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Acid-base disturbance and ventilatory response to changes in plasma osmolality in Pekin ducks

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Abstract. The effects of acute changes in plasma osmolality on blood acid-base status and ventilation were investigated in the Pekin duck, *Anas platyrhynchos*. Hyperosmolality due to intravenous infusion of hypertonic NaCl or sucrose caused a prolonged acidosis (so-called dilution acidosis), which was attributable to a decrease in estimated strong ion difference due to a fall in the plasma $[Na^+]:[Cl^-]$ ratio. Ventilation did not increase in response to the acidosis, and was actually depressed in some birds. Pa_{CO_2} increased by 3.5 ± 1.5 Torr and Pa_{O_2} decreased by 4 ± 2 Torr over the 2 h experimental period in all animals. It is suggested that the extracellular acidosis due to hyperosmolality is accompanied by an intracellular alkalosis which may suppress chemoreceptor stimulation, resulting in no ventilatory increase. Hyposmolality had no effect on acid-base status or respiration.

Acid-base state, plasma osmolality (duck); Bird, Pekin duck; Plasma osmolality, acid-base state (duck); Plasma osmolality, ventilation (duck)

Changes in extracellular osmolality are often accompanied by changes in extracellular and intracellular water volumes, electrolyte concentrations, and acid-base parameters. Acute hyperosmolality, due to essentially non-penetrating solutes such as sucrose or NaCl, leads to a prolonged extracellular acidosis, which has been termed dilution acidosis (Sotos *et al.*, 1962; Makoff *et al.*, 1970). Dilution acidosis has been examined in mammals, and a similar plasma acidosis has been demonstrated in teleosts and amphibians in response to a hypertonic environment (Wilkes and McMahon, 1986; Walker *et al.*, 1990). The conventional explanation of this acidosis is based upon the dilution of plasma by the movement of intracellular water to the extracellular space in response to the osmotic gradient created by hypertonic infusion. Due to the continuous tissue production of CO_2 and its ready diffusion across cell membranes, the dilution would only measurably reduce bicarbonate concentration, resulting in a drop in extracellular pH (pHe). Bicarbonate generation and equilibration is believed to be inhibited during extracellular hyperosmolarity because of perturbation of intermediary cell meta-

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bolism (Chang *et al.*, 1975; Makoff *et al.*, 1970), although this is controversial. The development of the extracellular acidosis is accompanied by an intracellular alkalosis in muscle and erythrocytes (Adler *et al.*, 1975; Makoff *et al.*, 1970).

Dilution of the extracellular space by infusion of isotonic or hypotonic fluids generally does not result in a measurable acidemia (see Garella *et al.*, 1975), although rapid infusion of massive volumes of isotonic fluid can transiently increase the hydrogen ion concentration ($[H^+]$; Shires and Holman, 1948; Rosenbaum *et al.*, 1969). Infusion of freely diffusible solutes, such as urea, which do not cause a shift of water from the intracellular compartment or affect intracellular pH (pHi; Adler *et al.*, 1975), either induces extracellular acidosis (Sotos *et al.*, 1962) or has no effect on pHe (Winters *et al.*, 1964).

Normally, extracellular acid-base disturbances elicit compensatory changes in respiration. The degree of respiratory compensation has never been measured during dilution acidosis, but the literature shows anomalous changes in blood gases. In studies with rabbits and dogs, which were allowed to breathe normally during dilution acidosis, Pa_{CO_2} either decreased slightly or actually increased even after a fall in arterial pH (pHa) of 0.3 pH units, suggesting a lack of ventilatory compensation (Sotos *et al.*, 1962; Asano *et al.*, 1966). The same decrease in pHa caused by infusion of acids approximately doubled ventilation in rabbits (Maskrey and Trenchard, 1989; Nattie, 1983) and decreased Pa_{CO_2} 8 Torr (Nattie, 1983). The objectives of this study were to identify the ionic and other changes leading to acid-base disturbance during acute plasma osmolality changes, and to measure the degree of respiratory compensation.

