

Electrolytes and Acid-Base Balance in Hypothermia

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ABSTRACT

Dogs were cooled in an ice-water bath, and plasma electrolytes were measured at heart temperatures of 38°C, 28°C and 25°C. A 'cold acidosis' occurred during hypothermia that is attributable largely to temperature-influenced physico-chemical factors related to the buffer systems. A slight respiratory depression is of greater importance in decreasing plasma pH at lower body temperature than at normal body temperature.

PREVIOUS studies of electrolyte and acid-base balance changes in hypothermia have been done using artificial respiration, or measuring only a few of the constituents that make up the acid-base pattern. This study was designed to show the effects of hypothermia, during spontaneous respiration, on most of the electrolytes that make up the acid-base picture. The following measurements were made on dogs at normal and at two hypothermic temperatures: blood pH, plasma CO₂, electrolyte and protein concentrations, osmolarity, hematocrit and heart rate.

The results of this study show that the acidosis associated with hypothermia can be attributed to a combination of physico-chemical and physiological effects. The term 'cold acidosis' is suggested to designate the acidosis of hypothermia.

METHODS

Eight dogs, in the postabsorptive state, were anesthetized with sodium pentobarbital (30 mg/kg) intraperitoneally. Additional sodium pentobarbital (maximum 60 mg) was given intravenously, as needed, to keep shivering at a minimal level. The right jugular vein was exposed, and a cardiac catheter which enclosed a copper constantan thermocouple was inserted in the right atrium. Temperature readings were made from this thermocouple with a Leeds and Northrop 'Speedomax.' The left carotid artery was exposed and blood samples were removed either through an inserted T tube or directly from the artery. Samples were collected anaerobically into oiled, heparinized syringes. After an aliquot for pH was taken, the sample was

transferred under mineral oil, centrifuged and the plasma removed without exposure to air. Two control samples, taken 30 minutes apart, were drawn. The dog was then immersed in an icewater bath. When cardiac temperature was approximately 30°C, the dog was removed from the bath and one sample was obtained, followed by another 30 minutes later. The dog was then reimmersed in the icewater until cardiac temperature reached 25°C, at which time another blood sample was obtained. Heart rate was measured from the electrocardiographic tracing, and blood pH with the Cambridge pH meter. The temperature of the pH sample was adjusted to the cardiac temperature of the dog at the time of sampling, thus eliminating the need for a temperature correction factor. Osmolarity was measured by freezing point depression, using a Fiske Osmometer. Hematocrits and plasma concentrations of protein, Na, K, Cl and Mg, were measured by methods described elsewhere (1). In addition, plasma was analyzed for carbon dioxide (2) and calcium (3).

STATISTICAL METHODS

The results are expressed as means and standard deviations. Variance analysis was done using the average values of the two control samples, and two 28.6°C samples and the single 25.5°C sample. If the sample showed a statistically significant difference by variance analysis it was further examined for significance, using critical differences. The level of significance was chosen as $P < .05$. Heart rate did not have homogeneity of variance, and was analyzed by the Freidman test (4).

RESULTS

Table 1 summarizes the data, and is arranged to show the mean values, standard deviations and statistically significant changes at the three

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TABLE 1. SUMMARY OF EFFECTS OF HYPOTHERMIA, AVERAGE OF EIGHT DOGS

	Mean	Mean	Mean
Heart temp., C°	38.1±1.2	28.6*±.4	25.5*±.6
Heart rate/min.	184±44	100*±14	72*±15
Hematocrit, %	46.2±4.6	53.5*±3.8	54.3†±3.3
Plasma protein gm %	6.6±.4	6.7±.4	6.5±.5
mOs/l.	303±5	302±4	301±4
pH at body temp.	7.40±.04	7.25*±.05	7.21†±.08
Mg, mEq/l.	1.59±.11	1.60±.07	1.69*†±.08
Ca, mEq/l.	5.13±.19	5.24*±.28	5.3†±.22
K, mEq/l.	3.6±.3	3.3±.2	3.4±.1
Na, mEq/l.	150±4	145*±3	146†±4
Cl, mEq/l.	109±2	107±2	108±2
Total CO ₂ , mm/l.	25.7±2.9	26.8±3.2	27.6†±3.5

* Indicates statistically significant difference from the next higher temperature.

† Indicates statistically significant difference from control value.

heart temperatures. The mean heart temperatures were: 38.1°C for the control period, 28.6°C for the first cold period and 25.5°C for the second cold period. The standard deviations of 1.2, 0.4 and 0.6°C, for each of the periods, respectively, indicate that there was very little variation from dog to dog within any given situation. Analysis of variance revealed no significant differences between animals within each period.

Heart rate fell progressively as the animals cooled. Hematocrit increased 7-8 \bar{v} in the cold, but there was no evidence of a progressive change from the first cold period to the second. Plasma protein concentration and osmolarity did not change. Plasma pH fell an average of 0.15 and 0.19 \bar{v} from control in each of the cold periods. In both cold periods, pH was significantly lower than in the control, but there was no significant change from one cold period to the other. Plasma potassium and chloride concentrations did not change from control values.

The changes in the following are statistically significant, but are of small magnitude. Plasma calcium concentration increased and plasma sodium concentration decreased during the first cold period, without further change in the second period. Plasma magnesium concentration and plasma carbon dioxide content were higher than control values only in the second cold period.

DISCUSSION

Frank shivering, artificial respiration and chemical anesthesia, can all in themselves affect the acid-base and electrolyte pattern of the body fluids. The existence of these factors to unknown degrees may largely account for the conflicting results frequently reported. In the present study, artificial respiration was eliminated, and shivering was kept minimal with barbiturate anesthesia.

