**Abstract**

This clinical observation relates blood pCO₂, solubility, total CO₂ content, oxygenator FiCO₂ and ventilation rate, CO₂ transfer, and respiratory quotient during hypothermic cardiopulmonary bypass.

Techniques employed to obtain the above parameters include blood gas analysis, temperature correction, gas and blood flow settings, mass spectrometry, Kelman’s algorithm of the Singer-Hasting nomogram, and O₂ and CO₂ transfer calculations.

Membrane lung O₂ and CO₂ transfer curves demonstrate the following respiratory quotient (RQ) and CO₂ blood content requirements for two common hypothermic pCO₂ management techniques:

<table>
<thead>
<tr>
<th>TECHNIQUE</th>
<th>COOLING</th>
<th>WARMING</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH-Stat</td>
<td>CO₂ content increase, RQ lower than normal</td>
<td>CO₂ content decrease, RQ much greater than normal</td>
</tr>
<tr>
<td>Alpha-Stat</td>
<td>CO₂ content constant, RQ normal</td>
<td>CO₂ content constant, RQ normal</td>
</tr>
</tbody>
</table>

Oxygen, carbon dioxide transfer versus patient temperature plots from hypothermic CPB demonstrate the perfusionist’s complete control of blood CO₂ content and blood pCO₂.

**Introduction**

The pH of a solution is indirectly proportional to the hydrogen ion concentration in that medium. In the body the primary source of free hydrogen ions is from the dissociation of water.

\[ \text{H}_2\text{O} \xrightarrow{p\text{K}_w} \text{H}^+ + \text{OH}^- \quad \text{Eq. 1} \]

This reaction is governed by the dissociation constant (pK_w) of water. As temperature decreases the pK_w parallels this decline resulting in fewer free hydrogen ions and a resulting higher pH. The intracellular hydroxyl/hydrogen ion concentration (OH⁻/H⁺) remains constant at a ratio of 1.0 ± .3 at any temperature as the result of chemical and electrical equilibrium. Therefore the intracellular pH may be said to remain constant with changing temperature.

A buffer may be defined as any substance capable of donating or receiving a proton in an attempt to maintain a constant pH.

\[ \text{H}^- \text{Buffer} \xrightarrow{p\text{K}_w} \text{H}^+ + \text{Buffer}^- \quad \text{Eq. 2} \]

Three primary buffer systems found in humans are the bicarbonate, phosphate, and protein systems. In order to receive a proton (free hydrogen ion), a buffer must be in the dissociated or proper charge state. The ability of a buffer to dissociate or be in the proper charge state during hypothermia is dependent upon the pK for that buffer system.

As temperature decreases and the pK_w of water decreases, the pK of a buffer system must parallel this change in order to remain effective. It has been shown that during hypothermia the major normothermic buffer system, bicarbonate, is inadequate. A protein buffer system, specifically the imi-
zole portion of histidine found in plasma and red
blood cells, has a pK which parallels the pK of
neutrality (pKw) and is therefore the primary hypo­
thermic buffer system. Like all buffers, imidazole
must lose a proton during dissociation and be in the
proper charge state in order to be effective. The
imidazole protein minus a proton is identified as
alpha imidazole.

As the solubility increases with decreasing tem­
perature, a constant C02 content will result at a
lower pC02. In order to maintain hypothermic
biological neutrality, and the OH- | H+ ratio, the
imidazole protein buffer charge state, and total
CO2 content must remain constant. This strategy is
defined as alpha-stat. The end result is a decrease in
the pC02 due to increased carbon dioxide solubility
and will result in a concomitantly high actual
blood pH.

During cardiopulmonary bypass (CPB) the
easiest method of controlling the acid-base status is
through manipulation of the respiratory compo­
nent. Normothermic blood pH is proportional to
the metabolic and respiratory components.

\[
pH \propto \frac{\text{Metabolic}}{\text{Respiratory}} \propto \frac{\alpha}{\frac{\text{Base Excess}}{\text{pCO2}}} \quad \text{Eq. 3}
\]

Alteration in the acid-base status by manipu­
lating the carbon dioxide content may be illustrated
with the Henderson-Hasselback equation as shown
in Equation 3.

Carbon dioxide is carried primarily as bicarbon­
ate and dissolved in solution. Dissolved carbon
dioxide content is related to the partial pressure of
the gas and the solubility as follows in Equation 4.

\[
\text{CO2 volumes } \% = \text{pCO2 (mmHg)} \times \text{Solubility (mlCO2/mmHg/100 ml blood)} \quad \text{Eq. 4}
\]

During CPB the perfusionist regulates the respira­	ory acid-base component by selecting an artifi­
cial lung ventilation rate adequate to alter CO2
content yielding a desired blood pCO2. In order to
adequately quantify the physiological results of a
specific acid-base management technique, the
perfusionist must know the actual (temperature cor­
tected) pCO2 and pH values to determine CO2 gas
content, CO2 transfer (VCO2) and determine the
proper oxygenator ventilation rate.

