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RENAL REABSORPTION OF BICARBONATE DURING ACUTE RESPIRATORY ALKALOSIS *

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It has long been recognized that acute respiratory alkalosis depresses the renal reabsorption of bicarbonate (1, 2), but the exact nature of the reabsorptive limit has not been defined. In the present studies, it has been demonstrated that acute reduction of plasma carbon dioxide tension depresses bicarbonate reabsorption to a rate which is essentially constant over a wide range of plasma bicarbonate concentrations. This pattern is analogous to that found in the normal but differs from that previously observed in acute respiratory acidosis, where reabsorption rises as a curvilinear function of plasma bicarbonate concentration (3).

MATERIALS AND METHODS

Twelve experiments were performed on female mongrel dogs anesthetized with sodium pentobarbital. Prior to each experiment, hydrochloric acid was infused in order to decrease the plasma bicarbonate concentration to roughly 10 mEq. per L. An endotracheal tube fitted with an inflatable balloon was introduced into the trachea and connected either to a calibrated volume displacement ventilator (Etsten Ventilator) or to a Mine Safety "Pneophore." Respiratory movements were inhibited by the administration of gallamine triethiodide (Flaxedil®) so that respiratory exchange could be controlled by the ventilator. Plasma pCO_2 was decreased to approximately 20 mm. Hg by hyperventilation while the dogs were breathing 100 per cent oxygen. When pCO_2 had been steadily maintained for at least one hour and adequate urine flow (2.2 to 5.8 ml. per minute) achieved by constant infusion of isotonic mannitol or isotonic saline solution, plasma bicarbonate concentration was progressively elevated by intravenous infusion of 0.142 to 0.535 M sodium bicarbonate to final values of approximately 35 to 45 mEq. per L. In most experiments it was necessary to increase ventilation slightly in order to prevent the rise in CO_2 tension that usually followed the rapid infusion of sodium bicarbonate. In most experiments there was a progressive reduction in blood pressure as blood pH approached 7.9 to 8.0. This hypotension was often accompanied by a drop in urine flow, as well as by hemoglobinemia and hemoglobinuria, and collection periods in which both hypotension and reduction in urine flow occurred were excluded from the study.

The clearance of exogenous creatinine was used as a measure of glomerular filtration rate. Urine was collected under mineral oil through an inlying catheter, and the bladder was emptied by manual compression at the beginning and at the end of each 10 minute collection period. Heparinized blood samples were drawn anaerobically from the femoral artery. Plasma and urine were analyzed for creatinine by a modification of the method of Bonsnes and Taussky (4) and for total CO_2 by the manometric method of Van Slyke. Blood and urine pH were measured anaerobically at 37° C. with a syringe type Cambridge Research Model pH meter. In a few experiments pH was measured at room temperature, using a factor of 0.01 unit per degrees C. for the correction to 37° C. Carbon dioxide tension in the blood and urine was calculated from the Henderson-Hasselbalch equation, using a pK′ for carbonic acid of 6.1 and a solubility factor equal to 0.0301 for plasma and 0.0309 for urine. Bicarbonate concentration was calculated as the difference between total CO_2 content and the dissolved carbon dioxide. Filtered bicarbonate was taken as the product of the filtration rate and the plasma bicarbonate concentration, corrected by a Donnan factor of 1.05.

RESULTS

Tables I through III show the data from three representative experiments. Plasma bicarbonate concentration was raised from initial levels of approximately 10 mEq. per L. to final values of 45, 39 and 35 mEq. per L., respectively. It is apparent that there was nearly complete reabsorption of bicarbonate during the initial periods when plasma bicarbonate concentration was 15 mEq. per L. or below. As plasma level was elevated to the range of 16 to 20 mEq. per L., frank bicarbonate excretion began and reabsorption promptly reached

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TABLE I

*Effect of acute sustained respiratory alkalosis on bicarbonate reabsorption during progressive elevation of plasma bicarbonate levels**