Acidosis of Hypothermia. Hypothermia produced a fall in plasma pH in this study, and this fall in pH was accompanied by only a small rise in plasma carbon dioxide content. The fall in plasma pH that occurs in hypothermia, uncomplicated by artificial respiration or shivering, can be ascribed to two factors related to carbon dioxide: one physico-chemical and the other physiological. The physico-chemical factor is related to the changes in solubility of the gas, the dissociation of carbonic acid, and changes in the protein buffer systems at lowered temperatures. The physiological factor is the depressed respiration and resultant accumulation of carbonic acid.

A fall in temperature increases the solubility of carbon dioxide, but at the same time decreases the dissociation of carbonic acid into hydrogen and bicarbonate ions. These two effects oppose each other in changing pH, and whether pH will rise or fall depends upon the relative magnitude of these changes. In addition, cation made available from protein enters the bicarbonate-carbonic acid buffer system when there is a decrease in temperature (5-7).

Table 2 has been compiled to show the partition of the carbonic acid-bicarbonate buffer system found in this study (*part A*) and to show how the fall in temperature would affect pH if there were no respiratory depression (*part B*). In table 2A, the values for bicarbonate and carbonic acid have been calculated from the Henderson-Hasselbalch equation.¹ In table 2B, the values for carbonic

¹The dissociation constants (pK) for the lower temperatures were derived from the known pK at 38°C (6.10) plus the increment of 0.005 $\bar{v}/1^{\circ}\text{C}$ fall in temperature (8). Calculated plasma pK value at 28°C = 6.14; at 25°C = 6.16. The partial pressure of carbon dioxide (pCO₂) was calculated from the known solubility (α) in plasma at 38°C, plus the increment

TABLE 2. PLASMA CONCENTRATIONS

Temp.	pH	Total CO ₂	BHCO ₃	H ₂ CO ₃	pCO ₂
°C		mm/l.	mm/l.	mm/l.	mm Hg
<i>A. Data from this experiment</i>					
			(der.)*	(der.)	(der.)
38	7.40	25.7	24.5	1.2	40
28.6	7.25	26.8	24.9	1.9	50
25.5	7.21	27.6	25.3	2.3	55
<i>B. Derived when pCO₂ is kept constant</i>					
	(der.)	(der.)	(from A)	(der.)	(ass.)
38	7.40	25.7	24.5	1.2	40
28	7.35	26.4	24.9	1.5	40
25	7.34	27.0	25.3	1.7	40

A. Effect of hypothermia on the carbonic acid-bicarbonate buffer system. B. Calculated effect of respiration maintaining constant pCO₂.

* (der.) = derived. (ass.) = assumed.

acid concentration were calculated using the same constants, with pCO₂ kept constant at 40 mm Hg. The bicarbonate concentrations are the values taken from the experimental results; the increased concentrations at the lower temperatures can be ascribed to cation released from hemoglobin at the lower temperature.² The total CO₂ is the sum of the bicarbonate and the derived carbonic acid values. pH was derived using the Henderson-Hasselbalch equation with the appropriate pK value as described.

From table 2B, it can be seen that if pCO₂ were kept constant, there would be a fall of .05 ν from control in the first cold period, and .06 ν in the second cold period. Thus, at the lower temperature the increase in solubility of the carbon dioxide plays a greater role in determining pH than do the changes in pK of the bicarbonate and protein buffer systems. These pH changes are probably underestimated, since the assumption has been made that the increased intracellular dissociation of carbon dioxide is similarly balanced by the intracellular fluid buffers.

that occurs in water at the lower temperatures, taken from the International Critical Tables. Plasma α at 38°C = .0308. Calculated values: α at 28°C = 0.0382, at 25°C = 0.0416.

² *In vitro*, blood pH remains constant despite a fall in temperature, when pCO₂ is kept constant (5, 7). This cannot be directly applied to the intact animal, since the hemoglobin change is in equilibrium with all of the extracellular fluid (i.e., plasma plus interstitial fluid).

When the experimental results are compared with the values derived when pCO₂ is kept constant (table 2), the changes are in the same direction. However, the measured experimental changes in pH, carbonic acid, and pCO₂ are of greater magnitude. The rise in pCO₂ points out that there was some respiratory depression. Again the physico-chemical changes at the lower temperature are important. If the increases in pCO₂ secondary to a respiratory depression were to take place at normal body temperature, pH would fall 0.06 ν and 0.08 ν compared with the observed decrements of 0.15 and 0.19 ν . Thus, small increases in pCO₂ decrease pH much more at lower body temperatures. While it is not possible to assign fixed values to the influence of the physico-chemical factor and the physiological factor of depressed respiration, the above calculations indicate that more than half of the pH decrease can be assigned to the physico-chemical factors. It should be noted that the temperature-invoked changes can be applied to cold extremities, even in the absence of general hypothermia. The respiratory depression found here may be due to, or accentuated by, the chemical anesthesia. Since the change in acid-base balance in hypothermia is due in large part to temperature sensitive factors, the term 'cold acidosis' is proposed to describe the fall in plasma pH found at lowered body temperature. It is of interest to compare the plasma electrolyte concentrations in 'cold acidosis' with those of a respiratory acidosis. In a respiratory acidosis, imposed by the inhalation of a high carbon dioxide concentration there is a rise in plasma sodium, potassium and bicarbonate levels and a fall in plasma concentrations of chloride and phosphate (9). The different electrolyte patterns in the two types of acidosis support the concept that the changes in 'cold acidosis' are not primarily the result of carbon dioxide retention.

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