

# TEMPERATURE CORRECTION OF ARTERIAL BLOOD pH AND CO<sub>2</sub> TENSION IN NEWBORN INFANTS: A NEW SOLUTION FOR AN OLD PROBLEM

A. MADANI, M.D., F. HABIBZADEH,\* M.D., AND M. YADOLLAHIE,\* M.D.

*From the Division of Neonatology, Department of Pediatrics, Shiraz University of Medical Sciences, and  
\*National Iranian Oil Company Outpatient Polyclinics, Shiraz, I. R. Iran.*

## ABSTRACT

The acid-base status and arterial blood gas change with temperature variation. To determine the changes in arterial pH and pCO<sub>2</sub>, arterial blood samples of 50 neonates with different clinical conditions were examined at temperatures of 35 to 42°C with an increment of 0.5°C, which resulted in two nonlinear equations with perfect fit on data. The temperature correction factors of these equations, unlike factors of the previously proposed linear equations, are not, themselves, functions of temperature. The arterial pH increases by 0.014 to 0.015 units, and pCO<sub>2</sub> decreases by 4.15-4.35%, with a 1°C drop in body temperature.

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## INTRODUCTION

Although water has only a very slight tendency to ionize, the products H<sup>+</sup> and OH<sup>-</sup> have very profound biological effects. Protein structure and function, optimal reaction rates of important enzyme systems, and intracellular concentrations of crucial metabolic intermediates are all critically dependent on the activity of H<sup>+</sup> and OH<sup>-</sup>. Normal enzyme structure and function depend on a constant and usually neutral electrochemical environment, because electrochemical charge states and binding are largely responsible for maintaining normal protein conformational structure and active sites of enzymes.

Acid-base regulatory systems provide, in most cases, a neutral intracellular milieu in which H<sup>+</sup> and OH<sup>-</sup> ions are equal in number, thus maintaining a constant ratio [H]/[OH]= 1 which preserves normal charged ionic states of

cytosolic intermediary metabolites, and maintains active sites of critical enzymes functional.<sup>1</sup> Keeping a constant intracellular [H<sup>+</sup>]/[OH<sup>-</sup>] at 37°C requires buffering systems that sustain intracellular pH around 6.8 to 6.9. This is facilitated by keeping arterial blood pH at about 7.4 for 'neutrality'. This means that blood and extracellular fluid are normally relatively alkaline at neutral intracellular pH. This normal intracellular to extracellular H<sup>+</sup> gradient allows for unloading of acidic products of cellular metabolism, including CO<sub>2</sub>, to extracellular spaces and blood.<sup>1,2</sup>

The acid-base status and arterial blood gas, however, change with temperature variation.<sup>2-6</sup> By far the most important and dominant protein buffer is the imidazole R-group of the amino acid histidine which is abundant in most proteins. As temperature drops, the imidazole protein buffer changes its pK<sub>a</sub> in parallel with pK<sub>w</sub> of water.<sup>1</sup> A parallel change in pH, when temperature falls, maintains the fraction of unprotonated histidine imidazole groups constant.<sup>1</sup> This constant net charge provides for normal protein structure and function as well as other aspects of intracellular homeostasis.

Employing the newly-advented medical techniques such as hypothermic cardiopulmonary bypass surgery increasingly challenges physicians with the problem of evaluating and

**Correspondence:** F. Habibzadeh, P.O. Box 71955-575, I.R. Iran.

E-Mail: habibzaf@pearl.sums.ac.ir

Fax: 071-661001

Tel: 071-664481

maintaining their patients' health at temperatures largely distant from what they have dealt with before.<sup>7,8</sup> Neonates, especially premature infants, due to their special characteristics, that is the higher-than adults body surface to weight ratio, are more prone to hypothermia. This requires one to pay more attention to physiologic alterations that occur during hypo-/hyperthermia when examining neonates. Since neonates, whether full-term or premature, are highly susceptible to hypothermia, we decided to reevaluate this topic and thus conducted this study to determine the effect of temperature on arterial blood pH and pCO<sub>2</sub>, the two most important acid-base determinants in neonate infants.

**PATIENTS AND METHODS**

Heparinized arterial blood samples of 50 neonates with a variety of surgical and medical disorders, in different clinical conditions and gestational age, who were admitted to the neonatal ICU of Nemazee Hospital, Shiraz, Iran, were transferred anaerobically to a blood-gas analyzer. The machine was calibrated routinely.

