

## Temperature Correction of Arterial Blood-Gas Parameters: A Comparative Review of Methodology

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THERAPY for arterial blood-gas abnormalities and acid-base disturbances is generally instituted with the assumption that the reported parameters are accurate. Although recent advances in the technology of blood-gas measurement ensure precise, reproducible measurements of the  $P_{O_2}$ ,  $P_{CO_2}$ , and  $pH$  of *in vitro* samples, any discrepancy between patient body temperature and the temperature of the blood sample at the time of analysis may still introduce a source of error that significantly impairs clinical interpretation of blood-gas data.<sup>1</sup> Confusion regarding the feasibility or the necessity to apply temperature correction to blood-gas results<sup>2</sup> appears to originate from hesitancy to add further mathematical complexity to a high-technology area that is already intimidating to many medical personnel. There also appears to be uncertainty as to how the "corrected" results will be interpreted by physicians or therapists unaccustomed to their use.

An arterial blood-gas sample is a glimpse into a biological system at an instant in time. Any measurement system which does not eliminate or correct for artificial *in vitro* variations in the measured variables cannot provide an accurate picture of the patient's clinical status. Previous reports describe tables,<sup>3-7</sup> alignment nomograms,<sup>1,8-12</sup> slide rule computations,<sup>13</sup> and various computer programs<sup>14-21</sup> designed to calculate acid-base parameters and to correct arterial or venous blood-gas values for temperature discrepancies. Some of these reports contain minor or major inaccuracies in the correction formulas. We will review the essentials for understanding the method-

ology of temperature correction and we have compared the accuracy and convenience of the available empirical and theoretically derived correction systems.

### $pH$

Anaerobic cooling of blood samples is associated with an increase in measured  $pH$ . Stadie and Martin<sup>22</sup> analyzed  $CO_2$  carriage by human blood at 15° C and 38° C and derived the empirical equation

$$pH = pH_{38} - 0.022(T - 38) \quad (1)$$

where  $pH$  is the  $pH$  value *in vivo*, corrected to patient body temperature,  $pH_{38}$  is the  $pH$  *in vitro* measured at 38° C,  $T$  is the patient body temperature (° C), and 0.022 is an empirical correction factor. Rosenthal<sup>23</sup> and others<sup>5,24-26</sup> subsequently established a more precise correction factor for  $\Delta pH/\Delta T$  of 0.015  $pH$  units/° C. Adamsons<sup>25</sup> has confirmed that this factor is independent of hematocrit but varies with changes in  $pH$  and plasma  $CO_2$  content ( $[CO_2]$ ), expressed as mm/l. Kelman and Nunn substituted measured carbon dioxide partial pressure for  $[CO_2]$  and derived an accurate, if unwieldy, correction factor,<sup>1</sup> but Severinghaus<sup>13</sup> has subsequently modified Adamsons' equation to a convenient form:

$$\Delta pH/\Delta T = 0.0146 - 0.0065(7.4 - pH_m) \quad (2)$$

The correction factor  $\Delta pH/\Delta T$  is used to correct the measured  $pH$  by substitution into the formula

$$pH = pH_m - (\Delta pH/\Delta T)(\Delta T) \quad (3)$$

where  $pH$  is the  $pH$  *in vivo* corrected to patient body temperature,  $pH_m$  is the  $pH$  *in vitro* measured by electrode at 37° C, and  $\Delta T$  is the temperature discrepancy, body temperature - electrode temperature (° C). Figure 1 illustrates the high degree of correlation ( $r = 0.967$ ) between  $pH$  values calculated using the Kelman and Nunn formula and equation 2. We have chosen the Severinghaus modification for our computer algorithm (See the Appendix) because of its compact format.

