THE EFFECT OF ACUTE ELEVATION OF THE PLASMA CHLORIDE CONCENTRATION ON THE RENAL EXCRETION OF BICARBONATE DURING ACUTE RESPIRATORY ACIDOSIS [1]

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It has been postulated recently that renal bicarbonate reabsorption is *entirely* dependent on the exchange of hydrogen ions, derived from the dissociation of carbonic acid within the cells of the renal tubule, for the fixed base of filtered bicarbonate in the tubular urine (1–3). According to this theory, an elevation of the CO_2 tension of the extracellular fluid results in an increase in the rate of bicarbonate reabsorption because it leads to an increase in the rate of hydrogen ion secretion.

Earlier studies, however, indicate that chloride reabsorption may interfere with bicarbonate reabsorption presumably because of competition between these two ions for some common transport mechanism in the proximal tubule (4). Since plasma pCO_2 was apparently within normal range in those experiments, it was thought of interest to study the effect of hyperchloremia on bicarbonate reabsorption in the presence of an elevated extracellular pCO_2.

Our results indicate that under these circumstances the rate of bicarbonate reabsorption does not depend entirely on the CO_2 tension, but may, in part, depend upon the rate of chloride ion reabsorption.

METHODS

Normal adult mongrel female dogs were anesthetized by the intravenous administration of 0.46 to 0.62 mg. of sodium pentobarbital per kilogram of body weight. The trachea was cannulated with a "Y"-shaped glass tube, the two free arms of which served as inspiratory and expiratory airways by means of flutter valves. The animals breathed spontaneously throughout the entire experiment. The abdomen was opened by a midline incision and each ureter cannulated with a polyethylene tube. The abdomen was then closed by a continuous silk suture and the polyethylene tubes brought through the suture line, care being taken not to kink the ureters and tubes. Urine was collected directly under mineral oil contained in a graduated cylinder.

During the successive periods of study, the dog breathed first room air, then a mixture of CO_2 and air containing 10 per cent of CO_2.

The different solutions were administered at desired rates by means of a constant-speed Bowman pump via a cannulated brachial vein. As the operative procedure was begun, the animal was given intravenously within a 5 to 24-minute period 400 ml. of a 0.15 molar sodium bicarbonate solution containing 0.375 Gram per cent of creatinine. Then a sustaining infusion containing from 0.93 Gram per cent of $NaHCO_3$ to 1.175 Gram per cent of $NaHCO_3$ (0.11 to 0.14 molar solution) was administered at rates varying between 6.4 and 18.5 ml. per minute. This infusion also contained an amount of creatinine such that the dog received 15 mgm. of creatinine per minute. When the operative procedures were completed, a fifteen to thirty-minute equilibration period was allowed. Then control determinations were made, the animal breathing room air and receiving the sustaining infusion. The dog then inhaled the air-CO_2 mixture and after thirty minutes of administration of this mixture, a second set of determinations was made, the dog still receiving the same sustaining infusion as during the first set of determinations. Chloride loading was then accomplished by the rapid administration of a priming injection of 30 to 45 ml. of a 3.33 Gram per cent of sodium chloride solution. The sustaining infusion was then changed to one containing 1.68 Gram per cent to 2.3 Gram per cent of $NaHCO_3$ (0.2 M to 0.27 M) and 4.35 Gram per cent to 7.6 Gram per cent of NaCl. It was delivered at rates of from 3.2 to 6.4 ml. per minute. After thirty minutes of administration of this infusion, determinations were again made. In some experiments the first control period (room air breathing) was omitted. The exogenous creatinine clearance was taken as equal to the glomerular filtration rate (GFR).

Arterial blood samples were obtained at the midpoint of each clearance period from a needle inserted into a femoral artery. The blood was collected anaerobically and rendered incoagulable with heparin. The pH of the whole blood was determined immediately on a 0.5-ml.