Carbon dioxide transfer across a membrane may be
represented by the Fick Formula:

\[
\dot{V}_{CO2} = \frac{D_{CO2} \times (C_1 - C_2)_{CO2}}{\Delta X} \quad \text{Eq. 5}
\]

Where: \( \dot{V}_{CO2} \) = ml CO2/min.
D_{CO2} = Diffusion coefficient
(ml CO2 \times cm/minute)
(C_1 - C_2)_{CO2} = CO2 concentration gradient
X = CO2 diffusion distance (cm)

Assuming the temperature and solubility are
constant, the above equation may be rewritten as:

\[
\dot{V}_{CO2} = D_{CO2} \times \frac{(\text{pCO2,1} - \text{pCO2,2})}{\Delta X} \quad \text{Eq. 6}
\]

In a parallel channel gas transfer device such as a
membrane blood oxygenator, the amount of CO2
transferred per unit time is a function of the mean
driving force, the partial pressure difference for
CO2.

The mean driving force for CO2 between the gas
and blood streams is determined by the CO2 partial
pressure gradients between the arterial and venous
blood and the inspired and expired gases*. Carbon
dioxide transfer is linearly proportional to the CO2
driving force under constant ventilation, blood
flow, and membrane boundary layer conditions. The
venous blood pCO2 is a major determinant of
CO2 transfer in a fixed oxygenator design.

Oxygen transfer approximation by measuring
blood oxygen content is common in the study of
artificial oxygenating devices. The direct mea­
urement of CO2 transfer in artificial lungs was not
reported until 1974 (Snider et al.). Early inves­
tigators estimated VCO2 by the Fick Formula. Car­
bondioxide content determination by the VanSlyke
apparatus was cumbersome, and less accurate pre­
dictions were made employing pCO2, pH and % O2
saturation of hemoglobin using a nomogram.

Clinical calculation of carbon dioxide transfer
can be determined by measuring the artificial lung
inlet and outlet ventilating gas % CO2 and multi­
plying the difference by the total gas sweep
rate. Correlation between the outlet ventilating
gas pCO2 and outlet blood pCO2 (PaCO2) has been
demonstrated with some success. However, few

*LMΔpCO2 is the log mean driving force for CO2. It is
calculated as follows:

\[
\text{LMΔpCO2} = \Delta P_1 - \Delta P_2 \quad \text{where } \Delta P_1 = (P_vCO2 - P_inCO2) \quad \text{ln}(\Delta P_1 - \Delta P_2) \\
\Delta P_2 = (P_aCO2 - P_exCO2)
\]

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TABLE 1
Group I and Group II control characteristics for the pH-stat and alpha-stat management techniques.

<table>
<thead>
<tr>
<th></th>
<th>TEMPERATURE CORRECTED AT 28°C</th>
<th>NOT TEMPERATURE CORRECTED AT 37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACID BASE STATUS</strong></td>
<td><strong>pCO₂ 35-45 mmHg pH 7.35-7.45</strong></td>
<td><strong>pCO₂ 58-67 mmHg pH 7.25-7.33</strong></td>
</tr>
<tr>
<td>Group I</td>
<td>pH-Stat</td>
<td>Alpha-Stat</td>
</tr>
<tr>
<td></td>
<td>pCO₂ 25-35 mmHg pH 7.45-7.58</td>
<td>pCO₂ 35-45 mmHg pH 7.35-7.45</td>
</tr>
</tbody>
</table>

"Actual blood values"

reports exist illustrating the CO₂ transfer requirements to maintain a specific acid-base status during hypothermic CPB. The CO₂ transfer rate is determined by the CO₂ driving force regulated by the venous blood pCO₂, ventilating gas pCO₂ and sweep rate, as well as the artificial lung design and gas path boundary phenomena. The perfusionist may select the oxygenator CO₂ driving force to achieve the oxygenator respiratory quotient (RQ), which is the ratio of carbon dioxide transfer to oxygen transfer (VCO₂/VO₂), to achieve a desired blood CO₂ content and pCO₂.

The CO₂ transfer requirements to maintain two different acid-base management strategies are presented in this paper. Both strategies are related to different temperature control mechanisms. A "pH-stat" management technique is presented in which actual blood pH and pCO₂ are maintained at 37°C temperature corrected normal values. This technique is commonly associated with homeotherms such as man. Poikilotherms however exhibit an "alpha-stat" strategy during hypothermia in which the pCO₂ is allowed to decrease, resulting in a high pH, normal OH⁻/H⁺ ratio, constant CO₂ content, and biological neutrality. The pCO₂ and pH requirements for each technique are presented in Table One.

Methods

Cardiopulmonary bypass was initiated using a Cobe CML membrane oxygenator on 22 adult patients undergoing open-heart surgery. Fourteen were randomly chosen to be managed by pH-stat and 8 by alpha-stat. Arterial and venous blood gas data were collected at every degree centigrade change in nasopharyngeal temperature during the cooling and warming phases. Oxygen transfer in ml O₂/minute/m² body surface area was calculated as previously reported. The oxygenator was ventilated at a constant gas sweep rate of 10 L/min, as recommended by the manufacturer. The arterial pO₂ and pCO₂ were controlled by varying the ventilating gas FiCO₂ and FiO₂.

