A Technique for Extrapolation of Analyzed Values of Blood pH, pCO_2 and pO_2 to Hypothermic States

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PURPOSE/ABSTRACT

It is the purpose of this paper to review the work of other authors on the influence of temperature changes on blood pH, pCO_2, and pO_2 in vitro. Composite, easy to use diagrams based on these works will be presented here for use by the clinician employing hypothermia in the treatment of his patient. It is not the purpose of this paper to recommend the ideal acid base status that will lead to the best patient care during hypothermia, although this question will be discussed.

INTRODUCTION

Error in the interpretation of blood pH, pCO_2, and pO_2 arises from three possible sources. First, improper calibration procedure for the blood gas analyzer by the operator may lead to questionable clinical results. The problems remaining are changes in the blood which occur with improper sampling techniques[1-3], and temperature differences between the clinical subject and the measuring electrode water bath.[1 5-14]

The majority of blood gas alterations that occur once the blood is drawn into a syringe fall into four categories;[2-4] 1) diffusion of gas through the syringe wall, 2) leakage between the syringe plunger and barrel, 3) trapping air bubbles within the sample, and 4) continuing cellular metabolism. The above mechanisms are exaggerated with aggitation of the sample and increased time delay between sampling and measurement. Diffusion of gases through various types of syringes is well studied and no significant differences in blood gas studies employing glass and polypropylene syringes have been demonstrated over a four hour time delay between sampling and measurement.[4 15] Leaving a bubble of room air equal to 10% of the sample volume in the syringe is sufficient to induce a marked change in pO_2 when blood is aggitated between sampling and measurement with essentially no change in pH and pCO_2.[3] Blood, like any other tissue, consumes oxygen and produces CO_2 and hydrogen ions.

The effects of storing blood at 37° C have been quantitated.[16-17] When the original pO_2 is greater than 150mmHg the rate of decay of the pO_2 is 2.7mmHg/minute of storage.[16] When the original pO_2 is less than 100mmHg the decay is about .4mmHg/minute of storage.[17] The decay is considerably less at room temperature and insignificant when the sample is stored in ice.[2] The loss of CO_2 gas from a polypropylene syringe stored in ice between sampling and measurement is not significant enough to alter pH and blood gas assessment.[15]

The majority of blood gas inaccuracies created by missampling and delaying between sampling and measurement can be avoided by collecting the sample anerobically in a glass or polypropylene syringe, evacuating any air bubbles carefully, capping securely, and storing in ice until the measurement may be made.

PROBLEM

When blood is warmed *in vitro* without exposure to air (holding gas contents constant), the pH falls and the pCO_2 and pO_2 rise.[4 8 10-12 18] When a blood sample is drawn from a hypothermic patient on total heart-lung bypass, taken to the blood gas analyzer and exposed to a water bath at 37° C, the values reported from the analyzer reflect similar changes. Ideally, the analyzer bath temperature should be placed at the hypothermic patient's temperature and the apparatus recalibrated. Matching the analyzer to each patient is not always practical. Therefore, if the reported results are to reflect the absolute value of the blood pH and blood gases *in vivo* (at the lower temperature), the reported results must be temperature corrected to offset the physical change *in vitro*.

The accurate correction of pH, pCO_2, and pO_2 from the temperature of the measuring instrument to the body temperature involves linear and logarithmic factors.[12] The procedures for temperature correction available to date are time consuming mathematical operations that often take the clinician more time than the analysis itself.[18] However, these mathematical functions are easily computerized and several algorithms are presently available.[13 18] Reliable formulas for computer implementation are presented in the following text. For the clinician who does not have access to an interactive computer system, the following diagrams are presented for use and their reliability and limitations explained.

TEMPERATURE CORRECTION OF pH

As early as 1948 T. B. Rosenthal described the effects of changing temperature on the pH of blood *in vitro* by reporting the slope of the pH versus temperature curve to be -0.0147 pH units/° C for whole blood between 18° C and 37° C. In 1952, Graig confirmed Rosenthal's constant (-0.0147 pH units/° C) and reported the following formula for correction of pH for changes of whole blood temperature *in vitro:*

$$pH_t = pH_{37°C} + .0149(37° C - t)$$

where t is the temperature at which the blood was shed *in vivo* and the analyzer sampling chamber is at 37° C.