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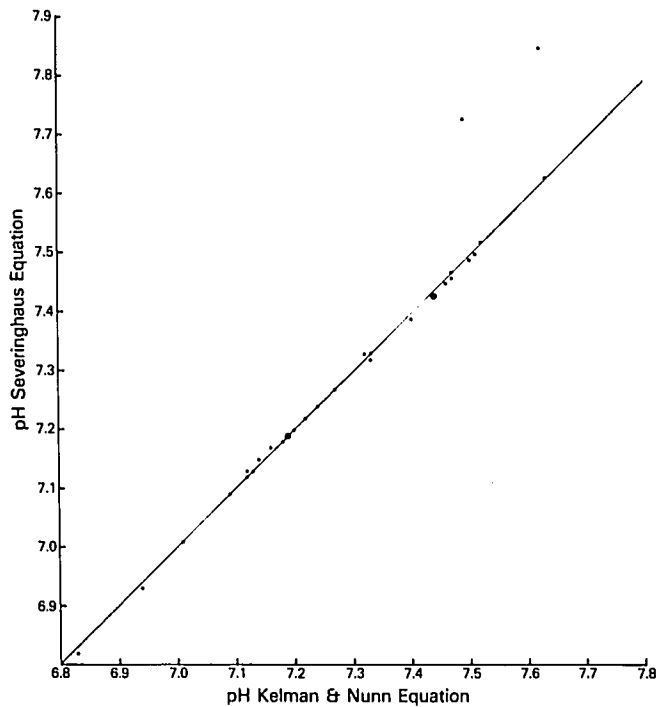


FIG. 1. Temperature-corrected pH values, Kelman and Nunn equation vs. Severinghaus equation,  $r = 0.967$ ,  $n = 29$ .

### $P_{CO_2}$

The physical dissolution of carbon dioxide or any other gaseous molecule in a liquid is described by Henry's Law:

$$X_{\text{gas}} = S \times P_{\text{gas}} \quad (4)$$

$X_{\text{gas}}$  is the concentration of gas molecules in the liquid phase in mm/l,  $S$  is the coefficient of solubility of the gas in the liquid, and  $P_{\text{gas}}$  is the partial pressure of the gas molecules in torr. Therefore, direct electrode measurements of  $P_{CO_2}$  actually reflect the ratio  $X_{CO_2}/S_{CO_2}$ , and both of these values are temperature-dependent:  $S$  because of the physicochemical properties of the molecules in solution, and  $X$  because of the relationship between temperature and the  $pK$  of carbonic acid which determines the actual molecular concentration of the various forms of that molecule in solution.<sup>7</sup> In addition, the  $pK$  itself may be altered by temperature-induced  $pH$  changes,<sup>27</sup> as described above. Of all the components of the Henderson-Hasselbalch equation, only  $[HCO_3^-]$  is independent of temperature.<sup>28</sup> Therefore,  $P_{CO_2}$  must be corrected to patient body temperature to accurately reflect conditions *in vivo* for both acid-base status and carbon dioxide partial pressures. Bradley *et al.*<sup>3</sup> proposed that over a modest range of temperature changes, the multiple factors which alter  $P_{CO_2}$  with temperature could be accounted for by the simple relationship

$$P_{CO_2} = P_{mCO_2} \times 10^{f_{CO_2}(\Delta T)} \quad (5)$$

where  $P_{CO_2}$  is the  $P_{CO_2}$  *in vivo* corrected to body temperature,  $P_{mCO_2}$  is the  $P_{CO_2}$  *in vitro* measured by electrode at 37° C,  $f_{CO_2}$  is the  $CO_2$  temperature correction factor observed to be 0.019, and  $\Delta T$  is the temperature discrepancy, body temperature – electrode temperature (° C). This general relationship and the use of the empirical factor 0.019, an exponent, appears to be universally accepted and is incorporated in our temperature correction program.

### $P_{O_2}$

The effect of temperature on both the solubility of oxygen in plasma and on the affinity of hemoglobin for oxygen makes temperature correction of measured oxygen tensions in the blood a complex matter. Complete saturation of hemoglobin with oxygen can be assumed regardless of temperature when  $P_{O_2}$  is 250 torr or greater.<sup>4</sup> Under these circumstances, a correction factor of 0.0052 has been determined empirically by Nunn *et al.*<sup>6</sup> for use in an equation analogous to that described above for  $P_{CO_2}$ :