Methods

Experimental preparation. Thirteen female Pekin ducks (*Anas platyrhynchos*), weighing 2.6–3.7 kg, were obtained from the Animal Care Facility of the University of British Columbia and housed indoors in wire cages with free access to food and water. At least 2 days before the experiments, a polyvinyl chloride (PVC VIII, Bolab, AZ) cannula was placed in the brachial artery and ulnar vein of each animal so that the vessels were connected in an exteriorized loop. The ends of the cannula were inserted approximately 5 cm into each vessel under local anaesthetic (Xylocaine 2%; Astra, Ontario). Pretreating the cannula with TD-MAC heparin (Polysciences, PA) and continuous flow through the cannula ensured its patency for several weeks. The animals were allowed at least 48 h to recover.

Measurements. Arterial blood samples (0.8 ml) were drawn anaerobically and immediately placed on ice to arrest erythrocyte metabolism (Scheid and Kawashiro, 1975). A 0.4 ml portion of the sample was used to measure blood gases (P_{CO_2} and P_{O_2}) and pH using a blood/gas analyzer (IL813; Instrumentation Laboratory, MA) maintained at duck body temperature (40 °C). The IL813 was calibrated before each sample using commercially prepared gas mixtures and pH standards. The remainder

of the blood sample was centrifuged and the plasma decanted and immediately frozen. Plasma Na^+ and K^+ concentrations ($[Na^+]$, $[K^+]$) were determined by flame photometry (IL943; Instrumentation Laboratory, MA), plasma Cl^- concentration ($[Cl^-]$) using a Buchler digital chloridometer (4–2500; Buchler Instruments, NJ) and plasma osmolality was measured with a vapor pressure osmometer (5500; Wescor, UT). Plasma lactate concentration was determined in two ducks during each of the three treatments in the hyperosmolality series by the method of Noll (1974). The arterial side of the cannula was also attached to a pressure transducer (Elcomatic 715A; Harvard Instruments, MA) calibrated by mercury manometer for measurement of mean arterial blood pressure and heart rate. Temperature was monitored in several ducks by rectal thermometer and did not change throughout the experiment.

Ventilation was measured by whole body plethysmography. Ventilatory changes in body volume were measured as changes in pressure due to air flow through a Fleisch 0 pneumotachograph connected to a port in the plethysmograph. The airflow signal was measured with a gas pressure transducer (Hewlett-Packard 275A) and integrated to yield tidal volume. The system was calibrated with known volumes of air delivered by hand-driven syringe. Ventilation ($\dot{V}_I$) was calculated as the product of tidal volume and respiratory frequency.

Protocol. Each duck was weighed and placed in a temperature-controlled body plethysmograph. Wings and legs were lightly restrained with filament tape. The head of the animal extended out of the plethysmograph through a dental dam collar and the catheters were led out of an air-tight hole. The animals were then left undisturbed for 45 min to allow them to adjust to their surroundings. A 1 h control period followed in which three blood samples were drawn for analysis, and measurements of resting ventilation, blood pressure and heart rate were taken every 10 min. Eight ducks were each infused with three different solutions (4 M NaCl, 2.4 M sucrose, or 0.15 M NaCl) in random order (as outlined below), with at least a 48 h recovery period between infusions.

Each animal received 7.5 mmol/kg body wt of 4 M sodium chloride (NaCl) infused over 15 min (total volume 5–6 ml). Since this infusion always stimulated salt gland secretion, plasma osmotic pressure was maintained for the duration of the experiment by subsequent infusion of a 540 mM NaCl solution at a rate of 0.1 ml/min to approximately match salt gland secretion. Blood samples were taken at 5, 10 and 15 min, then every 15 min for the remainder of the first hour, and every 30 min in the following hour. These 2 h are termed the infusion period throughout this paper. The total volume of blood removed during each experiment was 8.8 ml. Cardiovascular and respiratory parameters were measured every 5 min for the first hour and every 10 min during the second hour. Each animal also received an equivalent osmotic load of 2.4 M sucrose over approximately 25 min (total volume 18–22 ml), and 5–6 ml of isotonic saline (isotonic control infusion). A maintenance infusion was not required during these infusions since salt gland secretion was insignificant.