Rosenthal stated that the slope coefficient numerical value was independent of abnormal concentrations of hemoglobin, plasma proteins and bicarbonate. However, when Adamson[19] studied the effects of pH, CO_2 content, degree of oxygenation, and RBC concentration on Rosenthal's factor, they found no significant differences in the

$\Delta pH/°C$ over a range of 20% to 60% hematocrit, but as the hematocrit was lowered to 5% the $\Delta pH/°C$ approached that of plasma, .0118 pH units/°C. At comparable pH's and CO_2 content, they revealed no significant differences in the $\Delta pH/°C$ of oxygenated and reduced blood. Austin[6] reported similar findings in their small series of patients.

Rosenthal and Austin concluded that because large changes in the major buffer systems of whole blood did not vary the slope constant significantly in their investigations, illness and disease would not effect the constant. However, Adamson found the $\Delta pH/°C$ to be smallest at low pH, low protein concentrations and high CO_2 content. The constant increased with raising pH, raising protein concentration and lowering CO_2 content. Thus, Adamson concluded that, over the physiological range of pH, it is best to express temperature correction of pH as a function of CO_2 content and pH employing the following equation:

$$\Delta pH/°C = .0146 - .005(7.4 - pH_{37°C}) + .00005(20 - CO_2)$$

where .0146 is the $\Delta pH/°C$ of whole blood with a plasma CO_2 content of 20 mMole/Liter and a pH = 7.4. The calculated $\Delta pH/°C$ is then substituted into the equation:

$$pH_t = pH_{37°C} + \Delta pH/°C(37°C - t)$$

Figure 1 presents a series of isobars generated using Adamson's work holding the temperature corrected pCO_2 constant at 40mmHg ±1mmHg for commonly employed *in vivo* hypothermia temperatures. The pH of whole blood analyzed at 37°C is on the abscissa and the temperature corrected pH value is on the ordinate. The temperature corrected pH is obtained by locating the measured pH at 37°C on the abscissa, going directly up to the intersection point of the appropriate *in vivo* temperature isobar, and then reading the corresponding value from the ordinate. For rapid approximation of pH change due to temperature difference, a factor of .015 pH units/°C may be employed.

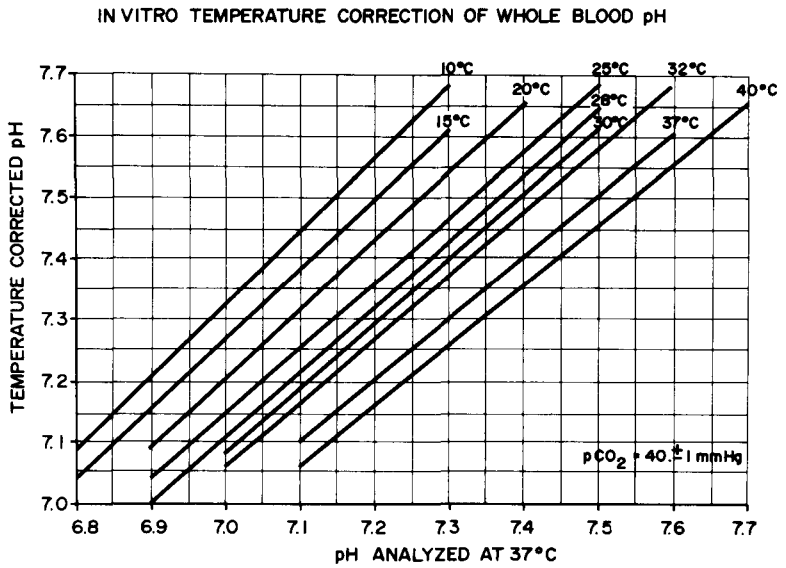

Figure 1

TEMPERATURE CORRECTION OF pCO_2

Henry's Law describes the relationship between the concentration of a gas in solution, the gas' solubility in that non-blood solution and the partial pressure of that gas:

$$\text{concentration} = \text{solubility} \times \text{partial pressure}$$

If the volume of a gas in solution is not allowed to change when warmed in an analyzer, then a partial pressure at one temperature is easily converted to the value corresponding to another temperature as a function of the solubility which is temperature dependent. The effect of temperature changes on the partial pressure of CO_2 is only partially explained by solubility changes. CO_2 is in equilibrium with hydrogen ions, and the temperature dependence of the pCO_2 becomes a function of the temperature dependence of pH and changes in the pK of carbonic acid with temperature.[13 18]

Since the plasma bicarbonate level does not change with temperature, the effect of temperature on the pCO_2 may be calculated from the Henderson-Hasselback Equation substituting the appropriate solubility and pK for the temperature. Bradley[5] has described the relationship between the pCO_2 and temperature change as:

$$\log pCO_2/\Delta T = F_{CO_2}$$

where F_{CO_2} is the correction coefficient for CO_2. The temperature corrected pCO_2 may be found by employing the formula:

$$pCO_{2t} = pCO_2(37°C) \times 10\ F_{CO_2(t-37)}$$

The temperature isobars in Figure 2 are generated using this equation and the mean F_{CO_2} for a pH of 7.4 at all temperature ranges ($F_{CO_2} = .019$).[5 8 14] The measured pCO_2 at 37° C is on the abscissa and the temperature corrected pCO_2 on the ordinate. This diagram may be used in the same fashion as Figure 1.

