Alveolar Air Equations

To the Editor — Story’s letter1 raises interesting questions about the alveolar gas equations. Essentially, these indicate the alveolar partial pressures of oxygen and carbon dioxide in terms of barometric pressure, uptake (or output), and alveolar ventilation. They are simply based on conservation of mass.

Alveolar gas equations exist in many versions for different purposes: some versions are accurate, some less accurate, and some only approximate. Accurate versions are required for determination of alveolar PaO2 in the calculation of venous admixture, for example. Perhaps the most satisfactory version for the anesthesiologist is that of Filley, Machintosh, and Wright,2 which does not require inert gases, such as nitrous oxide, to be in equilibrium.

Some approximate versions give a clearer indication of the quantitative relevance of clinically important variables and so are a valuable teaching aid. For this purpose, I favor the following:

\[ PAO_2 = Pd (FIO_2 + \dot{V}CO_2 / \dot{V}A) \]
\[ PAcO2 = Pd (FIO2 - \dot{V}CO2 / \dot{V}A) \]

The first is accurate if expired minute volume is used to calculate \( \dot{V}A \), the second is only approximate. Nevertheless, it is quite adequate as a basis for consideration of problems of gas exchange in such situations as high altitude, malignant hyperpyrexia, or ventilatory failure.

These versions of the "universal" alveolar air equation make it quite clear that \( PAO_2 \), is not really a function of \( PA_{CO2} \), as Story explains, even though some versions of the alveolar gas equation give this impression. However, if inspired concentrations and respiratory exchange ratio remain constant, then changes in alveolar ventilation alter \( PAO_2 \) and \( PA_{CO2} \) in different directions, the magnitude of the changes being related to the respiratory exchange ratio. Therefore, it is a case of post hoc rather than propter hoc.

It should be stressed that \( \dot{V}CO_2 \) and \( \dot{V}O_2 \) in these equations are output and uptake, respectively, and not production and consumption, as Story states. In the case of oxygen, uptake and consumption seldom differ greatly. However, for carbon dioxide, output may differ greatly from production in an unstable state. This has considerable clinical relevance. Patients seldom die in a steady state.

Alveolar air equations are at their simplest when \( FIO_2 = 1.0 \). Then:

\[ PAO_2 = Ph - PH_O2 - PA_{CO2} \]

and no corrections are required. An opening parenthesis is missing from Story’s equation (1) immediately before Ph. This may have caused confusion.

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References


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Cerebral Oxygenation during Deep Hypothermic Cardiopulmonary Bypass: Is Hemoglobin Relevant?

To the Editor — I was fascinated by Dexter and Hindman’s model of cerebral oxygen delivery.1 To examine the behavior of their model in more detail, I loaded the equations into a Hewlett Packard HP 48GX programmable calculator and examined their behavior under a variety of conditions, using the calculator’s Equation Solver application.

This examination led me to conclude that it is not the shift in \( P_{O2} \) alone that is responsible for the change in the relation between \( SvO_2 \) and \( CMR_{CO2} \) (percentage of maximal CMRO2) seen with hypothermia, but rather the interaction between that shift and the relation between interstitial oxygen tension (PinO2) and \( CMR_{CO2} \). In brief, the target (or basal) CMR determines the PinO2 (and therefore the Pao2) needed to support that CMR. The authors chose a model (Michalis-Menken kinetics, eq. 9)2 that requires relatively high PinO2 to support high CMR. As the Pao2 shifts left with hypothermia, it is not surprising to find that the high Pao2, which is determined

Anesthesiology, V 85, No 4, Oct 1996
by the high \( \text{PinO}_2 \), corresponds to higher and higher \( \text{SvO}_2 \). Although this model for the relation between \( \text{PinO}_2 \) and CMR\(_\text{O}_2 \) has some support experimentally,\(^1\) neither this relation nor the target CMR\(_\text{O}_2 \) has been measured in humans. If the true target CMR\(_\text{O}_2 \) or the relation between \( \text{PinO}_2 \) and CMR\(_\text{O}_2 \) in humans were such that lower values of \( \text{PinO}_2 \) could support adequate CMR\(_\text{O}_2 \) at hypothermia, then the shift in \( \text{P}_{\text{O}_2} \) with hypothermia would not result in such dramatic changes in the relation between CMR\(_\text{O}_2 \) and \( \text{SvO}_2 \). In examining this issue, I found that even very subtle, minor changes in the relation between \( \text{PinO}_2 \) and CMR\(_\text{O}_2 \) produced major alterations in the way the relation between \( \text{SvO}_2 \) and CMR\(_\text{O}_2 \) changes with temperature.