Three ducks were infused with the NaCl load under the same protocol to measure

the resultant change in extracellular fluid volume and hematocrit. Extracellular fluid volume was measured by injecting 5 μCi of ^{36}Cl in two animals and ^{22}Na in the third animal. After 30 min equilibration, 3 × 0.5 ml arterial blood samples were taken over 15 min and the 4 M NaCl was then infused. Blood samples were taken at 10-min intervals for 130 min. The blood was centrifuged and duplicate 100-μl plasma samples were transferred to 4 ml of Aquasol scintillation cocktail for measurement of ^{36}Cl on a liquid scintillation counter (LS9000, Beckman, CA), while samples were measured for ^{22}Na in a Minaxi 5000 gamma counter (Canberra-Packard, Ont.)

In five other ducks, plasma hyposmolality was induced by withdrawing arterial blood which was concurrently replaced with an equal volume of sterile, deionized water maintained in a water bath at 40 °C. The purpose of this experiment was to determine whether dilution without hyperosmolarity or extracellular fluid volume increases would affect acid-base balance. Each 10 ml aliquot of blood was immediately centrifuged, the plasma decanted and the red blood cells reinfused. The control period was identical to that described above, but during the experimental period, measurements were made and samples taken after every 40 ml of blood exchanged. The measurements were taken as described above, except blood gases were not analyzed. Red cell water content was measured by drying packed red blood cells at 105 °C to a constant weight.

Calculations and statistics. Data were analysed as the difference from the resting control value by analysis of variance and Tukey's post-hoc test, assuming significance when $P < 0.05$. pHa was converted to $[H^+]$ for statistical analysis. The bicarbonate concentration was calculated using the Henderson-Hasselbalch equation, assuming a solubility coefficient of 0.0282 mmol · L^{-1} · $mmHg^{-1}$ and a pK_1 of 6.090 (Helbacka *et al.*, 1964). [SID] was calculated as $[SID] = ([Na^+] + [K^+]) - ([Cl^-] + [lactate^-])$. All data are shown as differences (mean ± S.E.) from the mean resting value established in the 1 h control period before each infusion. Data from the NaCl and sucrose infusion experiments are compared to the isotonic control infusion experiment.

Results

Infusion of 4 M NaCl caused a significant mean increase in extracellular fluid volume of 10 ± 5%. The expansion was complete 30 min after the start of infusion and was maintained for the rest of the sampling period. This extracellular fluid volume expansion must have been due to the movement of intracellular water since the volume of the NaCl infusate never exceeded 1% of extracellular fluid volume. Resting hematocrit was 39 ± 4% and decreased 4 ± 2% with the infusion.

There were no significant changes in plasma osmolality, $[Na^+]$ or $[Cl^-]$ during the control infusion period. Plasma osmolality increased by a maximum of 31 ± 1 and 27 ± 2 mosm/kg above control during the NaCl and sucrose infusions and remained significantly higher throughout the infusion period (fig. 1). Plasma $[Na^+]$ increased and