Time	Plasma		GFR*	Urine flow	HCO_3^-		
	pCO_2	HCO_3			Filtered	Excreted	Reabsorbed
min.	*mm. Hg*	*mEq./L.*	*ml./min.*	*ml./min.*	*mEq./min.*	*μEq./min.*	*mEq./100 ml. GF‡*
Dog No. 8, 11.0 Kg.							
−130	NaCl 0.154 M at 7 cc./min.						
−60	Dog breathing 100% O_2						
−2	$NaHCO_3$ 0.142 M at 7 cc./min.						
0–10	16	6.7	30.1	5.6	0.20	18	0.60
10–20	17	10.6	32.4	6.1	0.34	30	0.96
22	$NaHCO_3$ 0.240 M at 7 cc./min.						
25–35	17	13.3	34.2	6.1	0.46	37	1.24
35–45	17	16.9	36.7	6.3	0.62	60	1.53
47	$NaHCO_3$ 0.300 M at 7 cc./min.						
50–60	19	23.3	34.1	5.8	0.80	133	1.96
60–70	21	29.2	33.1	6.9	0.97	299	2.03
72	$NaHCO_3$ 0.350 M at 7 cc./min.						
75–85	22	33.5	29.0	7.4	0.97	396	1.98
85–95	22	36.9	30.7	8.4	1.13	547	1.90
97	$NaHCO_3$ 0.400 M at 7 cc./min.						
100–110	21	42.4	30.1	8.8	1.28	671	2.02
110–120	21	45.5	29.3	9.3	1.33	770	1.91

* Plasma bicarbonate values have been corrected by a Donnan factor of 1.05.
† Glomerular filtration rate.
‡ Glomerular filtrate.

a maximal constant rate of approximately 1.9 to 2.0 mEq. per 100 cc. of glomerular filtrate. In the three experiments pCO_2 ranged between 16 and 26 mm. Hg with an average value of approximately 20 mm. Hg.

The results of all 12 experiments are shown in Figure 1. On the abscissa is plasma bicarbonate concentration in milliequivalents per liter and on the ordinate bicarbonate reabsorption in mEq. per 100 cc., glomerular filtrate (GF). It can be seen that at plasma levels of 5 to 15 mEq. per L. there was nearly complete reabsorption of bicarbonate.

Frank excretion of bicarbonate usually began at plasma levels of 15 to 18 mEq. per L. At levels from 20 to 45 mEq. per L. reabsorption was virtually constant, averaging 1.9 mEq. per 100 cc. of glomerular filtrate. Variations in glomerular filtration rate during the course of the experiment were usually small and differed from the control values by no more than 20 per cent.

Plasma carbon dioxide tension for each experimental period is shown in the upper part of Figure 1. The extreme values for carbon dioxide tension were 13 and 26 mm. Hg, but the majority of the points lay between 17 and 22 mm. Hg.

DISCUSSION

The data indicate that during acute reduction of pCO_2 to approximately 20 mm. Hg, bicarbonate reabsorption is depressed to a rate which is independent of plasma bicarbonate concentration and which is essentially constant at an average value of 1.9 mEq. per 100 cc. of glomerular filtrate. In contrast, during acute respiratory acidosis the reabsorption of bicarbonate increases as a curvilinear function of plasma concentration (3), suggesting that the transport limits imposed by elevation and reduction of carbon dioxide tension are different in nature.

It is noteworthy that the reabsorptive pattern in acute respiratory alkalosis is similar to that of the normal, while the pattern in acute respiratory acidosis is analogous to that found with partial inhibition of carbonic anhydrase (Figure 2). The finding of two different reabsorptive patterns

TABLE II

*Effect of acute sustained respiratory alkalosis on bicarbonate reabsorption during progressive elevation of plasma bicarbonate levels**