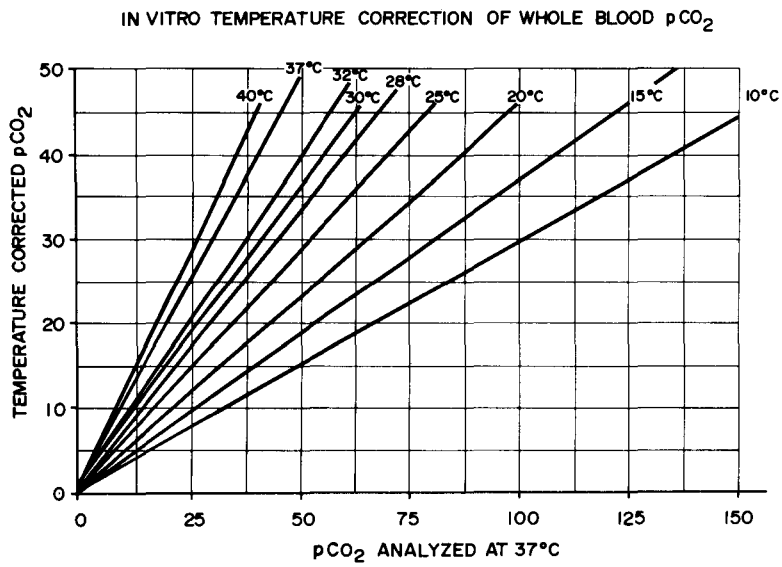

Figure 2

Bradley, Stuppel and Severinghaus, in 1956, theoretically calculated the F_{CO_2} for a pH of 7.4 and temperature of 37° C to be 0.0185. They state that the calculated F_{CO_2} varies with temperature range and pH. At a pH of 7.4 F_{CO_2} is .0212 at 20 -26° C and .0185 at 34–40° C. At temperatures of 34–40° C pH causes the F_{CO_2} to vary from .0175 at 7.0 to .0194 at 7.8. Nunn empirically confirmed the mean value of .019 for F_{CO_2}. Using .019 facilitates temperature correction and does not incur significant interpretation error in teh physiological ranges of pH. In temperature corrections of pCO_2 for *in vivo* temperatures between 30–37° C the change in the pCO_2 is 4.7 to 4.1% per °C.[5 10]

TEMPERATURE CORRECTION OF pO_2

In 1956 Bradley[5] assumed that oxygen content and percent saturation of hemoglobin would not change with temperature alterations *in vitro* in an anaerobic environment. They concluded that, since the pH and temperature of whole blood change when warmed in analysis, temperature correction of pO_2 is only a function of these two families of curves. They presented the equation:

$$pO_{2t} = 10^{F_{O_2}(t-37)} \times pO_{2,\,37°C}$$

where F_{O_2} is the correction coefficient for O_2 and has the calculated value of .0247 for small temperature differences in near physiological pH ranges. Their experimental confirmation was not significant. Nunn,[10] using fresh whole blood, found that the F_{O_2} rose with decreasing hemoglobin saturation from .0052 at a hemoglobin saturation of 100% to .032 at 83%. The F_{O_2} was unchanged with further decrease of hemoglobin saturation. They further suggested that the F_{O_2} for desaturated hemoglobin blood must also be dependent on actual temperature pCO_2 and hemoglobin concentration.

Kelman and Nunn[1] studied the effects of hemoglobin saturation on the F_{O_2} and generated the following equation in 1966:

$$F_{O_2} = .0052 + .0268\,(1 - e^{-.3x})$$

where x is the percent saturation of hemoglobin with oxygen.