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TABLE I

Effect of sodium chloride infusion on the excretion of chloride and bicarbonate during acute respiratory acidosis in the anesthetized dog

Expt. No.	Period	Urine flow ml./min.	GFR ml./min.	Plasma				Urine			Bicarbonate					Chloride	
				Cl^- mEq./L.	HCO_3^- mEq./L.	pH	pCO_2 mm. Hg	Cl^- mEq./L.	HCO_3^- mEq./L.	pH	Filtered μEq./min.	Excreted μEq./min.	Reabsorbed μEq./min.	Reabsorbed mEq. per L. of filtrate	Reabsorbate mEq./L.	Reabsorbed mEq. per L. of filtrate	Reabsorbate mEq./L.
	Air	2.0	52.8	102.8	34.2	7.53	43	7.0	183.6	7.90	1,897	367	1,530	29.0	30.1	107.7	111.9
1	CO_2	2.7	55.8	95.9	41.3	7.27	93	5.0	140.8	7.75	2,422	373	2,049	36.8	38.6	100.5	105.5
	CO_2+5% NaCl	9.4	50.3	127.0	40.1	7.25	95	98.0	68.0	7.41	2,119	636	1,483	29.5	36.2	115.2	141.7
	Air	2.08	36.3	98.0	39.3	7.46	57	3.0	155.8	7.77	1,499	323	1,177	32.5	34.4	103.0	108.9
2	CO_2	2.33	38.7	92.4	45.0	7.25	106	1.3	115.7	7.59	1,824	269	1,555	40.6	42.8	97.0	103.0
	CO_2+5% NaCl	9.47	37.3	127.3	44.7	7.20	120	104.0	63.0	7.25	1,756	597	1,150	30.9	41.4	107.0	143.7
	Air	4.81	61.6	101.2	35.0	7.49	48	24.8	85.9	7.70	2,259	410	1,849	30.0	32.7	105.0	113.6
3	CO_2	5.01	58.1	95.0	43.4	7.26	101	11.4	67.2	7.47	2,647	337	2,310	39.8	43.5	99.0	107.9
	CO_2+5% NaCl	15.4	52.4	143.0	44.6	7.25	117	113.6	46.9	7.19	2,450	722	1,728	33.0	46.7	117.0	165.5
	Air	4.0	76.8	102.3	32.3	7.46	47	57.3	124.1	7.81	2,601	480	2,121	27.5	29.1	104.3	110.1
4	CO_2	3.1	64.3	97.6	38.8	7.27	88	33.3	108.9	7.66	2,620	332	2,288	35.6	37.4	101.0	106.0
	CO_2+5% NaCl	16.2	63.8	132.7	39.7	7.24	96	117.3	49.3	7.30	2,655	795	1,861	29.2	39.1	109.9	149.5
	CO_2	2.3	85.7	105.0	34.5	7.24	84	37.5	165.9	7.70	3,097	377	2,720	31.8	32.6	108.8	111.7
5	CO_2+4.35% NaCl	11.5	102.4	122.9	34.8	7.21	90	131.5	91.6	7.49	3,741	1,049	2,697	26.4	29.7	114.2	128.7
	CO_2+4% NaCl +0.5% KCl	12.5	104.4	141.3	33.7	7.18	92	141.0	93.7	7.48	3,695	1,172	2,519	24.2	27.5	131.5	149.4
6	CO_2	9.0	47.9	89.0	48.9	7.41	80	1.6	74.2	7.64	2,458	668	1,790	37.4	46.1	93.2	114.8
	CO_2+5% NaCl	10.9	46.7	115.2	46.1	7.37	83	38.5	75.7	7.71	2,258	825	1,433	30.8	40.2	112.0	146.4
7	CO_2	3.6	36.2	81.9	54.5	7.38	97	0.9	115.2	7.65	2,068	413	1,652	45.8	50.9	85.9	95.4
	CO_2+5% NaCl	7.3	37.4	109.8	52.2	7.32	105	62.4	91.0	7.50	2,047	662	1,386	37.1	46.1	103.2	128.3
8	CO_2	5.66	53.6	87.0	46.3	7.32	94	3.0	99.6	7.60	2,602	564	1,988	38.1	42.6	91.1	98.7
	CO_2+5% NaCl	6.76	52.6	119.5	40.9	7.29	89	72.5	85.2	7.52	2,257	575	1,682	31.9	36.7	116.1	133.6
9	CO_2	4.44	47.0	85.8	48.4	7.43	75	8.9	148.6	7.67	2,385	660	1,725	36.7	40.5	89.1	98.5
	CO_2+7.6% NaCl	10.5	52.6	110.3	44.4	7.35	84	88.6	79.9	7.48	2,451	838	1,613	30.7	38.3	96.9	121.0
	Air	6.56	46.1	88.4	47.2	7.61	49	13.5	150.2	7.83	2,287	984	1,303	28.3	33.0	90.9	106.1
10	CO_2	7.67	43.1	80.5	57.7	7.42	92	5.5	124.2	7.69	2,609	951	1,658	38.6	46.9	83.5	102.5
	CO_2+5% NaCl	11.0	48.5	110.1	51.7	7.37	92	71.5	109.2	7.59	2,636	1,202	1,434	29.6	38.3	99.4	128.6