Time	Plasma		GFR*	Urine flow	HCO_3^-		
	pCO_2	HCO_3			Filtered	Excreted	Reabsorbed
min.	*mm. Hg*	*mEq./L.*	*ml./min.*	*ml./min.*	*mEq./min.*	*μEq./min.*	*mEq./100 ml. GF*
Dog No. 12, 17.0 Kg.							
–95	Dog breathing 100% O_2						
–65	Mannitol 50 Gm./L. at 7 cc./min.						
–2	Mannitol 20 Gm./L., $NaHCO_3$ 0.166 M at 7 cc./min.						
0–10	25	11.6	62.6	3.2	0.73	1	1.16
10–20	25	12.3	66.7	2.7	0.82	1	1.23
20–30	24	12.9	67.7	2.2	0.87	1	1.28
30–40	24	13.5	61.0	1.8	0.82	1	1.34
42	$NaHCO_3$ 0.238 M at 7 cc./min.						
45–55	23	15.6	71.6	1.5	1.12	2	1.56
55–65	23	17.3	72.7	1.5	1.26	12	1.72
67	$NaHCO_3$ 0.300 M at 7 cc./min.						
70–80	24	19.7	72.3	1.5	1.42	38	1.91
80–90	24	21.5	86.6	1.9	1.86	120	2.01
92	$NaHCO_3$ 0.380 M at 7 cc./min.						
95–105	23	23.1	86.4	2.8	2.00	233	2.05
105–115	23	25.0	75.1	3.1	1.88	325	2.07
117	$NaHCO_3$ 0.452 M at 7 cc./min.						
120–130	23	26.9	77.5	4.0	2.09	469	2.09
130–140	23	28.8	71.3	5.1	2.05	621	2.00
142	$NaHCO_3$ 0.535 M at 7 cc./min.						
145–155	23	31.3	69.9	6.1	2.19	765	2.04
155–165	24	33.3	74.7	8.1	2.49	927	2.09
165–175	25	35.4	70.0	9.0	2.48	1,029	2.07
175–185	25	37.6	70.3	11.0	2.64	1,155	2.11
185–195	26	39.4	67.5	12.2	2.66	1,297	2.02

* See footnotes, Table I.

TABLE III

*Effect of acute sustained respiratory alkalosis on bicarbonate reabsorption during progressive elevation of plasma bicarbonate levels**

Time	Plasma		GFR*	Urine flow	HCO_3^-		
	pCO_2	HCO_3			Filtered	Excreted	Reabsorbed
min.	*mm. Hg*	*mEq./L.*	*ml./min.*	*ml./min.*	*mEq./min.*	*μEq./min.*	*mEq./100 ml. GF*
Dog No. 1, 16.4 Kg.							
–65	Dog breathing 100% O_2						
–30	Mannitol 50 Gm./L. at 7 cc./min.						
0–10	18	10.4	43.9	5.3	0.46	17	1.01
10–20	17	10.8	44.0	5.6	0.48	20	1.05
22	Mannitol 25 Gm./L., $NaHCO_3$ 0.166 M at 7 cc./min.						
40–50	19	14.6	43.6	5.9	0.64	39	1.38
50–60	17	16.1	49.3	6.4	0.79	55	1.49
62	$NaHCO_3$ 0.238 M at 7 cc./min.						
80–90	18	22.2	50.8	6.1	1.13	197	1.84
90–100	18	24.5	51.9	5.9	1.27	304	1.85
120	$NaHCO_3$ 0.300 M at 7 cc./min.						
120–130	21	33.0	47.3	6.0	1.56	635	1.96
130–140	21	35.2	44.5	5.8	1.57	711	1.93

* See footnotes, Table I.

might be accounted for if it is assumed, as has previously been suggested, that bicarbonate reabsorption takes place by means of a two step process involving a nonenzymatic and an enzymatic component, either of which can be rate-limiting (3, 5). According to this view, hydrogen ion secretion occurs as a first step in the reabsorptive mechanism and takes place independently of the enzymatic process within the tubular cell (3). A second step involving the enzyme, carbonic anhydrase, is concerned with the removal of hydroxyl ion released in the cell by the hydrogen secretory process. The specific role of the enzyme might be either to catalyze the reaction of $OH^- + CO_2 \overset{CA}{\rightleftarrows} HCO_3^-$, or alternatively to provide hydrogen ions for the neutralization of the OH^- ions by the reaction $H_2O + CO_2 \overset{CA}{\rightleftarrows} H_2CO_3$.

