

Temperature Correction of P_{CO_2} and pH in Estimating Acid-Base Status:

An Example of the Emperor's New Clothes?

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IT IS GENERALLY AGREED that at the normal temperature of man, 37° C, the ideal (normal) values of arterial pH and P_{CO_2} are 7.42 and 40 mmHg, respectively.¹ With a different patient temperature, however, most typically lower than normal, the ideal values are less obvious. Until recently, it appeared that the position expressed in 1965 represented a clinical consensus:

Interaction of decreased metabolism, increased dead space, and increased solubility of CO_2 is such that if ventilation is held constant as body temperature is reduced, arterial P_{CO_2} falls about 40% as temperature falls from 37 to 25 degrees centigrade. . . . It appears desirable to avoid this low P_{CO_2} and the associated alkalosis from the standpoint of cardiac irritability, so the addition of CO_2 to inspired gas has been practiced by some groups doing hypothermic bypass procedures.²

In other words, in the hypothermic patient, it was suggested that the P_{CO_2} of arterial blood should be adjusted to keep the pH (*i.e.*, the pH of the blood at the patient temperature) equal to 7.42. Because blood gas tensions and pH value are measured in the laboratory at a standard temperature of 37° C, it is necessary to *correct* this laboratory value to the patient's temperature, to determine patient P_{CO_2} and pH . The underlying assumption of this approach is that 7.42 is the ideal corrected or patient pH at all patient temperatures.

Recently, Rahn has suggested that the proper reference value may be electrochemical neutrality, where $pH = pOH$.³ It follows that the normal offset of physiologic pH at 37° C (0.6 units alkaline of the neutral point at $pH = 6.8$) should be maintained when body temperature changes. With cooling, the pH of the neutral point rises, with warming it falls; hence, so also should blood pH .

It has been suggested that the defended parameter is the charge state of proteins, in turn dependent on the extent of dissociation of the peptide-linked histidine imidazole groups. By protecting from change the fractional dissociation of these proteins, a wide array of protein enzymatic and transport activities dependent on protein charge state are available to the organism at all body temperatures.⁴

Several observations support this hypothesis. In man, in the exercising warm muscle, and at the skin with cooling, the changes in pH maintain this 0.6 unit offset of the neutral point (fig. 1). It could be argued that man is unlikely to maintain properly the appropriate pH with cooling or warming in excess of the normal physiologic range. It seems more probable that in the normal range the response is appropriate, since the body buffer system (primarily imidazole of peptide-histidine) is necessary to ensure this result. (Malan, in a parallel argument, suggests that cooling a closed system with a single major buffer does not change the acid-base balance.⁵)

The results of studying many other vertebrate species with acclimation to different body temperatures are consistent with this interpretation. The same variation in blood pH is observed^{6,7} (fig. 2). And while HCO_3^- content varied somewhat over the 35 species of vertebrates examined, HCO_3^- content in each species was essentially constant with changing temperature.⁸

(It is tempting to speculate that homeostasis also is the basis for the observed change in P_{50} (the partial pressure of oxygen necessary to achieve 50 per cent hemoglobin saturation) with temperature: the change in P_{50} is just sufficient to maintain constant hemoglobin saturation with changing temperature, despite changing blood solubility. Note that this interpretation simplifies many clinically obscure arguments, for example, the problem of an altered P_{50} when transfusing cold blood, or the need to alter the P_{50} from the normal response in a hypothermic patient.)

An interesting byproduct of these observations is the nature of the corresponding change in P_{CO_2} . The pH is maintained in the proper range by keeping HCO_3^- constant. A constant HCO_3^- results when total blood CO_2