Regarding thermodynamic rules,<sup>9</sup> it was learned that the temperature-induced changes in pH and pCO<sub>2</sub> should obey the following equations:

$$pH_2 - pH_1 = K_{pH} \left( \frac{1}{T_2} - \frac{1}{T_1} \right) = \Delta pH = K_{pH} \Delta \frac{1}{T}$$

$$\log \left( \frac{p_2CO_2}{p_1CO_2} \right) = K_{pCO_2} \left( \frac{1}{T_2} - \frac{1}{T_1} \right) = \Delta \log(pCO_2) = K_{pCO_2} \Delta \frac{1}{T}$$

where T denotes absolute temperature, and K<sub>pH</sub> and K<sub>pCO<sub>2</sub></sub> are proportionality constants. The readings for each sample were performed for pH and pCO<sub>2</sub> at temperatures of 35 to 42°C with increments of 0.5°C. Comparing the readings at each two temperatures, yields 105 sets of data for each sample which amounts to a total of 5250 Δ<sub>T</sub><sup>-1</sup>, ΔpH, and Δlog(pCO<sub>2</sub>) values for all cases. To find the constant values of K<sub>pH</sub> and K<sub>pCO<sub>2</sub></sub>, employing SPSS for PC software, linear regression through the coordinate origin was performed.

**RESULTS**

Linear regression analysis resulted in the following equations:

$$(1) \quad \Delta pH = 1398.4024 \Delta \frac{1}{T}$$

$$(2) \quad \Delta \log(pCO_2) = -1797.4053 \Delta \frac{1}{T}$$

Obviously, as temperature drops, blood pH will increase and pCO<sub>2</sub> will decrease. As shown in Fig. 1, a perfect fit was obtained for both pH (r= 0.99, p< 0.00001), and pCO<sub>2</sub>(r= 0.99, p<0.00001).

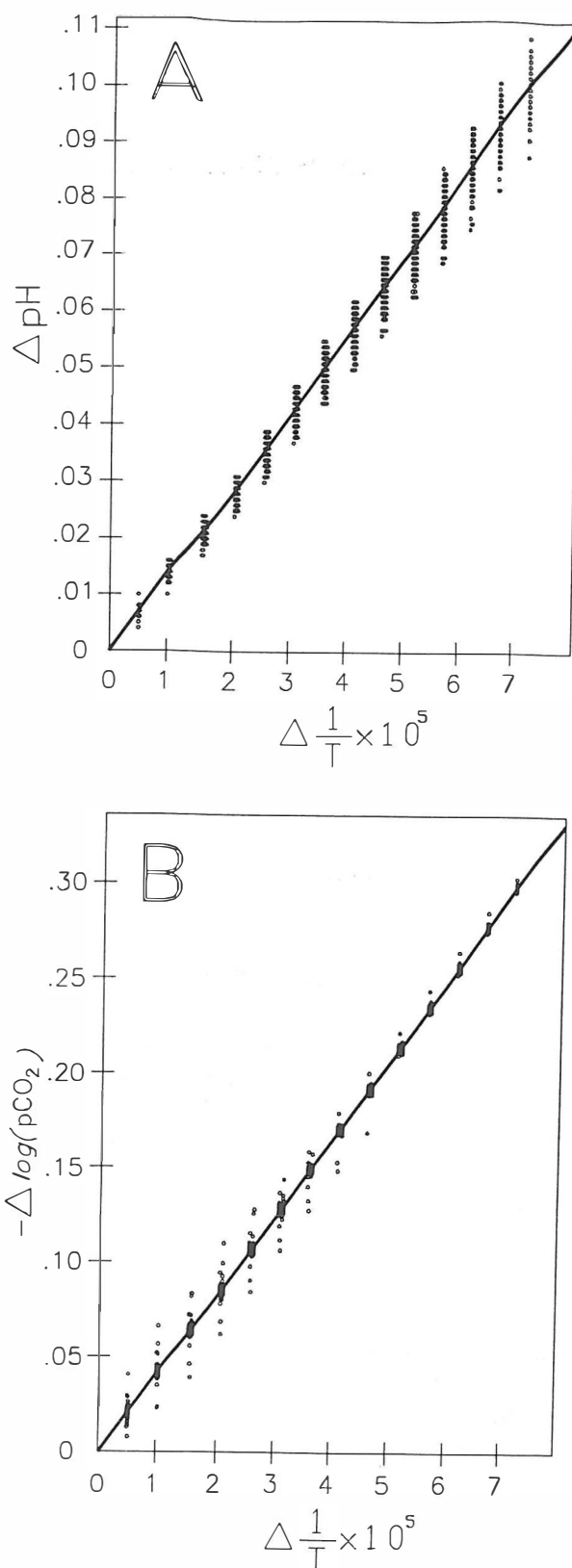


Fig. 1. The change of (A) arterial pH, and (B) pCO<sub>2</sub> with temperature.