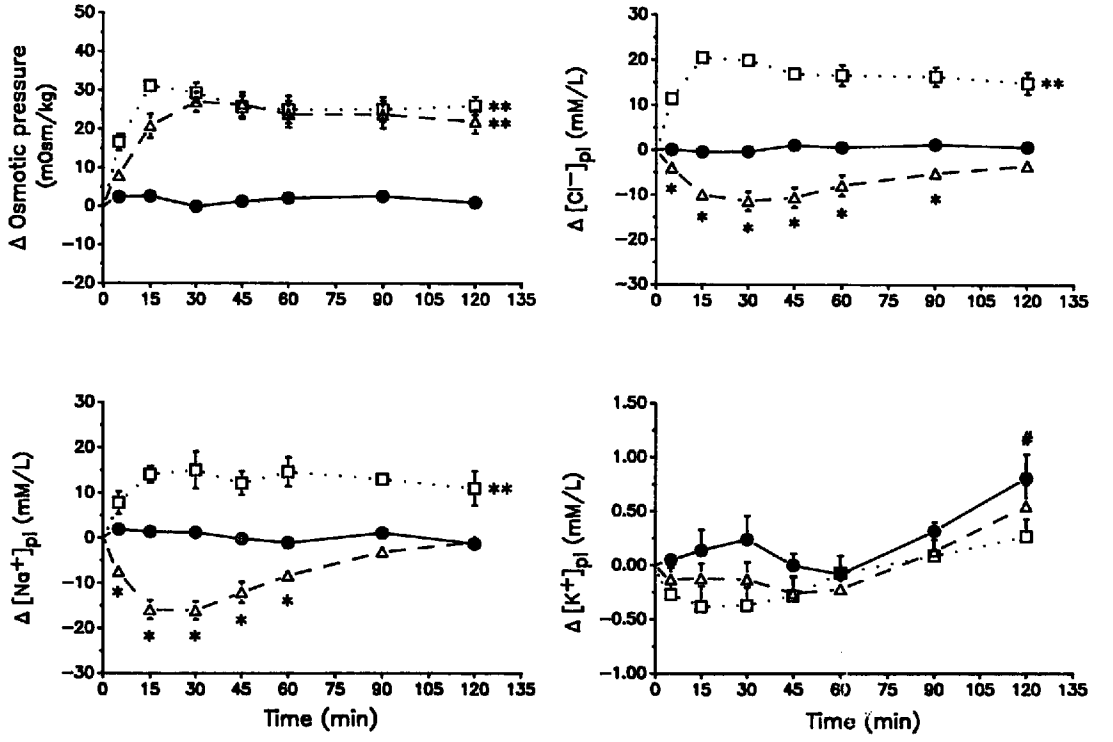

Fig. 1. Changes observed in osmotic pressure, plasma $[Na^+]$, $[Cl^-]$, and $[K^+]$ during control (isotonic saline), 4 M NaCl and 2.4 M sucrose infusions. Mean (± S.E.) differences from resting control values are shown. $n = 8$. ●, control; □, NaCl infusion; △, sucrose infusion. * Significantly different from rest ($P < 0.05$); ** significantly different from rest ($P < 0.05$) throughout infusion; # significantly different from 0 ($P < 0.05$) for all three treatments.

decreased a maximum of 15 ± 4 and 16 ± 2 meq./L with the NaCl and sucrose infusions, respectively ($P < 0.05$). However, plasma $[Cl^-]$ increased a maximum of 21 ± 1 meq./L and decreased a maximum of 11 ± 2 meq./L with the NaCl and sucrose infusions, respectively ($P < 0.05$). The increase in plasma $[Cl^-]$ remained significantly higher (5–6 meq./L) than the increase in plasma $[Na^+]$ throughout the NaCl infusion period and during the first hour of the sucrose infusion period. [SID] decreased significantly during the hypertonic infusions, primarily because of this change in the $[Na^+]:[Cl^-]$ ratio (table 1). Both plasma $[Na^+]$ and $[Cl^-]$ returned to control levels by the end of the sucrose infusion period. Plasma $[K^+]$ remained constant for the first 90 min and then increased slowly but significantly over the last 30 min during all three infusion periods. Plasma [lactate$^-$] did not change during any of the infusions (table 1).

With both hypertonic infusions, only minor changes in respiratory parameters were observed despite significant decreases in pHa. During the NaCl and sucrose infusion experiments, $\dot{V}_I$ did not change significantly from $\dot{V}_I$ during control infusion except for a transient 53% increase 15 min after the start of the NaCl infusion (fig. 2), due to small increases in both respiratory frequency and tidal volume. However, pHa decreased significantly within 5 min after the start of both the NaCl and sucrose infusions (fig. 2).

TABLE 1

Ionic, pHa and Pa_{CO_2} changes 30 min after the start of infusion, shown as the difference from resting control values (t = 0).

