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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 *p*H 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.[1] Confusion regarding the feasibility or the necessity to apply temperature correction to blood-gas results[2] 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 artifactual *in vitro* variations in the measured variables cannot provide an accurate picture of the patient's clinical status. Previous reports describe tables,[3–7] alignment nomograms,[1,8–12] slide rule computations,[13] and various computer programs[14–21] 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 methodology of temperature correction and we have compared the accuracy and convenience of the available empirical and theoretically derived correction systems.

*p*H

Anaerobic cooling of blood samples is associated with an increase in measured *p*H. Stadie and Martin[22] 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 *p*H is the *p*H value *in vivo*, corrected to patient body temperature, pH_{38} is the *p*H *in vitro* measured at 38° C, T is the patient body temperature (° C), and 0.022 is an empirical correction factor. Rosenthal[23] and others[5,24–26] subsequently established a more precise correction factor for $\Delta pH/\Delta T$ of 0.015 *p*H units/° C. Adamsons[25] has confirmed that this factor is independent of hematocrit but varies with changes in *p*H 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,[1] but Severinghaus[13] 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 *p*H by substitution into the formula

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

where *p*H is the *p*H *in vivo* corrected to patient body temperature, pH_m is the *p*H *in vitro* measured by electrode at 37° C, and ΔT is the temperature discrepancy, body temperature − electrode temperature (° C). Figure 1 illustrates the high degree of correlation ($r = 0.967$) between *p*H 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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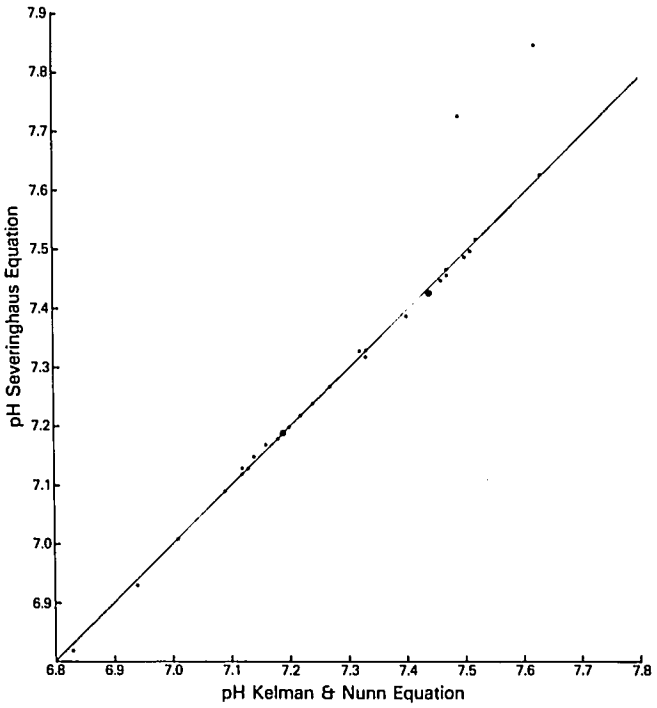

FIG. 1. Temperature-corrected *p*H values, Kelman and Nunn equation *vs.* Severinghaus equation, r = 0.967, n = 29.

P_{CO_2}

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

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

X_{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_{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 *p*K of carbonic acid which determines the actual molecular concentration of the various forms of that molecule in solution.[7] In addition, the *p*K itself may be altered by temperature-induced *p*H changes,[27] as described above. Of all the components of the Henderson-Hasselbalch equation, only $[HCO_3^-]$ is independent of temperature.[28] 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.*[3] 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 ΔT 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.[4] Under these circumstances, a correction factor of 0.0052 has been determined empirically by Nunn *et al.*[6] 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_mCO_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 ΔT 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.[13] 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.*[7] 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, *p*H 7.40

Equation Source	Maximum Deviation	Mean Deviation
Severinghaus[30]	0.002	0.001
Ruiz *et al.*[21]	0.001	<0.001
Hewlett-Packard[29]	0.002	<0.001
Burnett[7]	0.006	0.002