It has been suggested that the constant rate of reabsorption seen in the normal may be the consequence of a fixed maximal rate of hydrogen ion secretion which is determined by the carbon dioxide tension (perhaps through an effect on intracellular pH) (3). Thus, in the normal subject, this secretory step, rather than the enzymatic one, would be the slower of the two reactions leading to bicarbonate reabsorption and would be rate-limiting. The present study suggests that acute reduction in pCO_2 simply depresses the rate of hydrogen ion secretion and, therefore, of bicarbonate reabsorption to a new constant value. On the other hand, it has been postulated that, in acute respiratory acidosis or with partial inhibition of carbonic anhydrase, the rate of hydrogen ion secretion is high relative to enzyme activity and that the enzymatic step is rate-limiting. The evidence favoring

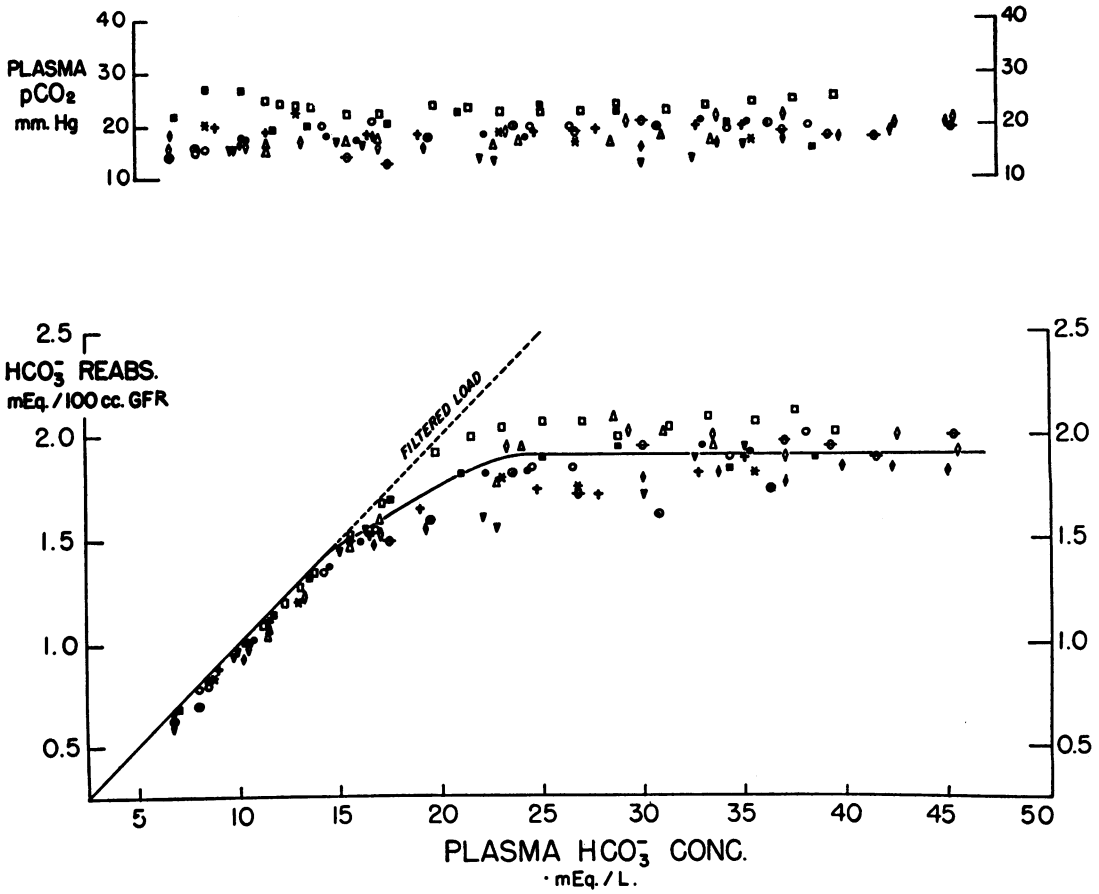

FIG. 1. EFFECT OF ACUTE SUSTAINED RESPIRATORY ALKALOSIS ON BICARBONATE REABSORPTION DURING PROGRESSIVE ELEVATION OF PLASMA BICARBONATE CONCENTRATION

The values for plasma bicarbonate have been corrected by a Donnan factor of 1.05.