	Isotonic saline	NaCl	Sucrose
Organic phosphates (mosm/kg)	0.0 ± 1.4	29.5 ± 2.6*	27.0 ± 2.5*
	(280 ± 6)	(282 ± 4)	(283 ± 5)
Na^+ (meq./L)	1.0 ± 1.6	15.0 ± 4.1*	− 16.0 ± 2.0*
	(147 ± 2)	(148 ± 5)	(148 ± 4)
K^+ (meq./L)	0.2 ± 0.2	− 0.4 ± 0.2	− 0.1 ± 0.2
	(2.4 ± 0.4)	(2.6 ± 0.6)	(2.5 ± 0.4)
Cl^- (meq./L)	0.0 ± 0.5	20.0 ± 1.2*	− 11.0 ± 2.1*
	(108 ± 2)	(108 ± 4)	(111 ± 3)
$Lactate^-$ (mmol/L)	− 0.1[a]	0.8[a]	0.2[a]
	(2.0)	(2.5)	(2.0)
SID	1.9 ± 4.1	− 6.5 ± 7.4*	− 5.1 ± 2.7*
	(43 ± 4)	(42 ± 10)	(41 ± 5)
pHa	0.00 ± 0.00	− 0.06 ± 0.01*	− 0.05 ± 0.01*
	(7.48 ± 0.03)	(7.48 ± 0.03)	(7.49 ± 0.03)
Pa_{CO_2} (Torr)	0.5 ± 0.7	2.0 ± 2.0	3.0 ± 1.6
	(29 ± 4)	(31 ± 3)	(31 ± 3)

n = 8; [a]n = 2; ( ) resting control values, mean ± S.E.
* Significantly different from isotonic saline (control).

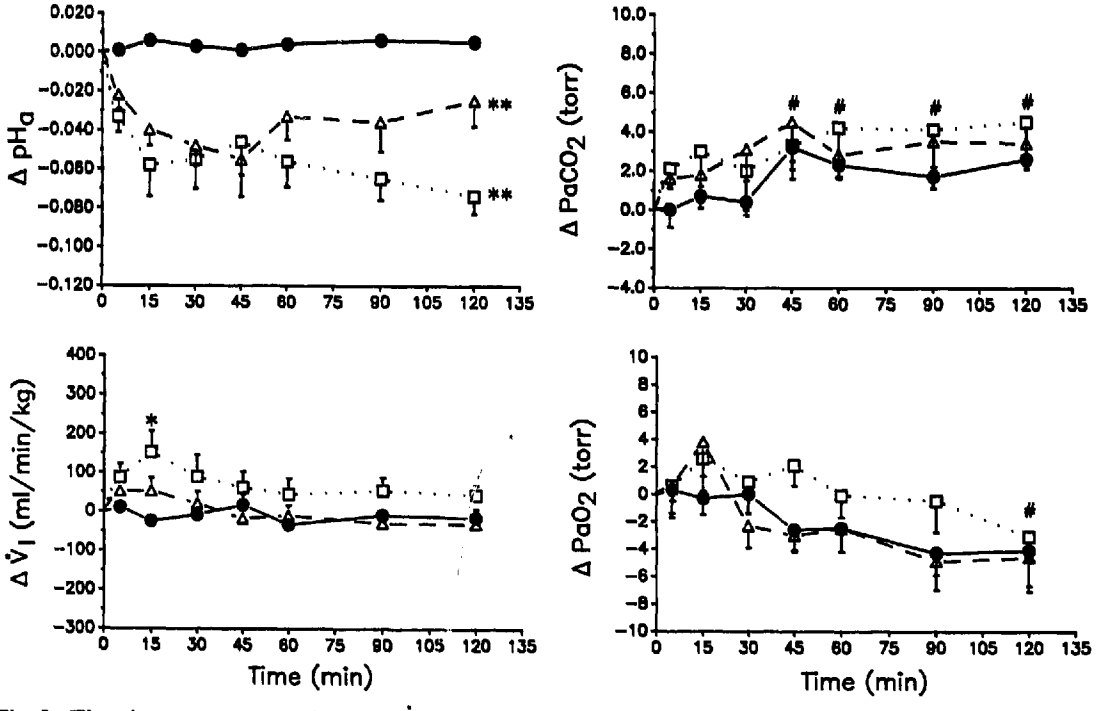

Fig. 2. The changes observed in pHa, $\dot{V}_I$, Pa_{CO_2} and Pa_{O_2} during control (isotonic saline), 4 M NaCl and 2.4 M sucrose infusions. Mean (± S.E.) differences from resting control values are shown. n = 8. ●, control; □, NaCl infusion; △, sucrose infusion. * Significantly different from rest ($P < 0.05$); ** significantly different from rest ($P < 0.05$) throughout infusion; # significantly different from 0 ($P < 0.05$) for all three treatments.