Kelman and Nunn's equation agreed with Hedley-Whyte, who demonstrated that the change in the pO_2 of whole blood at 100% hemoglobin oxygen saturation is in inverse proportion to the change in O_2 solubility as temperature is altered *in vitro*.[9]

If the temperature of anaerobically stored blood is changed, the change in pO_2 is offset by the change in oxygen affinity resulting in shifting of the oxyhemoglobin curve. However, at oxygen saturations of 83% and above, these factors do not offset each other.[12 18] Severinghaus[12] also explained that pO_2 changes with temperature because the dissociation curve and the pH change with temperature. Congruent with Bradley,[5] Severinghaus calculated the total anaerobic affect of temperature change on pO_2 by combining the effects of temperature and pH to arrive at $F_{O_2} = .031$, and stated that this F_{O_2} is not reliable at hemoglobin saturations greater than 95%.[12] Severinghaus further stated that the F_{O_2} varies from .030 to .032 over the range of pCO_2 from 0 to 100mmHg while maintaining the O_2 saturation of hemoglobin less than 83%.

Kelman, in 1968,[20] theoretically determined that the magnitude of F_{O_2} varies with the hemoglobin concentration, acid-base status of the blood and somewhat with temperature range especially when the hemoglobin saturation is less than 95%.

Thomas,[4] developed an algorithm for temperature correction of pO_2 that takes into account the effect of hematocrit, pCO_2, pH and oxygen saturation of hemoglobin

on the Fo_2. Implementing the computerizable algorithm is less complex, depending on the hemoglobin saturation, than employing three different temperature correction procedures: between 0-83%, Bradley;[5] between 83-100%, Severinghaus;[12] and above 100%, Hedley-Whyte.[9] Thomas reports his algorithm's agreement with Severinghaus and Nunn is quite satisfactory over the complete range of pO_2's encountered clinically and furthermore takes into account the effects of other variables.

Figures 3, 4, and 5 were generated by a digital computer employing the algorithm of Thomas. The temperature corrected pH and pCO_2 are held constant at 7.4 ±.01 pH units and 40 ±1mmHg respectively for all temperature isobars in all three figures. Figures 3, 4 and 5 are employed the same way as the previous figures. Figure 3 illustrates the effects of altering the hemoglobin concentration in temperature correction of pO_2 *in vitro*.

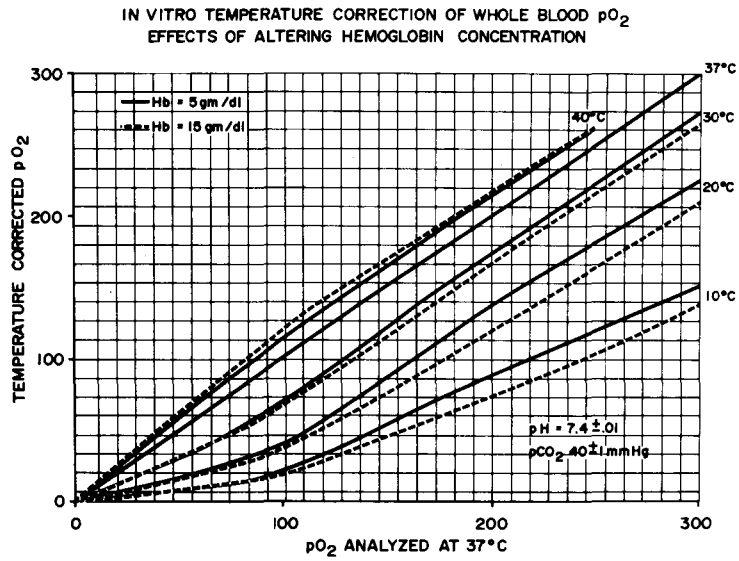

Figure 3

Figure 4 is the pO_2 measure at 37° C on the abscissa with the corrected pO_2 on the ordinate for a hemoglobin concentration of 15 grams per decaliter for measured pO_2's up to 700mmHg.

Figure 5 presents temperature correction isobars for pO_2's from 0–100 for accurate interpretation in the venous pO_2 range.

Thomas warns that because the temperature correction of pO_2 depends primarily on the slope of the oxyhemoglobin dissociation curve rather than on its position (P_{50}), severe abnormally shaped dissociation curves for aberrant forms of hemoglobin may cause temperature correction inconsistencies.