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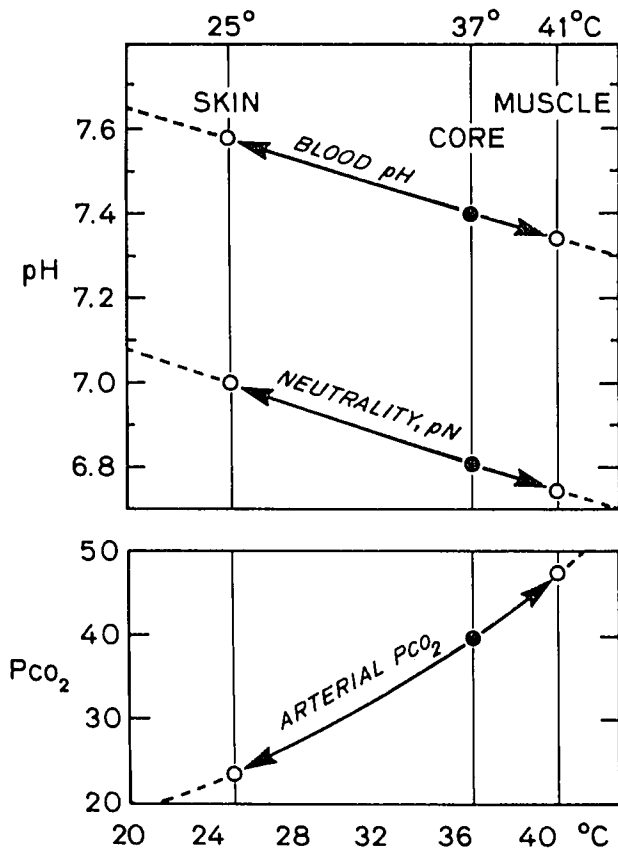


FIG. 1. Changes in arterial pH and P_{CO_2} in man as $37^\circ C$ blood arrives at the skin or exercising muscle at temperatures of $25^\circ C$ and $41^\circ C$, respectively. Neutrality of water, pN , changes in parallel with the changes in blood pH . Thus the relative alkalinity of the blood, or the ratio between $[OH]^-$ and $[H]^+$ ion remains constant. (After fig. 1, reference 3.)

content is constant, despite changing temperature. Then alveolar ventilation must increase, relative to oxygen consumption, with decreasing temperature, since a lower P_{CO_2} will compensate for rising solubility. The suggested practical rule using corrected P_{CO_2} is: for every ten-degree centigrade decrease in body temperature, the blood P_{CO_2} should decrease about 35 per cent.⁹

The net result is that minute ventilation should not markedly decrease with decreasing body temperature. This appears to be the actual response in poikilotherms, the group thought most likely to exhibit appropriate respiratory control responses with changing body temperature.

As can readily be appreciated from examination of figure 1, this approach suggests that the blood pH should be kept such that when the blood is warmed to $37^\circ C$, the pH is approximately 7.42. Then, if the patient's metabolic acid-base status is normal, the P_{CO_2} must be approximately 40 at $37^\circ C$. In other words, uncorrected

pH and P_{CO_2} , with the laboratory measurements made at $37^\circ C$, are the simplest means of assessing acid-base balance.

Rahn's hypothesis, that the most desirable pH is referenced to neutrality, is not yet fully accepted by the clinical community. (Both available data¹⁰ and the personal experience of the authors suggest that corrected values of arterial blood gas and pH determinations are most often used for management of acid-base balance.) However, the presumption that Rahn is correct is reinforced by animal studies, clinical impressions, and the failure to identify clearly contradictory findings.

Rahn's suggested approach appears favorable to the heart. In dogs, managing acid-base status according to the suggested criteria resulted in a 65 per cent increase in total left ventricular flow during cardiopulmonary bypass, with a 210 per cent increase in lactate metabolism.¹¹ There was no evidence of anaerobic metabolism. A recent study is particularly interesting.¹² In puppies studied after cardiac arrest for 1 h at $16^\circ C$, the seven animals with pH varied as in poikilotherms exhibited normal cardiac performance (as measured by the relation between stroke work index and left atrial pressure) post-bypass; however, in the seven held at $pH = 7.4$ throughout there was a 50 per cent depression in cardiac performance post-bypass. Ohmura reported similar results.¹³ There appear to be a number of centers which prefer to allow the P_{CO_2} to fall with temperature in performing cardiac surgery.^{14,15} In at least one center, the degree of hypocarbia is, on average, deliberately consistent with Rahn's recommendations.^{16,17}

Severinghaus proposed constant ventilation during hypothermia in 1958.¹⁸ But since then, concerns about cerebral function have been expressed because of the decrease in cerebral blood flow associated with hypo-