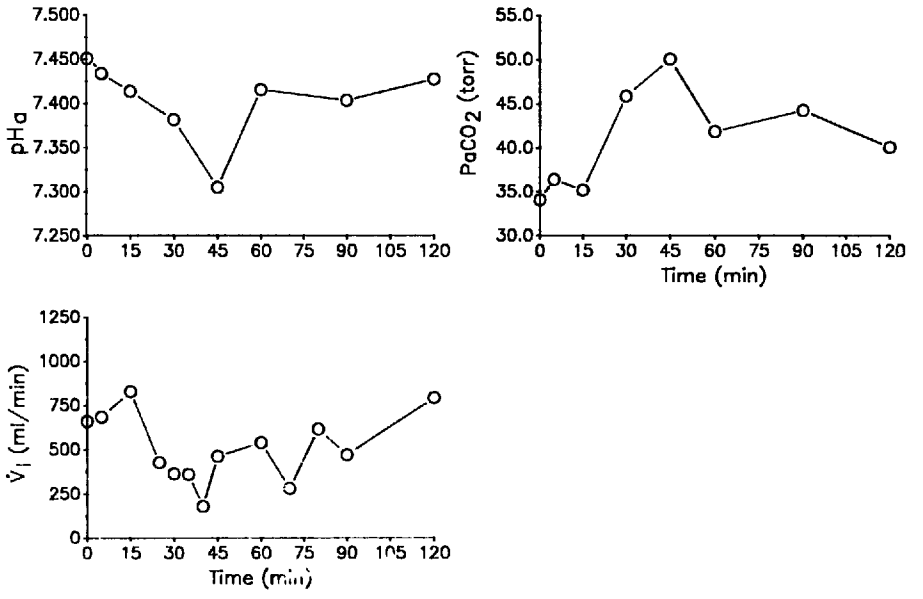

Fig. 3. The changes in pHa, $\dot{V}_I$, and Pa_{CO_2} measured in a single animal during infusion of 2.4 M sucrose (7.5 mM/kg).

In one animal, $\dot{V}_I$ decreased 45% by the end of the sucrose infusion and remained low for 90 min, despite a fall in pHa of 0.15 pH units and a rise in Pa_{CO_2} from 34 to 50 Torr (fig. 3). The reduction in $\dot{V}_I$ was almost entirely due to a decrease in respiratory frequency. Similar but less dramatic changes also occurred in two other sucrose infused animals. The pHa continued to decline throughout the NaCl experiment, but pHa began to recover 60 min after the start of the sucrose infusion. Neither $\dot{V}_I$ nor pHa changed significantly over the isotonic control infusion period. With the exception of the three sucrose-infused animals mentioned above, there was no change in the pattern of respiration, *i.e.* in tidal volume or respiratory frequency, during any of the infusions. There were no significant differences in Pa_{CO_2} or Pa_{O_2} among the three treatments at any time. Pa_{CO_2} increased significantly an average of 3.5 ± 1.5 Torr and Pa_{O_2} decreased significantly an average of 4 ± 2 Torr during all three infusion periods. Calculated bicarbonate concentration did not change significantly over the infusion periods. There were no significant changes in either mean arterial blood pressure or heart rate.

Replacement of plasma with deionized water did not elicit the changes in acid-base status caused by hyperosmolarity. There was a significant decrease in plasma osmolality of 21 ± 1 mosm/kg from the average control osmolality of 282 ± 3 mosm/kg. Plasma $[Na^+]$ decreased 8 ± 2 meq./L while plasma $[Cl^-]$ decreased 6 ± 2 meq./L ($P < 0.05$). There was no significant difference between the changes in plasma $[Na^+]$ and $[Cl^-]$ at the end of the experiment. There was no significant effect of hyposmolality on pHa, $\dot{V}_I$, hematocrit, $[K^+]$, red cell water content, or mean arterial blood pressure. Heart rate increased 60% by the end of the experimental period, but this change was not significant.