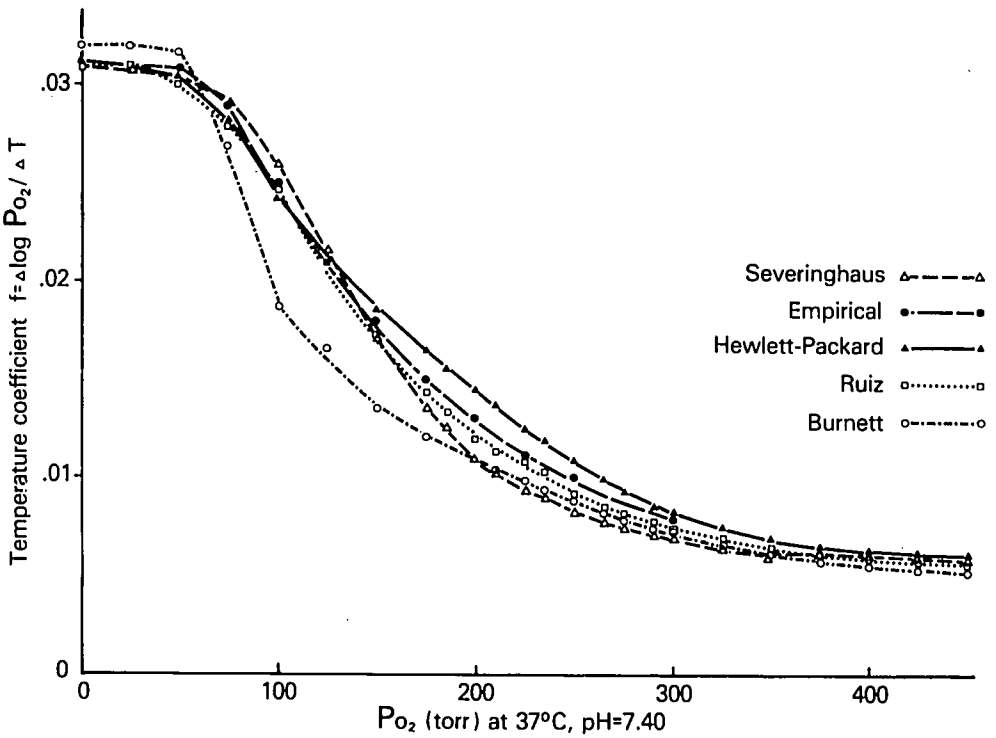

FIG. 2. Temperature correction coefficient, f_{O_2}, as a function of oxygen tension, estimated by the equations of Severinghaus, Ruiz, Burnett, and Hewlett-Packard. Empirical curve based upon original observations of Severinghaus.

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.*[21] and others[7,29] 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[30] from the Hill equation.[31] 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[32]:

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

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,[13] 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[13]

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

in computer programs[7,18,32] are based upon Adair's classic model[33] and are inaccurate at saturations below 40 per cent when compared to the observed standard oxyhemoglobin dissociation curve reported by Severinghaus.[13] The Roughton and Severinghaus modification of the Adair formula[34] and the mathematical curve-fit approaches of Aberman[35] and of Ruiz[21] 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[30] 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 step 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 *p*H 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,

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

where $[HCO_3^-]$ is bicarbonate concentration in mEq/l, *p*K is the dissociation constant for carbonic acid at *p*H 7.40 and 37° C equal to 6.1, and S = 0.0307 at 37° C. Bicarbonate concentration is temperature-independent.[28] If *p*H and P_{CO_2} are both measured at the same reference temperature, 37° 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

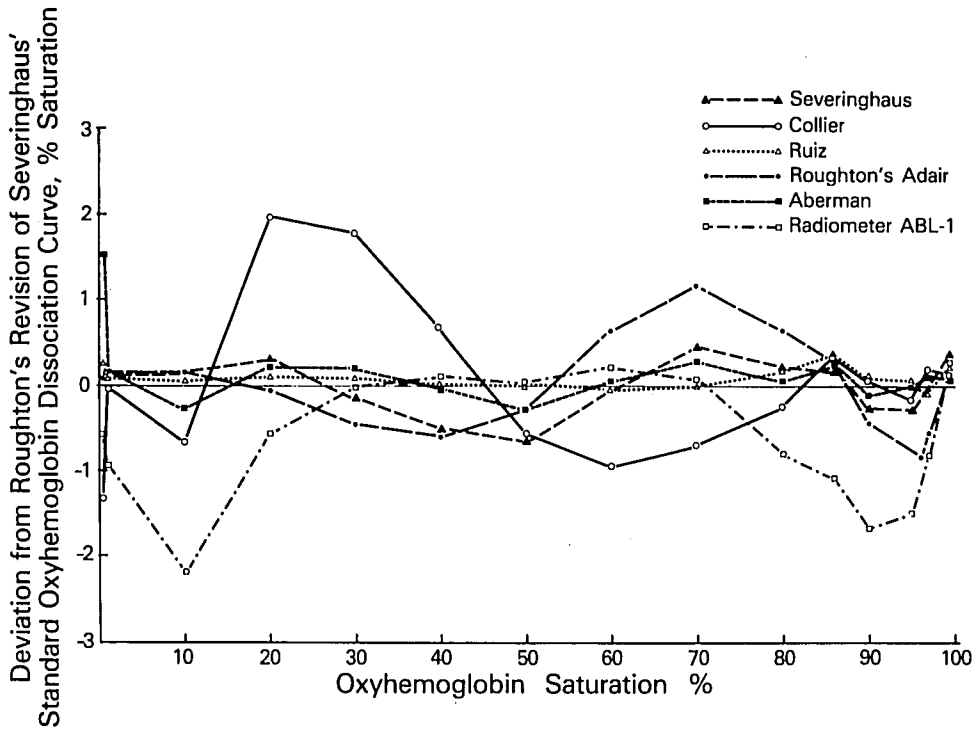

FIG. 3. Comparison of mathematical curve-fitting equations to the corrected observed standard oxyhemoglobin dissociation curve. Deviation in per cent saturation as a function of oxyhemoglobin saturation.

quantify, in mEq/l, the addition or deletion of nonvolatile, metabolically derived acids to the patient's extracellular fluid (ECF).[38] 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[39] or 12 mEq/l[40] and the equation

$$BE_{ecf} = [HCO_3^-] - 24 - [BC(7.4 - pH_m)]. \quad (13)$$

In order to rely only on directly measured values, we have chosen for our algorithm the relatively compact, exceptionally accurate equation[12]

$$BE_{ecf} = 37(e^A - 1)$$

where

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

and

$$Y = \ln (P_{m}CO_2/40)$$

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 *p*H, P_{CO_2}, P_{O_2}, 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 ΔT (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 ΔT 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.