portion of the sample and the rest of the sample was delivered under mineral oil into a centrifuge tube and centrifuged. The plasma was then immediately analyzed for CO_2 content.

Creatinine was determined in diluted urine and protein free filtrates of plasma by the method of Kennedy, Hilton, and Berliner (5). Total CO_2 in plasma and urine was determined by the manometric extraction technique of Van Slyke and Neill (6). The pH of the whole blood and urine was determined anaerobically at room temperature with a Beckman model G pH meter equipped with a syringe-type glass electrode. A correction factor (7) of 0.014 pH units per degree of difference between room and body temperatures was used in the calculation of the pH. Concentrations of bicarbonate and dissolved CO_2 were calculated from the Henderson-Hasselbalch equation employing a pK′ of 6.1 for carbonic acid, and an α equal to 0.0301 for plasma and 0.0309 for urine. The concentrations of sodium and potassium in plasma and urine were determined with an internal standard flame photometer. Chloride concentration in the plasma was determined on protein-free filtrates of plasma according to the method of Schales and Schales (8). A modified Volhard titration method (9) was used in determining the chloride concentrations of urine. The amount of each ion filtered per minute was calculated by multiplying its plasma concentration by the glomerular filtration rate. A Donnan distribution factor of 0.95 for Na^+ and K^+ and 1.05 for Cl^- and HCO_3^- was employed in this calculation. The rate of excretion of each ion was calculated by multiplying its urine concentration by the urine flow. The rate of reabsorption of water or any ion was taken as the difference between its rate of filtration and its rate of excretion. To facilitate the analysis and the discussion of the results, the amount of a given ion reabsorbed per liter of glomerular filtrate was also calculated by dividing the rate of reabsorption of that ion expressed in mEq. per min. by the filtration rate expressed in ml. per min. The concentration of each ion in the volume of water reabsorbed or "reabsorbate" was calculated by dividing the rate of reabsorption of each ion (mEq. per min.) by the rate of water reabsorption (ml. per min.), the resultant concentration being expressed in terms of mEq. per L.

RESULTS

Ten experiments were performed on ten animals. The results are summarized in Table I and the protocol of one of these experiments is given in Table II. In four experiments (Nos. 1, 2, 3, and 4) the animals were studied, first, while breathing room air and receiving intravenously an infusion containing a 0.11 molar solution of sodium bicarbonate delivered at a rate of 6.4 ml. per minute, then while breathing the air-CO_2 mixture and receiving the same infusion, and finally while continuing to breath the same air-CO_2 mixture but receiving intravenously a 0.2 molar solution of $NaHCO_3$ containing 5 Gram per cent of NaCl. In one experiment (No. 5) the animal was studied initially while breathing the air-CO_2 mixture and receiving intravenously a 0.11 molar solution of

TABLE II

Experiment illustrating the effect of sodium chloride infusion on the excretion and reabsorption of bicarbonate during acute respiratory acidosis