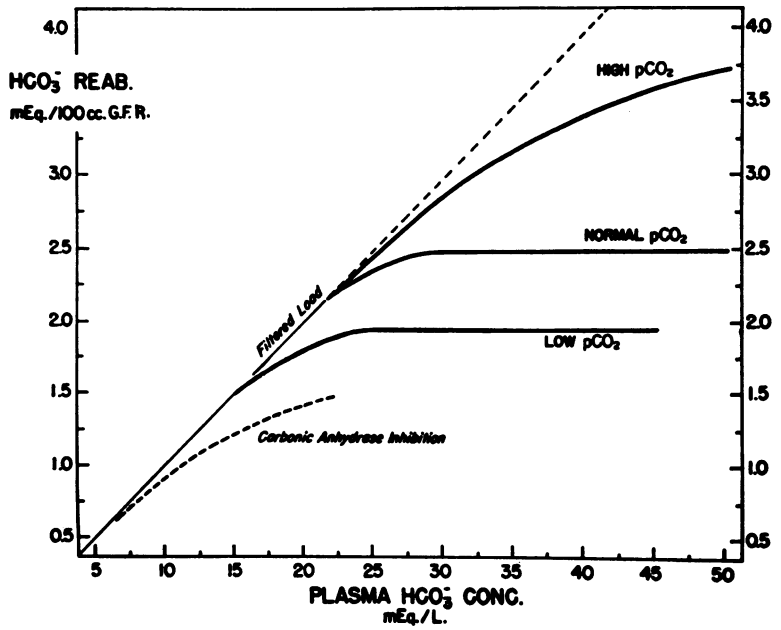

FIG. 2. DIAGRAM OF THE RELATIONSHIP BETWEEN PLASMA BICARBONATE CONCENTRATION AND REABSORPTIVE RATE WITH HIGH, NORMAL AND LOW PLASMA CARBON DIOXIDE TENSIONS AND WITH PARTIAL INHIBITION OF CARBONIC ANHYDRASE

this hypothesis has been discussed in detail elsewhere (3, 5). Regardless of these theoretical considerations, it seems clear that the pattern of the bicarbonate reabsorptive process may vary significantly under various experimental conditions.

SUMMARY

Renal reabsorption of bicarbonate was studied during acute, sustained respiratory alkalosis while plasma bicarbonate concentration was progressively elevated from approximately 10 mEq. per L. to final values ranging between 35 and 45 mEq. per L. With plasma carbon dioxide tensions of approximately 20 mm. Hg, reabsorption was depressed to an essentially constant rate averaging 1.9 mEq. per 100 cc. of glomerular filtrate. These data suggest that in the patient with acute respiratory alkalosis, as in the normal subject, carbon dioxide tension directly determines a fixed limit for bicarbonate reabsorption. This pattern contrasts with that seen in acute respiratory acidosis and with partial inhibition of carbonic anhydrase, where reabsorption rises as a curvilinear function of plasma bicarbonate concentration.

REFERENCES

1. Davies, H. W., Haldane, J. B. S., and Kennaway, E. L. Experiments on the regulation of the blood's alkalinity. J. Physiol. (Lond.) 1920, **54**, 32.
2. McCance, R. A., and Widdowson, E. M. The response of the kidney to an alkalosis during salt deficiency. Proc. roy. Soc. Med. 1936, **120**, 228.
3. Schwartz, W. B., Falbriard, A., and Lemieux, G. The kinetics of bicarbonate reabsorption during acute respiratory acidosis. J. clin. Invest. 1959, **38**, 939.
4. Bonsnes, R. W., and Taussky, H. H. On the colorimetric determination of creatinine by the Jaffé reaction. J. biol. Chem. 1945, **158**, 581.
5. Schwartz, W. B., Falbriard, A., and Relman, A. S. An analysis of bicarbonate reabsorption during partial inhibition of carbonic anhydrase. J. clin. Invest. 1958, **37**, 744.