$$P_{O_2} = P_{mO_2} \times 10^{f_{O_2}(\Delta T)} \quad (6)$$

$P_{O_2}$  is the  $P_{O_2}$  *in vivo* corrected to patient body temperature,  $P_{mO_2}$  is the  $P_{O_2}$  *in vitro* measured by electrodes at 37° C,  $f_{O_2}$  is the temperature correction factor for oxygen, and  $\Delta T$  is the temperature discrepancy, body temperature – electrode temperature (° C). Nunn and his colleagues observed a progressive increase in  $f_{O_2}$  with decreasing saturation to a maximum  $f_{O_2}$  of 0.032 at 83 per cent saturation, a correction factor in very close agreement with the  $f_{O_2}$  value of 0.031 found by Severinghaus under similar conditions.<sup>13</sup> The  $f_{O_2}$  is relatively constant at saturations below 85 per cent due to the offsetting influences of oxygen solubility and oxyhemoglobin dissociation. Burnett *et al.*<sup>7</sup> described the complex relationship between  $f_{O_2}$  and saturation as

$$f_{O_2} = 0.032 - 0.0268e^{(0.3x-30)} \quad (7)$$

where  $x$  is the per cent desaturation of hemoglobin, and  $e$  is the base of the natural logarithm.

TABLE 1. Absolute Deviation from Observed  $P_{O_2}$  Temperature Coefficient ( $f$ ) When Various Curve-Fitting Equations Are Used to Calculate  $f = \Delta \log P_{O_2}/\Delta T$ , Range 0 to 450 torr at 37°C, pH 7.40

Equation Source	Maximum Deviation	Mean Deviation
Severinghaus <sup>30</sup>	0.002	0.001
Ruiz <i>et al.</i> <sup>21</sup>	0.001	<0.001
Hewlett-Packard <sup>29</sup>	0.002	<0.001
Burnett <sup>7</sup>	0.006	0.002

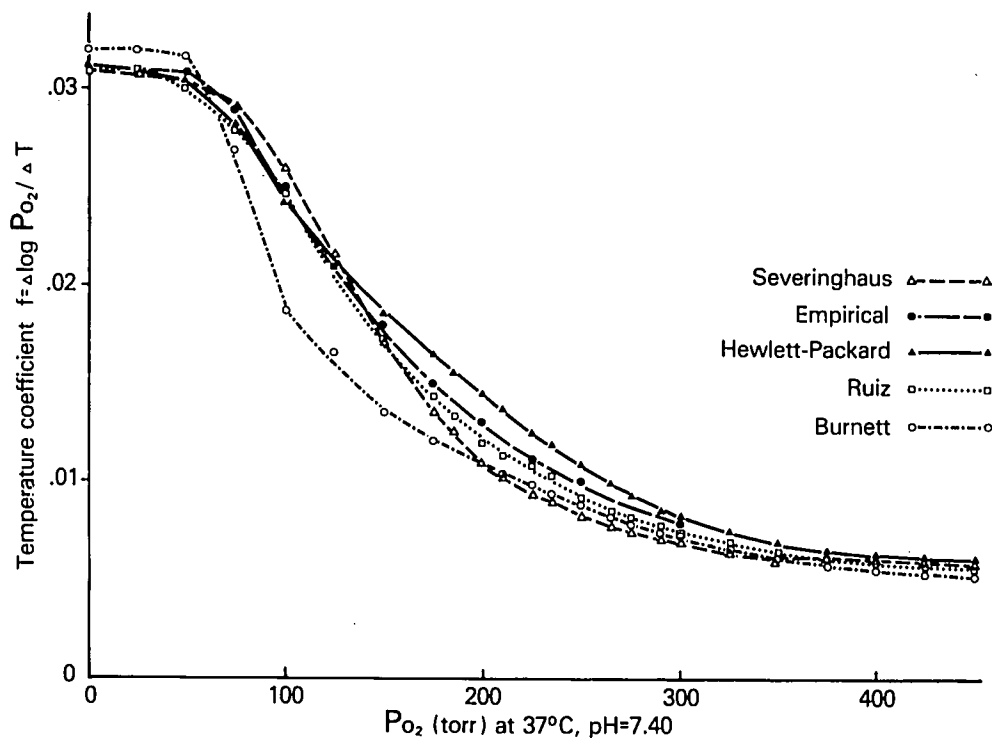


FIG. 2. Temperature correction coefficient,  $f_{O_2}$ , as a function of oxygen tension, estimated by the equations of Severinghaus, Ruiz, Burnett, and Hewlett-Packard. Empirical curve based upon original observations of Severinghaus.