Discussion

Analysis of acid-base status. Since calculated plasma bicarbonate did not change significantly during the infusions, it was felt that Stewart's approach to acid-base balance (Stewart, 1983) could provide a useful analysis of the available data and insight into the cause of the acidosis. According to Stewart, in salt solutions such as blood and cerebrospinal fluid (CSF), $[H^+]$, $[OH^-]$, and $[HCO_3^-]$ are dependent variables whose concentrations are determined by the three independent variables of the solution, which are the strong ion difference ([SID]), total weak acid concentration, and P_{CO_2}. Despite inherent technical and conceptual problems, this analysis of acid-base balance can offer an informative approach to acid-base disturbances associated with large changes in electrolyte concentrations. The only significant change in the measured independent variables in this study in the first 45 min was a mean decrease of 5.8 meq./L in estimated [SID] during hyperosmolality (table 1). This decrease was almost entirely due to excess Cl^-, resulting in a decrease in the plasma $[Na^+]:[Cl^-]$ ratio, as has been measured in mammals (Sotos *et al.*, 1962; Makoff *et al.*, 1970; Anderson and Jennings, 1988). The decrease in [SID] was independent of whether plasma $[Na^+]$ and $[Cl^-]$ were increased (NaCl infusion) or decreased (sucrose infusion). There is no doubt that this estimate of [SID] contains error, but the change in [SID] is larger than the possible error, and it does account for most of the measured pH change as calculated by Stewart's approach. Total weak acid concentration (protein) was not measured, but since plasma protein concentration in ducks is very low, any change in protein concentration would be minor compared to the change in [SID]. There was a small increase in Pa_{CO_2} which occurred during all of the treatments, but this did not measurably affect pHa, at least in the control animals. Since $\dot{V}_I$ did not significantly decrease during the treatments, it is likely that the increase in Pa_{CO_2} was due to a decrease in parabronchial ventilation during the relatively long restraint period.

The cellular mechanism underlying the hyperchloremia during dilution acidosis is not known. Hyperosmolality presumably causes ion transport alterations which decrease the cation : anion ratio, resulting in acidemia. The acidosis is independent of whether the hyperosmolarity is produced with ionic or non-ionic substances. Based on the most recent studies listed below, the term dilution acidosis is an inappropriate description of the acidosis caused by hyperosmolality since neither dilution nor expansion of the extracellular space alone accounts for the observed acidosis. Hyposmolality with or without volume expansion has no measurable effect on pHa (Chang *et al.*, 1975; current study), and volume contraction alkalosis occurring in association with chloride deficiency can be corrected by replacing Cl^- without restoring volume (Luke and Galla, 1983). Further studies of the ion transport effects of hyperosmolality will be required in order to understand the nature of the acidosis.

Constancy of plasma $[K^+]$. It is noteworthy that plasma $[K^+]$ did not decrease significantly (although there was a trend toward a decrease) when extracellular fluid volume was expanded with either hypertonic solution, indicating that total K^+ increased

extracellularly. The K^+ shift is simultaneous with the decrease in pH (Makoff *et al.*, 1970; present study), and may be a passive readjustment to maintain a normal $[K^+]_i/[K^+]_e$ ratio. Other studies (Makoff *et al.*, 1970; Wathen *et al.*, 1982) have observed significant increases in extracellular $[K^+]$ with hypertonic saline and mannitol infusions, although the loads infused were significantly larger than in this study. Such a flux could change membrane potential in the direction of hyperpolarization, although the small magnitude of this efflux would render any membrane potential change insignificant.

Respiratory compensation. When evaluating the ventilatory response to an acidosis, the acid-base status of the extracellular fluid, intracellular fluid and the CSF (including brain interstitial fluid) must all be considered for their effect on chemoreceptor activity. In respiratory acidosis, arterial, CSF and intracellular pH all decrease (see Roos and Boron, 1981) and $\dot{V}_I$ increases significantly. During systemic metabolic acidosis, the resultant hyperventilation of spontaneously breathing animals can change CSF pH paradoxically because of the high permeability of the blood-CSF barrier to CO_2 and its relatively low permeability to ions (Robin *et al.*, 1958). Systemic pHe and pHi are decreased, but CSF pH and brain pHi may not be, resulting in some attenuation of the ventilatory response. However, during dilution acidosis, a concomitant, systemic, intracellular alkalosis develops (Adler *et al.*, 1975; Makoff *et al.*, 1970). Potential changes to CSF pH and brain pHi are unknown, but there is clearly no accompanying, compensatory increase in ventilation. We are unable to determine unequivocally the reason for the lack of respiratory compensation from this study, but two possibilities are worthy of discussion.