Time	GFR	Urine flow	Reabsorbate volume	Plasma			Urine			Bicarbonate*				
					HCO_3^-	pCO_2		HCO_3^-	pCO_2	Filtered	Excreted	Reabsorbed	Reabsorbed per L. filt.	Conc. in reabsorbate
min.	*ml./min.*	*ml./min.*	*ml./min.*	pH	*mEq./L.*	*mm. Hg*	pH	*mEq./L.*	*mm. Hg*	*μEq./min.*	*μEq./min.*	*μEq./min.*	*mEq.*	*mEq./L.*
				Dog 10, ♀, 15.9 Kg., breathing room air										
0–8	prime: 400 ml. 0.375% Creatinine in 1.25% $NaHCO_3$													
8	Begin infusion: 0.081% Creatinine in 1.175% $NaHCO_3$ at 18.5 ml. per min.													
77–81	46.8	6.25	40.5	7.61	47.2	49	7.84	154.2	91	2,321	964	1,357	29.0	33.5
82–86	45.4	6.87	38.5	7.61	47.2	49	7.82	146.2	90	2,252	1,004	1,248	27.5	32.4
86	Begin inhale 10% CO_2 and 90% air for duration of experiment													
116–119	44.0	8.34	35.7	7.42	57.7	92	7.68	120.7	103	2,666	1,007	1,659	37.7	46.5
120–123	42.1	7.0	35.1	7.42	57.7	92	7.69	127.7	106	2,551	894	1,657	39.4	47.2
123.5	prime: 45 ml. of 3.33% NaCl													
124	Change infusion to: 0.278% Creatinine and 2.3% $NaHCO_3$ in 5% NaCl at 5.4 ml. per min.													
154–157	48.3	11.18	37.1	7.37	51.7	92	7.59	110.2	115	2,627	1,232	1,395	28.9	37.6
158–161	48.7	10.82	37.9	7.37	51.7	92	7.58	108.2	116	2,644	1,171	1,473	30.2	38.9

* See methods section for calculations of derived data.

$NaHCO_3$ administered at the rate of 6.4 ml. per minute. The chloride loading was then accomplished first by the administration of a 0.2 molar solution of $NaHCO_3$ containing 4.35 Gram per cent of NaCl at the same rate, then by changing the infusion to a 0.2 molar solution of $NaHCO_3$ containing 4.0 Gram per cent of NaCl and 0.5 Gram per cent of KCl delivered at the same rate of 6.4 ml. per min. Because the urine flow always rose sharply in these first five experiments when the hypertonic chloride infusion was given, an attempt was made to prevent this in the last five experiments (Nos. 6, 7, 8, 9, and 10) by administering a 0.11 to 0.14 molar solution of $NaHCO_3$ at higher rates, *i.e.*, 11 to 18.5 ml. per min. The chloride loading was then achieved by administering a 0.2 to 0.27 molar solution of $NaHCO_3$ containing 5 to 7.6 Gram per cent of NaCl at slower rates of 3.2 or 5.4 ml. per min. In four of these last five experiments (Nos. 6, 7, 8, and 9) the initial period of breathing room air was omitted.

In all experiments, during chloride loading, the amount of chloride filtered and the amount of chloride excreted in the urine both increased. Concomitantly, moreover, the rate of chloride reabsorption increased, as well as the concentration of chloride in the reabsorbate and the amount of chloride reabsorbed per liter of glomerular filtrate.

In all experiments, the load of filtered bicarbonate remained essentially unchanged during chloride loading, rising slightly in four experiments (Nos. 4, 5, 9, and 10) and decreasing slightly in six experiments (Nos. 1, 2, 3, 6, 7, and 8). In all experiments, however, whether the filtered bicarbonate slightly rose or decreased, the amount of HCO_3^- excreted in the urine increased during chloride loading and the amount of HCO_3^- reabsorbed per liter of glomerular filtrate decreased.

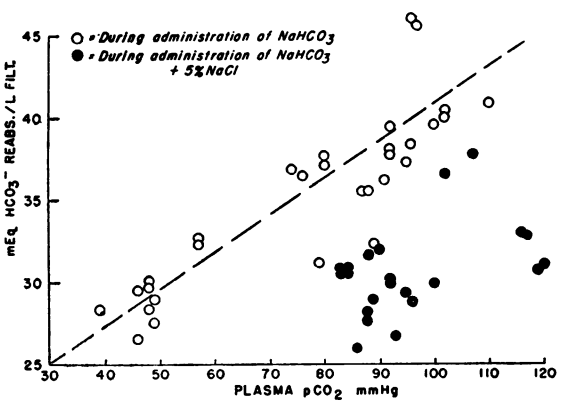

FIG. 1. RELATIONSHIP BETWEEN PLASMA CO_2 TENSION AND AMOUNT OF BICARBONATE REABSORBED PER LITER OF GLOMERULAR FILTRATE IN ACUTE RESPIRATORY ACIDOSIS BEFORE AND DURING INFUSION OF SODIUM CHLORIDE