Currently, the most widely used formulas for estimation of  $f_{O_2}$  are based upon  $P_{O_2}$  rather than upon saturation, avoiding the practical difficulties of direct measurement of saturation. These formulas, however, can generate minor inaccuracies because of the variations in the oxyhemoglobin dissociation curve seen in the general population. Ruiz *et al.*<sup>21</sup> and others<sup>7,29</sup> have used mathematical curve-fitting techniques to derive programmable equations which closely approximate the curvilinear empirical relationship between  $f_{O_2}$  and  $P_{O_2}$  initially observed by Severinghaus. A relatively simple formula

$$\Delta \ln P_{O_2} / \Delta T = 0.058(A + 1)^{-1} + 0.013 \quad (8)$$

where

$$A = 0.243 \times (P_{O_2} / 100)^{3.88}$$

has been derived recently by Severinghaus<sup>30</sup> from the Hill equation.<sup>31</sup> From comparison of the mean and maximum deviations from the observed correction factor associated with the various curve-fitting equations for  $f_{O_2}$  (table 1), and superimposition of the respective coefficient *vs.*  $P_{O_2}$  curves (fig. 2), we conclude that the Severinghaus formula, equation 8, is the most useful clinically because it offers ease of programming without significant loss of accuracy. Because it is based upon a natural logarithm, however, it is necessary to convert the Severinghaus temperature coefficient to base 10 prior to comparison with other equations or substitutions into equation 6.

### Saturation

If direct measurement of saturation is not possible, saturation values must be estimated from "virtual"  $P_{O_2}$  values. Virtual  $P_{O_2}$  is a theoretical value which permits calculation of oxygen saturation assuming a normal "standard" oxyhemoglobin dissociation relationship, and therefore requires some mechanism by which measured  $P_{O_2}$  is initially adjusted to standard conditions of *pH* 7.40,  $P_{CO_2}$  40 torr, and temperature 37° C. Therefore, virtual  $P_{O_2}$  is not a measured or physiologic variable but a theoretical, calculated value.

Calculation of virtual  $P_{O_2}$  for purposes of estimating hemoglobin saturation with oxygen is an initial step in temperature correction of measured  $P_{O_2}$  in arterial blood and can be accomplished according to the equation of Kelman<sup>32</sup>:

$$P_{O_2} = P_{mO_2} \times 10^{(0.40(pH_m - 7.4) + 0.06(\log 40 - \log P_{mCO_2}))} \quad (9)$$

where  $P_{O_2}$  is virtual  $P_{O_2}$ ,  $P_{mO_2}$  is the  $P_{O_2}$  *in vitro* measured by electrodes at 37° C,  $pH_m$  is *pH in vitro* measured by electrodes at 37° C, and  $P_{mCO_2}$  is the  $P_{CO_2}$  *in vitro* measured by electrodes at 37° C. This equation, included in our algorithm, utilizes directly measured variables, and unlike the comparable equation suggested by Severinghaus,<sup>13</sup> does not require prior calculation of base excess.

There are many equations available for translation of the calculated value for virtual  $P_{O_2}$  into percentage hemoglobin saturation. Many of those suitable for use

TABLE 2. ERROR (Mean/Maximum) in Per Cent Saturation Associated with Various Equations Used to Estimate Hemoglobin Saturation from Measured  $P_{O_2}$ ; Comparison with the Standard Oxyhemoglobin Dissociation Curve of Severinghaus<sup>13</sup>

Equation Source	Saturation Range (Per Cent)		
	1.0-100	10.0-97	98-100
Severinghaus <sup>30</sup>	0.42/0.72	0.26/0.64	0.46/0.72
Aberman <sup>35</sup>	0.10/0.30	0.15/0.29	0.08/0.30
Ruiz <sup>21</sup>	0.13/0.34	0.09/0.33	0.15/0.34
Adair-Roughton <sup>36</sup>	0.21/1.17	0.48/1.17	0.11/0.25
Adair-Collier <sup>7</sup>	0.28/1.97	0.64/1.97	0.26/0.33
Radiometer ABL-1 <sup>36</sup>	0.37/2.18	0.76/2.18	0.23/0.42