The first possible explanation is that stimulation of respiration may be due solely to central stimulation of chemoreceptors, and there simply may have been a lack of CSF pH change and, therefore, no central chemoreceptor stimulation during the dilution acidosis. However, in ducks, as in mammals, peripheral chemoreceptor contribution to respiration is approximately 20–40% (Milsom *et al.*, 1981). Infusion of lactic acid in Pekin ducks, causing a systemic acidosis comparable to that seen in the present study, immediately increased $\dot{V}_I$ 225% (Jones and Shimizu, unpubl.). Thus, the significant systemic acidosis caused by hyperosmolality should also have increased ventilation, even if central chemoreceptors were not stimulated.

A second possibility is that both peripheral and central chemoreceptors were stimulated by pHe changes, but there was concurrent development of a condition that inhibited normal chemoreceptor stimulation. This possibility would be valid even if only peripheral receptors were affected. A significant difference between respiratory/metabolic acidosis and dilution acidosis in mammals, is the development of intracellular alkalosis during the latter perturbation. Although pHi was not measured in this study, the similarity between dilution acidosis in mammals and in the duck makes the assumption of an intracellular alkalosis reasonable. Evidence for a repression of ventilation by hyperosmolality is best supported by the response of three ducks to the infusion of sucrose, as reported in the results of the present study. In the most extreme

case, neither a decrease in pHa of 0.15 units nor a 16 Torr increase in Pa_{CO_2} was capable of stimulating respiration either peripherally or centrally under the hyperosmolal conditions, and $\dot{V}_I$ actually decreased (fig. 3). This also tends to suggest that central receptors are affected by hyperosmolality since normally the large increase in Pa_{CO_2} would have decreased CSF pH and stimulated respiration. In ducks subjected to a period of submergence that resulted in a decrease in pHa of 0.2 pH units and an increase in Pa_{CO_2} from 32 to 57 Torr, $\dot{V}_I$ increased 350% upon emergence (Shimizu and Jones, 1987). In this case, both systemic and central pHe and pHi would be decreased. The possible effects of a concurrent extracellular acidosis and intracellular alkalosis on chemoreceptor threshold stimulation remain to be investigated. Some studies on the effects of osmolality changes on chemoreceptor activity, though, have been performed.

In cats, carotid body chemoreceptor activity increased when perfused *in vivo* with hyposmotic blood and decreased when perfused with blood made hyperosmotic with sucrose or NaCl (Gallego and Belmonte, 1979). The minimal osmolality variation necessary to obtain a detectable frequency change was 3–8% of the control. In the present study, plasma osmolality was increased 9–11% and decreased 7% of control values. However, superfused carotid bodies *in vitro* responded in exactly the opposite manner, with the authors concluding that the modifications in chemoreceptor activity *in vivo* were produced by changes in carotid body blood flow due to a direct effect of hypo- and hyperosmotic solutions on vascular muscle tone. However, this does not explain the *in vitro* results, unless presumably, the cardiovascular effects were much greater than the direct effects on the receptors. We did not observe any change in V_I during hyposmolality, and a depression in $\dot{V}_I$ in only a few animals during hyperosmolarity. It is possible that the stimulation of ventilation by the extracellular acidosis is approximately offset by a depression of ventilation due to an intracellular alkalosis during hyperosmolality, resulting in no ventilatory change. Gallego and Belmonte's protocol could easily have allowed development of an intracellular alkalosis without extracellular acidosis, since the carotid bodies were continuously flushed with fresh, hyperosmotic solution. Further work is required to fully explain these results. Hypertonic infusions have also been shown to inhibit thermal panting in mammals (Baker and Dawson, 1985), which again points to inhibitory effects of hyperosmolality on ventilation.

Summary. There has recently been some controversy over whether chemoreceptors respond to changes in intra- or extracellular pH, or both (Lassen, 1990; Nattie, 1990). The occurrence of a simultaneous extracellular acidosis and an intracellular alkalosis during acute hyperosmolality, coupled with no change in respiration, appears to offer a unique system for the further investigation of this issue.

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