Carbon dioxide transfer was estimated from calculated gas inlet and outlet CO₂ concentrations using the calibrated 100% O₂/room air and 100% CO₂ gas flow meter settings and exit gas mass spectrometer pCO₂ measurements. VCO₂ is reported as ml CO₂/min/m² body surface area.

Blood gas and pH measurements were taken at the initiation and termination of each cooling and warming phase. Mixed venous samples were "temperature corrected" to the venous blood temperature and arterial samples to the nasopharyngeal temperature.

The arterial pCO₂ and pH values were maintained within the limits for each technique outlined in Table One. The oxygen and carbon dioxide transfer were plotted with respect to temperature. The best fit curves were constructed using the least squares method.

Results

Figure One illustrates the carbon dioxide and oxygen transfers versus nasopharyngeal temperature for the pH-stat methodology. The pH, blood gas, and oxygenator ventilation parameters are listed at the beginning and end of each phase. The pH-stat blood CO₂ content increased dramatically to prevent a change in the arterial pCO₂ during the
FIGURE 1. Group I O₂ and CO₂ transfer rates during CPB cooling and warming phases. Cobe Membrane Lung (CML) ventilation settings are included.

FIGURE 2. Group II O₂ and CO₂ transfer rates during CPB cooling and warming phases. Cobe Membrane Lung (CML) ventilation settings are included.
cooling phase. The oxygenator RQ was less than 0.35 during this period. Upon the initiation of the warming phase, an oxygenator RQ greater than 1.5 was required to eliminate the CO₂ retained during the cooling phase and CO₂ produced as a result of increased patient metabolism.

An average oxygenator RQ of 0.7 was maintained during cooling to yield 37°C non-temperature corrected "normal values." During cooling, the CO₂ content is maintained and actual blood pCO₂ falls and pH rises. During the warming phase, a higher RQ was necessary to arrive at 37°C "normal" blood pCO₂ and pH at the end of the warming phase.

Discussion

When following the pH-stat acid-base management scheme, the actual (temperature corrected) arterial pH and blood gases are maintained at 37°C normal (pH = 7.35-7.45mmHg, pCO₂ = 35-40) values. In order to remain within the limits defined by this technique, the perfusionist must decrease the CO₂ driving force either by decreasing the oxygenator's gas sweep rate or increasing the ventilating gas FiCO₂. These perfusionist management actions will raise the CO₂ content and maintain the partial pressure in the face of increasing solubility (Figure One). During the warming phase, it becomes necessary to utilize a high oxygenator RQ in order to remove the CO₂ retained during cooling as well as the CO₂ produced by the patient tissue in order to achieve normal pCO₂ and pH values at 37°C.

In the alpha-stat technique, an oxygenator eugenermic RQ may be established at the initiation of normothermic CPB which results in normal 37°C non-temperature corrected values.¹¹⁰ Maintenance of uncorrected 37°C normal pH and pCO₂ values during the cooling phase will result in a constant CO₂ content, intracellular OH⁻/H⁺ ratio, and proper imidazole charge state.¹¹⁸,¹⁹ Figure Two illustrates a nearly constant oxygenator RQ during the cooling phase to maintain the non-temperature corrected normal values. During the warming phase a higher yet consistent RQ is required to remove the carbon dioxide produced by the patient tissue. Hyperventilation of the artificial lung to remove CO₂ retained in the cooling phase is not necessary as found with the pH-stat strategy.

When utilizing an alpha-stat technique, blood pH and pCO₂ should be analyzed at 37°C and not temperature corrected. Temperature correction of blood gases may be misleading due to the inability to accurately select a true core temperature as the result of internal gradients.¹ A constant blood CO₂ content, intracellular OH⁻/H⁺ ratio and alpha imidazole charge state may be assured during rapid cooling by maintaining 37°C non-temperature corrected normal values.² However, in order to accurately calculate O₂ and CO₂ transfer rates and monitor patient oxygenation (pO₂), actual temperature corrected blood values must be determined.

The arterial blood pCO₂ and CO₂ content during hypothermia are determined by the CO₂ transfer rate at the initiation of CPB and during rapid cooling. The CO₂ transfer rate is determined by the perfusionist selection of CO₂ driving force by varying the gas sweep rate and ventilating gas inlet pCO₂.

The proper ventilating gas sweep rate and FiCO₂ must be selected by the perfusionist to achieve a desired CO₂ transfer rate to alter CO₂ content and achieve the desired arterial pCO₂ at a given temperature. Both ventilation techniques require knowledge of the patient's blood gas status immediately prior to initiation of CPB and during the cooling phase either through frequent sampling or continuous monitoring.

Acknowledgment

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References