in computer programs<sup>7,18,32</sup> are based upon Adair's classic model<sup>33</sup> and are inaccurate at saturations below 40 per cent when compared to the observed standard oxyhemoglobin dissociation curve reported by Severinghaus.<sup>13</sup> The Roughton and Severinghaus modification of the Adair formula<sup>34</sup> and the mathematical curve-fit approaches of Aberman<sup>35</sup> and of Ruiz<sup>21</sup> give improved accuracy over the entire range of saturation at the cost of increased mathematical complexity. The modification of the Hill equation recently proposed by Severinghaus<sup>30</sup> is an acceptable compromise between accuracy over the clinically important range of saturations from 10-97 per cent (table 2 and fig. 3) and minimum computer program set requirements:

$$S = \{[(P_{O_2}^3 + 150 P_{O_2})^{-1} \times 23,400] + 1\}^{-1} \quad (10)$$

where  $S$  = per cent saturation of hemoglobin with oxygen, and  $P_{O_2}$  is the virtual  $P_{O_2}$ .

### Bicarbonate and $CO_2$ Content

Plasma bicarbonate concentration can be calculated easily by substituting measured  $pH$  and  $P_{CO_2}$  values and the  $CO_2$  solubility coefficient ( $S$ ) at the given measurement temperature into the Henderson-Hasselbalch equation:

$$pH = pK - \log [HCO_3^-]/(S \times P_{CO_2}) \quad (11)$$

Rearranging,

$$[HCO_3^-] = 0.0307 \times P_{mCO_2} \times 10^{(pH - 6.1)} \quad (12)$$

where  $[HCO_3^-]$  is bicarbonate concentration in mEq/l,  $pK$  is the dissociation constant for carbonic acid at  $pH$  7.40 and  $37^\circ C$  equal to 6.1, and  $S = 0.0307$  at  $37^\circ C$ . Bicarbonate concentration is temperature-independent.<sup>28</sup> If  $pH$  and  $P_{CO_2}$  are both measured at the same reference temperature,  $37^\circ C$  no further correction for patient temperature is needed. The  $CO_2$  content for all practical purposes, is the sum of  $CO_2$  present as  $[HCO_3^-]$  and as dissolved  $CO_2$  and it is calculated as  $[HCO_3^-] + (0.0307 \times P_{CO_2})$ .

### Base Excess

Reporting of base excess (BE) along with measured arterial blood-gas values permits the clinician to