As can be seen in Table I, bicarbonate reabsorption increased as the plasma pCO_2 rose, which confirms the work of other investigators (2, 3, 10). During chloride administration, however, there occurred a fall in the rate of bicarbonate reabsorption and a rise in the bicarbonate excretion, despite the persistence in the elevation of the plasma CO_2 tension. Figure 1 expresses graphically the relationship between the plasma pCO_2 and the amount of bicarbonate reabsorbed per liter of glomerular filtrate during the administration of the air-CO_2 mixture and the infusion of bicarbonate, both before and during chloride loading. The results observed before chloride loading are similar qualitatively and quantitatively to those reported by Brazeau and Gilman (2) as well as Dorman, Sullivan, and Pitts (3). The points representing such clearance periods are closely grouped along a straight line. However, the points representing the relationship between plasma pCO_2 and the amount of HCO_3^- reabsorbed per liter of glomerular filtrate during chloride loading are aberrant in their location from the first group of points. Indeed, during chloride administration, even at CO_2 tensions ranging between 90 and 100 mm. Hg, bicarbonate reabsorption falls to between 25 and 30 mEq. per liter of glomerular filtrate, values only found at CO_2 tensions of 35 to 50 mm. Hg before the chloride administration.

Plasma potassium levels were consistently between 1.8 and 2.8 mEq. per L. throughout all experiments with the exception of the final period of experiment No. 5 when the dog received KCl incorporated into the chloride infusion. Urine potassium excretion, with this latter period excepted, ranged between 35 and 104 μEq. per min. Both blood and urine values remained very steady throughout each experiment and potassium excretion did not appear to be influenced either by elevation of CO_2 tensions or by the combination of elevated pCO_2 and chloride loading.

DISCUSSION

The data presented above indicate that during acute respiratory acidosis, the renal excretion of bicarbonate was significantly increased by acute elevation of the plasma chloride concentration. Since the filtered load of bicarbonate remained essentially unchanged following the chloride infusions, the increased rate of bicarbonate excretion was entirely due to a reduction in the renal tubular reabsorption of bicarbonate. This occurred despite a tendency for extracellular CO_2 tension to increase during the chloride loading. There seem to be several theoretically possible explanations for this increase in HCO_3^- excretion: 1) Chloride loading interfered with H^+ secretion by the renal tubular cells, less HCO_3^- was converted to CO_2 and H_2O, more became available in the tubular fluid and was excreted as $NaHCO_3$; 2) Chloride loading did not interfere either actively or directly with the reabsorption of HCO_3^- but promoted an osmotic diuresis which caused more of the filtered HCO_3^- to be excreted; 3) The increase in chloride filtration and the subsequent increase in Cl^- reabsorption interfered directly with HCO_3^- reabsorption; or 4) HCO_3^- was actively secreted by the tubular cells.

It is unlikely that H^+ secretion was depressed by chloride loading in view of the fact that urine pH decreased and urine pCO_2 increased in most experiments following the chloride loading. The fall in urine pH *per se,* in alkaline urines such as these, could be explained solely by the fall in HCO_3^- concentration due to dilution (*i.e.,* osmotic diuresis) since the tubules are freely permeable to CO_2. However, the rise in urine CO_2 tension to values greater than that of the arterial plasma in the face of rising urine flows can best be explained on the basis of hydrogen ion addition to these urines resulting in titration of HCO_3^- to form additional carbonic acid. Such H^+ addition could come from distal tubular secretion of H^+ into a urine containing increasing amounts of HCO_3^-, or it could come from an increase in the excretion of acid buffers into this urine. Total buffer concentration was not measured in these experiments; but the concentration of one buffer (*i.e.,* creatinine) was measured and found to decrease. It does not seem unreasonable, therefore, to presume that the concentration of other buffers would likewise decrease as urine flow increased and hence the rise in urine pCO_2 appears to be the result of continued secretion of hydrogen ion into a highly alkaline urine. The decrease in HCO_3^- reabsorption following the chloride loading in the face of continued H^+ secretion must therefore be explained on the basis of some other mechanism.