DISCUSSION

In recent years, a controversy has developed among open heart team members: Is temperature correction of blood pH and gases necessary? The process of anaerobic temperature correction is to compensate for physical change in blood pH and gases

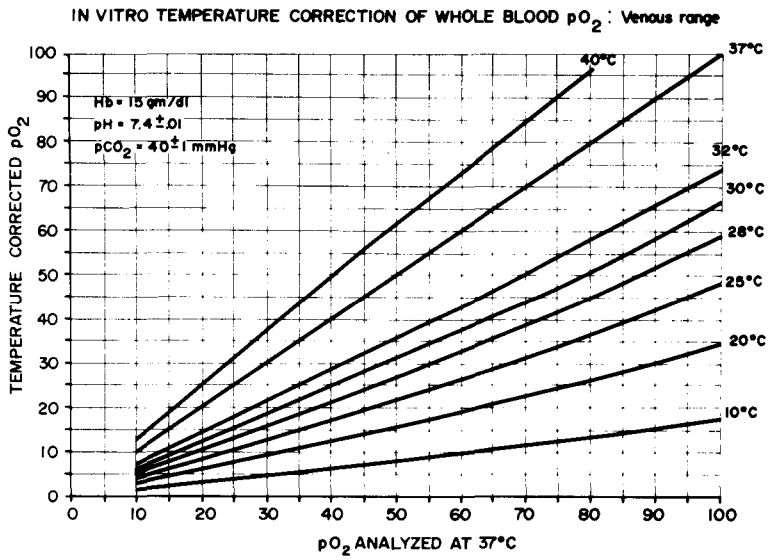

Figure 4

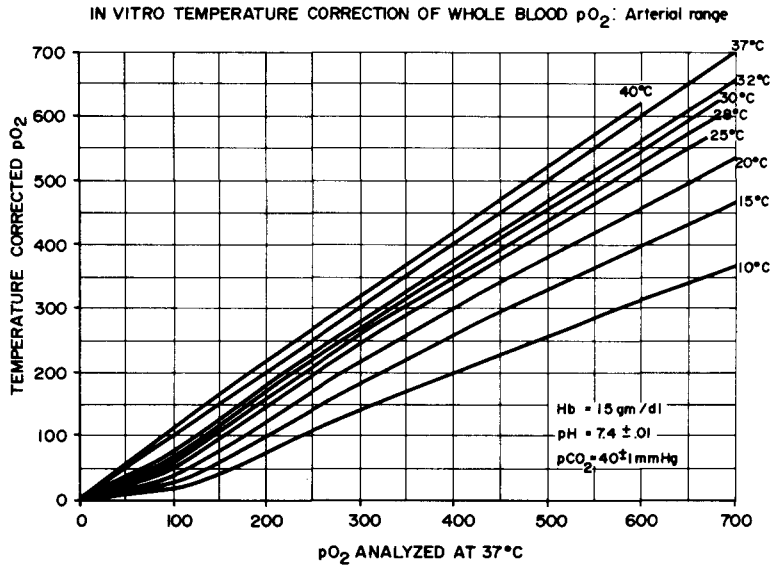

Figure 5

induced by the analyzer when patient temperature differs from that of the measurement instrument. The underlying problem is to establish what the ideal acid-base status to maintain during hypothermia is, which will insure optimal patient protection. If the clinician is interested in the absolute value of the blood pH and gases in the patient at temperatures other than 37° C, temperature correction is a necessity.

For example, if one ignores the process of temperature correction when the patient is at 28° C esophageal temperature and arterial blood results from the analyzer operating at 37° C are pO_2 = 290mmHg, pCO_2 = 42mmHg, pH = 7.38 (all within acceptable normal limits at 37° C), these results would temperature correct to pO_2 =

233mmHg, pCO_2 = 29mmHg and a pH = 7.51. A quick analysis shows this state to be respiratory alkalosis with an acceptable metabolic component. However, if the clinician wants 37° C normal values at a patient temperature of 28° C, the uncorrected values from the analyzer need to be about pO_2 = 300mmHg, pCO_2 = 56mmHg, and pH = 7.29 for the same patient. Classification of these uncorrected results in normothermic physiology would be respiratory acidosis, yet temperature correction yields 37° C normal values at a patient temperature of 28° C.

The optimal respiratory component to maintain during hypothermia is still in question. Dillard and co-workers, 1969,[21] recommended the use of respiratory alkalosis during deep hypothermia. Rahn, 1975,[22] concluded that respiratory alkalosis is optimal to maintain a normal intracellular environment during hypothermia. On the other hand, Subramanian, 1973,[23] does not employ the hyperventilation and respiratory alkalosis in deep hypothermia advocated by Dillard and Associates and prefers slight metabolic acidosis.

Unfortunately, alterations of the acid-base status with regard to protective or damaging effects are not well studied during hypothermia. The effects of varying the respiratory component and the accompanying changes in CO_2 content and pH are well understood in normothermic physiology. Until the optimal acid-base status to be maintained during hypothermia is well understood, the diagrams presented in this review may be used as guidelines for clinical research to answer this question.

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