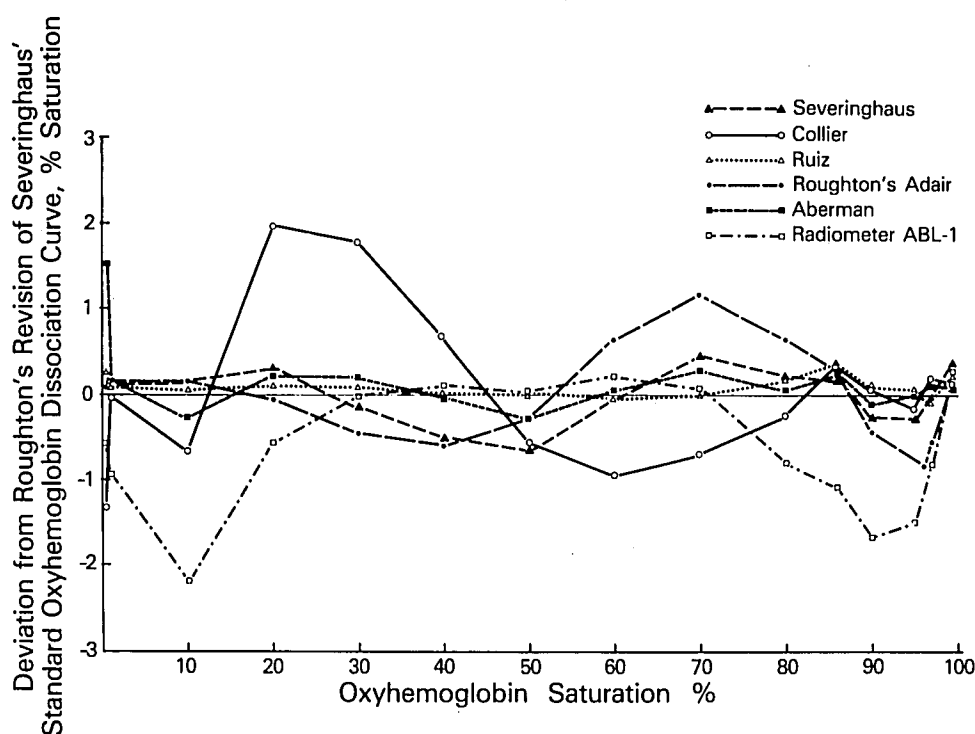


FIG. 3. Comparison of mathematical curve-fitting equations to the corrected observed standard oxyhemoglobin dissociation curve. Deviation in per cent saturation as a function of oxyhemoglobin saturation.

quantify, in mEq/l, the addition or deletion of nonvolatile, metabolically derived acids to the patient's extracellular fluid (ECF).<sup>38</sup> The hemoglobin in whole blood has a substantial capacity to buffer acid, but since about two-thirds of the ECF contains no hemoglobin, calculated estimates of total *in vivo* or "extracellular" BE can be provided using an assumed net buffer capacity (BC) of 10 mEq/l<sup>39</sup> or 12 mEq/l<sup>40</sup> and the equation

$$BE_{\text{cef}} = [\text{HCO}_3^-] - 24 - [\text{BC}(7.4 - pH_m)]. \quad (13)$$

In order to rely only on directly measured values, we have chosen for our algorithm the relatively compact, exceptionally accurate equation<sup>12</sup>

$$BE_{\text{cef}} = 37(e^A - 1)$$

where

$$A = (pH_m - 7.4 + 0.345Y)/(0.55 - 0.09Y) \quad (14)$$

and

$$Y = \ln(P_{m\text{CO}_2}/40)$$

None of the variables in equation 14 require temperature correction, but the equation is part of our algorithm to assist the clinician in the differential diagnosis of arterial blood-gas abnormalities.

### Summary

The need for accurate clinical diagnosis and appropriate intervention requires that a modern blood-gas laboratory have the means to correct for significant discrepancies between patient temperature and the temperature at which *in vitro* blood samples are analyzed. Recent advances in mini- and microcomputer technology permit application of any or all of the correction formulas above at modest cost and minimal inconvenience (See the Appendix). An expanded program for a TI-59 desk-top calculator and P-100C printer§ which gives labeled hard-copy readout of temperature-corrected pH, P<sub>CO<sub>2</sub></sub>, P<sub>O<sub>2</sub></sub>, and hemoglobin saturation values, as well as bicarbonate concentration and *in vivo* base excess is in daily clinical use in our operating room and is available from the authors upon request.

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## APPENDIX

*Temperature Correction of Arterial Blood Gases: Recommended Sequence of Equations.*

1. Enter and store measured body temperature ( $T$ , °C).
2. Calculate and store  $\Delta T$  ( $T$ -electrode temperature, °C).
3. Enter and store measured  $pH$  ( $pH_m$ ).
4. Calculate  $\Delta pH/\Delta T$  using equation 2 and store.
5. Enter measured  $P_{CO_2}$  ( $P_{mCO_2}$ ) and store.
6. Enter measured  $P_{O_2}$  ( $P_{mO_2}$ ) and store.
7. Calculate corrected  $pH$  using equation 3 and display the result.
8. Calculate corrected  $P_{CO_2}$  using equation 5 and display the result.
9. Calculate corrected  $P_{O_2}$  in three steps:
  - a. Substitute measured  $P_{O_2}$  into equation 8 and convert the result to base 10 to get a value for  $f_{O_2}$ .
  - b. Substitute this  $f_{O_2}$  value and the previously stored values for  $\Delta T$  and  $P_{mO_2}$  into equation 6 to obtain corrected  $P_{O_2}$ .
  - c. Display result.
- Note:* Division of solution to equation 8 by 2.31 converts it to base 10 logarithm if calculator has no preprogrammed function key for this purpose.
10. Calculate virtual  $P_{O_2}$  using equation 9 and store.
11. Calculate per cent saturation by substituting virtual  $P_{O_2}$  into equation 10. Display result.
12. Calculate bicarbonate using equation 12 and display result.
13. Calculate extracellular base excess using equation 14 and display result.