₂. The solid lines show the change in [CO₂]ₗ along the three RQ values. Since PaCO₂ was taken to be constant, aV[CO₂]ₗ was unrelated to the RQ, but increased with an increase in Vv/Q ratio. When the Vv/Q ratio was 0.85, aV[CO₂]ₗ was about 4 vol%. The broken lines show aV[CO₂]HE calculated from Eq. (3), these were about 33% aV[CO₂]ₗ regardless of the RQ and Vv/Q ratio.
Figure 2 shows that, when PaCO₂ is constant, [CO₂]* and venous PCO₂ are defined only by the V̇ₐ/Q ratio. This well controlled relationship will be ascribed to the interaction of the catalytic reaction rates of carbonic anhydrase in the red blood cell and the capillary endothelium.

The scale on the right ordinate shows PCO₂ given by Eq. (6). Since [CO₂]ₜₑ includes the change in carbamate concentration in the RBC⁴, the ratio [CO₂]ₜₑ/ [CO₂]* of Eq. (3) (0.328) was about 30% greater than the ratio [HCO₃⁻]ₜₑ/ [HCO₃⁻]* (0.252)⁵. If the a-v difference in PCO₂ were estimated from [CO₂]* by using Eq. (5), the change in PCO₂ will be greatly overestimated.

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