The simplest example of this would be a reduction in the target CMR\(_\text{O}_2 \), as might be seen with anesthesia, bypass, or hypothermia. Using the authors’ data for an infant at 17°C (Fig. 1), it can be seen that if the target CMR\(_\text{O}_2 \) were 90 ± 5%, the \( \text{SvO}_2 \) would lie in the range 97.3–100%, making it impossible to rely on \( \text{SvO}_2 \) to follow changes in CMR\(_\text{O}_2 \) until they become quite severe. Conversely, if the target CMR\(_\text{O}_2 \) were 85 ± 5%, the \( \text{SvO}_2 \) would lie in the range 78.6–97.3%, although this is different from the relation between \( \text{SvO}_2 \) and CMR\(_\text{O}_2 \) at normothermia, it might still be possible to use \( \text{SvO}_2 \) to follow trends in CMR\(_\text{O}_2 \).

Further examination of the Dexter-Hindman model suggested that hemoglobin saturation, and hemoglobin per se, are essentially irrelevant to cerebral oxygen delivery during deep hypothermia, because dissolved oxygen is adequate to provide almost all cerebral oxygen needs. For an infant at \( \text{Pao}_2 \geq 300 \text{ mmHg} \) and \( T = 18°C \), more than 90% of CMR\(_\text{O}_2 \) is provided by dissolved oxygen. Although there may be reasons to avoid hypoxemia during bypass (formation of bubbles during rewarming, generation of free radicals), this interpretation of the author’s model suggests the possibility of stroma-free perfusion during deep hypothermic bypass, which might have important implications for conservation of blood constituents and visualization of the surgical field during low-flow bypass. This interpretation also suggests that oxygen solubility enhancing agents (e.g., perfluorocarbons) may more effectively increase cerebral oxygen availability during low-flow deep hypothermic bypass than hemoglobin (erythrocytes or stroma-free hemoglobin); the ineffectiveness of hemoglobin preparations in this context is supported by other work from the authors.\(^3\)

Dexter and Hindman are to be commended for recognizing the importance of the shift in \( \text{P}_{\text{O}_2} \) on interpretation of \( \text{SvO}_2 \) during deep hypothermic bypass and for emphasizing the potential risks of widespread adoption of jugular venous bulb or cerebral near-infrared spectroscopy monitoring based on the assumption that a high \( \text{SvO}_2 \) implies adequate, or even lusurious, cerebral oxygen availability. However, given that very small changes in the model can produce major changes in how the relation between CMR\(_\text{O}_2 \) and \( \text{SvO}_2 \) changes with temperature, before we can draw conclusions about the role of

\( \text{SvO}_2 \) monitoring during bypass, it will be necessary to determine the target CMR\(_\text{O}_2 \) and the relation between \( \text{PinO}_2 \) and CMR\(_\text{O}_2 \) in humans both awake and anesthetized, on and off bypass, and at normothermia and hypothermia.

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References

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In Reply—Our computer simulations showed that the relation between cerebral venous oxygen saturation (\( \text{SvO}_2 \)) and CMR\(_\text{O}_2 \) depends on temperature. Hypothermia increases hemoglobin’s oxygen affinity. During profoundly hypothermic cardiopulmonary bypass (CPB), high \( \text{SvO}_2 \) can be the result of impaired oxygen transfer from hemoglobin to brain.\(^2\) \( \text{SvO}_2 \) may, under some circumstances, be an accurate monitor of CMR\(_\text{O}_2 \). However, our results showed that validation of near-infrared and internal jugular measurements of \( \text{SvO}_2 \), during normothermia does not imply that they have been validated under hypothermic conditions. We successfully used a computer simulation of a mathematical model to do a technology assessment. The model warned clinical investigators about potential misinterpretation of near-infrared and internal jugular measurements of \( \text{SvO}_2 \).

This model prediction has since been verified clinically. Du Plessis et al.\(^4\) simultaneously measured cerebral mitochondrial and cerebral hemoglobin saturations in children undergoing profoundly hypothermic CPB. During cooling and initiation of low-flow CPB, \( \text{SvO}_2 \) increased. In contrast, cerebral cytochrome saturation decreased. Therefore, oxygen availability at the mitochondrial level was diminished, despite high \( \text{SvO}_2 \). Together, our studies and those of Du Plessis et al. show that \( \text{SvO}_2 \) can be a poor monitor of the adequacy of cerebral oxygenation during profoundly hypothermic CPB.