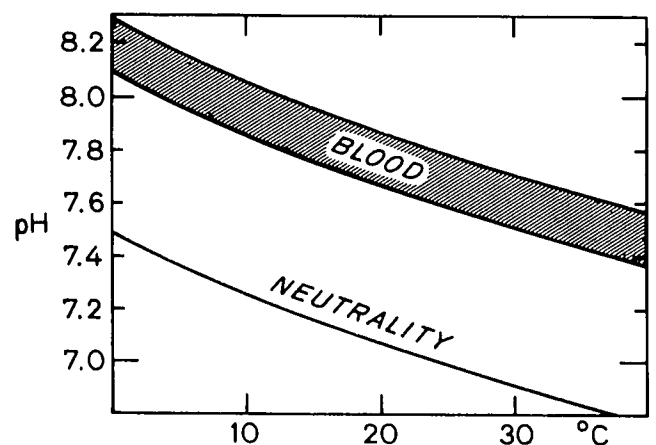


FIG. 2. Blood pH of exotherms, homeotherms, and the pH of neutral water as a function of body temperature. (After fig. 2, reference 3.)

carbia and normothermia.¹⁹ However, this concern appears inappropriate in reference to Rahn's hypothesis. Canine studies demonstrate that the reduction in blood flow with hypothermia is more nearly in 1:1 proportion to the reduction in whole body MR_{O_2} when minute ventilation is unchanged during cooling.¹³ Studies in rats¹⁹ and lambs²⁰ demonstrate that cerebral metabolism remained aerobic with equivalent decreases in P_{CO_2} vs. temperature. These studies all demonstrate that changes in cerebral blood flow with changing P_{CO_2} were maximal when near the P_{CO_2} suggested by Rahn for each temperature; a result strongly consistent with the observation that autoregulation is most sensitive in the middle of the desirable range. Finally, adding CO_2 to keep the corrected pH near 7.42 resulted in significant ventilatory effort in man under anesthesia.²¹ With an understanding of the nature of the decrease in cerebral blood flow, it appears that constant minute ventilation (and hence constant uncorrected pH) is preferable.

Our experience in 18 patients undergoing circulatory arrest in association with cardiopulmonary bypass supports these conclusions. In the first series of nine patients undergoing replacement of the aortic arch, we maintained minute ventilation, and added carbon dioxide during cooling to keep the (corrected) P_{CO_2} above 30 mmHg. Two arrhythmic cardiac arrests (with uncomplicated resuscitation) occurred between 26–28° C. We have gradually adopted Rahn's criteria. In our second series of nine patients, arrest occurred as the end stage of progressive bradycardia, with rapid cooling on bypass.²² In our last patient, an unanticipated variation in oxygenator gas flow immediately after circulatory arrest was demonstrated after the abrupt onset of brain swelling. Reducing the P_{CO_2} promptly corrected the problem (table 1).

It also is persuasive that no serious rebuttal to this view can be identified. Our literature search was fruitless. A recent letter to the *New England Journal of Medicine*¹⁰ suggesting that correction is unnecessary has not stimulated a single negative response in the first four months after publication. § We have not identified any investigator who is willing to offer a rebuttal, based on experimental data, to abandoning correction for acid-base management.

An important caveat must be remembered, however. Whenever gas tensions must be directly determined, as in comparison with alveolar or inspired values, correction is necessary to ensure proper interpretation. For example, it seems possible to manage patients by this approach using end-tidal P_{CO_2} measurements. But in this situation, the end-tidal value is measured at an external

§ Hansen JE: Personal communication.

TABLE 1. The Arterial Gas-tensions

Sample	Patient Temperature	Uncorrected		Corrected	
		P_{CO_2}	pH	P_{CO_2}	pH
Brain swelling After CO_2 tension reduced	20° C	74	7.14	35	7.39
	34° C	27	7.47	24	7.51

temperature. It must first be corrected to the patient temperature (using the gas laws) and used to estimate the actual arterial value. Then the estimated patient value must be corrected to 37° C (using the blood-gas laboratory correction algorithm in reverse). In such situations, there appears to be no escape from the hazards of a tricky calculation.

In summary, the use of the uncorrected value of pH in managing the hypothermic patient appears to be preferable, because the desired value does not change with temperature. For the management of acid-base status, the uncorrected P_{CO_2} should be used. (It appears that corrected P_{CO_2} is still required to characterize gas-equilibrium phenomena, as for example in estimation of an alveolar-arterial partial pressure gradient.) The concepts of metabolic and respiratory acidosis and alkalosis are appropriate; but uncorrected values should be used. Under normal circumstances, minute ventilation should not decrease or carbon dioxide be added to inspired gases with decreasing body temperature; and local variation in temperature of well-perfused tissue preserves optimal acid-base balance in all tissue, if balance is optimal in any one. These arguments appear equally correct for hyperthermic patients, below the denaturation temperature of approximately 41° C, although the corrections are then so small as to be of little practical significance.

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