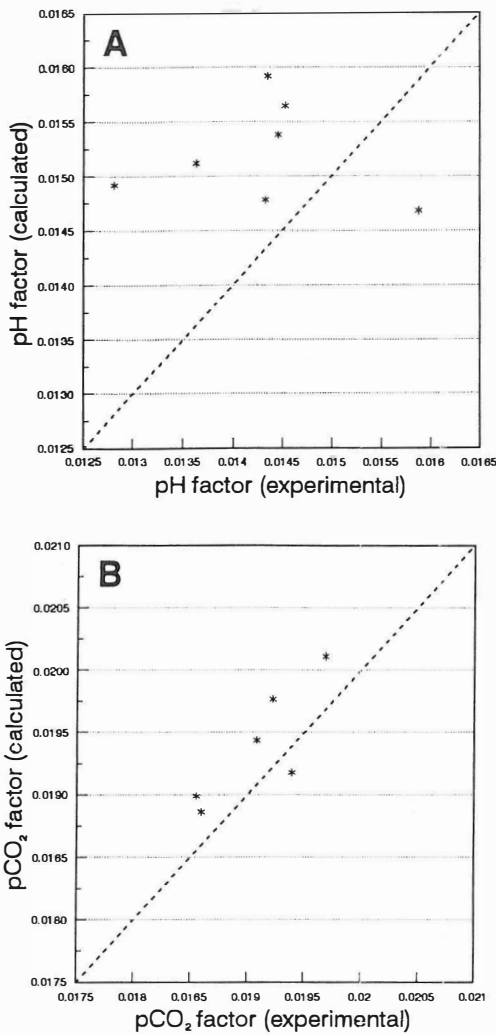


Fig. 2. Comparison of the experimentally derived<sup>4</sup> and the calculated temperature correction factors of (A) pH, and (B) pCO<sub>2</sub>. If the calculated data were exactly the same as the experimentally derived data, the points would fall on the dashed line.

DISCUSSION

Hypothermia is now firmly established as an adjunctive maneuver in open heart surgery. However, its use in various aspects of medical practice including repair and correction of major congenital defects in infants, neurological and cardiac surgery, requires knowledge of the respiratory and metabolic changes, including acid-base status, in man in deep hypothermia.<sup>10,11</sup> On the other hand, conditions with severe hyperthermia, such as malignant neuroleptic hyperthermia, also derange the acid-base equilibrium, and thus, require awareness of the temperature-induced changes in acid-base status.

There is much debate on the appropriate blood gas management of patients with hypo-/ hyperthermia, whether

the change in temperature is caused by accidents or induced intentionally.<sup>11-13</sup> An abundance of clinical experience has been acquired during the last years, during which operation of patients in hypothermia has become more common. There are two different strategies for blood gas management of patients in hypothermia; pH- stat and α - stat methods.<sup>7,11,12</sup> In the pH-stat method, the arterial pH is kept at 7.4 and the p<sub>a</sub>CO<sub>2</sub> is preserved at 40 mmHg, when measured at the patient's body temperature. In the α - stat strategy, however, the arterial pH and pCO<sub>2</sub> are maintained at 7.4 and 40 mmHg, respectively, when measured at 37°C.

When a patient is cooled down, the arterial pH will increase and the p<sub>a</sub>CO<sub>2</sub> will drop if measured at the patient's body temperature. To date, many attempts have been made to formulate this temperature-induced change of blood pH and pCO<sub>2</sub>.<sup>2,4-6</sup> Many of these endeavors have resulted in several linear models. However, the proportionality constants of these equations have been themselves functions of temperature.<sup>4-6</sup> This made researchers to use different proportionality values for different temperature ranges.<sup>4-6</sup>

The very good curve fit results obtained in this work support our initial thermodynamic assumptions. To reformulate our equations to the conventionally-used linear form,<sup>2,4-6</sup> Equ 1 can be rewritten as:

$$\begin{aligned} \Delta pH &= 1398.4024 \Delta \frac{1}{T} \\ &= 1398.4024 \left( \frac{1}{T_2} - \frac{1}{T_1} \right) \\ &= \frac{1398.4024}{T_1 T_2} (T_1 - T_2) \quad (3) \\ &= \frac{1398.4024}{T_1 T_2} (\theta_1 - \theta_2) \\ \Rightarrow \Delta pH &= \frac{1398.4024}{T_1 T_2} \Delta \theta \end{aligned}$$

Where θ designates temperature (°C). Using the same approach, Equ 2 can be also rewritten as:

$$\Delta \log (pCO_2) = \frac{1797.4053}{T_1 T_2} \Delta \theta \quad (4)$$

Comparing Equ's 3 and 4 with the commonly-used linear equations that have been employed by previous investigators,<sup>2,4-6</sup> that is:

$$\begin{aligned} \Delta pH &= f_{pH} \Delta \theta \\ \Delta \log (pCO_2) &= f_{pCO_2} \Delta \theta \end{aligned}$$

where  $f_{pH}$  and  $f_{pCO_2}$  are proportionality constants for pH and pCO<sub>2</sub>, respectively, indicates that:

$$\begin{aligned} f_{pH} &= \frac{1398.4024}{T_1 T_2} \\ \text{and} \quad f_{pCO_2} &= \frac{1797.4053}{T_1 T_2} \Delta \theta \end{aligned}$$

It is clear that a rise in temperature will increase  $f_{pH}$  and

decrease  $f_{pCO_2}$ , a fact that had been observed in previous experiments,<sup>4,6</sup> but had not yet been explained.

Comparing the calculated values, using Equ 5 for  $f_{pH}$ , with those experimentally derived values (Fig. 2A), showed a perfect match ( $r=0.99, p<0.00001$ ). This is also true for  $f_{pCO_2}$  (Fig. 2B) ( $r=0.99, p<0.00001$ ). The inherent variability of both  $f_{pH}$  and  $f_{pCO_2}$  in our model, that is in accord with the experimentally derived data, abolishes the need to use several equations for different temperature intervals.<sup>2,4,6</sup>

Although fetal hemoglobin has a slightly different buffering capacity than that of adults, since our model was not constructed upon any specific type of hemoglobin, the results generally can be applied to adults as well. The results indicate that normally, arterial pH increases by 0.014 to 0.015 units, and  $p_aCO_2$  decreases by 4.15- 4.35%, for each 1°C drop in body temperature.

### REFERENCES

1. Rahn H, Reeves RB, Howell BJ: Hydrogen ion regulation, temperature, and evolution. *Am Rev Respir Dis* 112: 165-72, 1975.
2. Ream AK, Reitz BA, Silverberg G: Temperature correction of  $pCO_2$  and pH in estimating acid-base status: an example of the emperor's new clothes? *Anesthesiology* 56 (1): 41-4, 1982.
3. Habibzadeh F, Yadollahie M: Temperature correction of the calculated alveolar oxygen tension. *Anesthesiology* 89 (4): 1042, 1998.
4. Greenburg AG, Moulder PV: Temperature coefficients for  $pCO_2$  and pH in whole blood finding  $Pco_2$  and pH at low temperatures. *Arch Surg* 91: 867-71, 1965.
5. Reeves RB: Temperature-induced changes in blood acid-base Status: pH and  $pCO_2$  in a binary buffer. *J Appl Physiol* 40(5): 752-61, 1976.
6. Bradley AF, Stupfel M, Severinghaus JW: Effect of temperature on  $pCO_2$  and  $pO_2$  of blood *in vitro*. *J Appl Physiol* 9: 201-4, 1956.
7. Kofstad J: Blood gases and hypothermia: some theoretical and practical considerations. *Scand J Clin Lab Invest Suppl* 224: 21-6, 1996.
8. Tallman RD Jr: Acid-base regulation, alpha-stat, and the emperor's new clothes. *J Cardiothoracic Vasc Anesth* 11(3): 282-8, 1997.
9. Alberty RA, Silbey RJ: Phase Equilibrium: One-Component Systems. In: *Physical Chemistry*. New York: John Wiley & Sons, pp. 179-195, 1992.
10. Barratt-Boyes BG, Simpson M, Neutze JM: Intracardiac surgery in neonates and infants using deep hypothermia with surface cooling and limited cardiopulmonary bypass. *Circulation* 43- 44 (Suppl): 25-30, 1971.
11. Kurth CD, O'Rourke MM, O'Hara IB, Uher B: Brain cooling efficiency with pH-stat and alpha-stat cardiopulmonary bypass in newborn pigs. *Circulation* 96 (9 Suppl): II- 358- 63, 1997.
12. Komberger E, Mair P, Hormann C, et al: Hemodynamics and oxygen metabolism in the pig during long- term hypothermia: comparison of 2 pH strategies. *Resuscitation* 30 (1): 43-50, 1995.
13. Goldsack C, Berridge JC: Acid-base management during cardiopulmonary bypass. Current trends in the United Kingdom. *Anesthesia* 51 (4): 396-8, 1996.