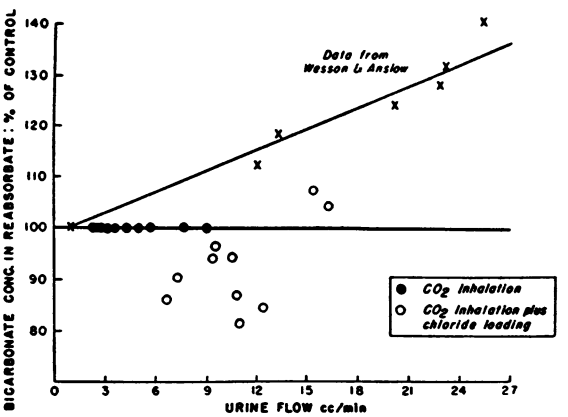

FIG. 2. PER CENT CHANGE IN BICARBONATE CONCENTRATION OF REABSORBATE PLOTTED AGAINST URINE FLOW

The points on the 100 per cent line represent control values observed during CO_2 inhalation. The open circles are the values obtained following the chloride loading, during continued CO_2 inhalation. The data from Wesson and Anslow (12) was obtained during mannitol diuresis under conditions of normal CO_2 tension.

It is difficult to hold that osmotic diuresis was responsible for the decreased reabsorption of bicarbonate because in 8 of 10 experiments there was a fall in the concentration of bicarbonate in the reabsorbate following the chloride loading. This occurred despite marked increases in urine flow and decreases in reabsorbate volume in four of these experiments (Nos. 1, 2, 5, and 9). If it is allowed that there is normally no limitation to the concentration of HCO_3^- in the reabsorbate one would expect that under a constant rate of HCO_3^- reabsorption (11) there would be an increase in HCO_3^- concentration of the reabsorbate as the urine volume increases and the volume of the reabsorbate falls. This has been shown by Wesson and Anslow (12) to occur during mannitol diuresis. In Figure 2 is plotted the per cent change in the bicarbonate concentration of the reabsorbate following chloride loading compared with the data of Wesson and Anslow (12) obtained under conditions of mannitol loading. During mannitol diu-

resis there is a progressive linear increase in the bicarbonate concentration of the reabsorbate as urine flow increases, whereas following chloride loading in most of our experiments there is a fall in the bicarbonate concentration of the reabsorbate as urine flow increases. Since it has also been shown that osmotic diuresis *per se* does not particularly increase the excretion of bicarbonate (13, 14) it is apparent that the increases in the excretion of bicarbonate and decreases in the reabsorption of bicarbonate following chloride loading are brought about by some other mechanism.

There remains the theoretical possibility that bicarbonate may have been secreted by the tubular cells and that such a secretion of HCO_3^- by the tubular cells may have been increased by chloride loading, thus accounting for the observed increase in excretion and apparent decrease in reabsorption of bicarbonate during chloride loading. It can only be stated in this regard that there is no direct experimental evidence that such a mechanism exists.

It appears then that during acute respiratory acidosis an increase in the amount of chloride reabsorbed interferes with the reabsorption of bicarbonate. This is in accord with the earlier observations made by Pitts and Lotspeich (4) on animals with presumably normal CO_2 tensions and is entirely consonant with the theory that there is competition between these two ions for a common reabsorptive transport mechanism. Indeed, it was originally suggested by these investigators that a dual process of bicarbonate reabsorption existed whereby most of the bicarbonate filtered at the glomerulus was reabsorbed by a specific anion transport in the proximal tubule. In this schema some of the bicarbonate ions not reabsorbed by the proximal tubule were reabsorbed in the distal tubule by a process involving exchange of H^+ ions originating within the tubular cells for Na^+ ions derived from the tubular urine.

It was later observed by Berliner (1) that following the administration of Diamox®, the amount of the additional bicarbonate excreted in the urine was too great to be accounted for solely by the abolition of the distal hydrogen ion secretory mechanism. Berliner therefore proposed that bicarbonate reabsorption throughout the *entire* renal tubule was dependent upon the hydrogen ion secretion mechanism. This concept was supported by the recent studies of Brazeau and Gilman (2) and Dorman, Sullivan, and Pitts (3). Working independently, these investigators noted that as the CO_2 tension of the extracellular fluid is raised, there is a concomitant linear increase in renal bicarbonate reabsorption. Since, presumably, H^+ secretion by the renal tubules increases with increasing pCO_2, they concluded that the increased rate of HCO_3^- reabsorption could best be explained by the assumption that the reabsorptive mechanism was entirely dependent upon the exchange of H^+ ions derived from carbonic acid in the tubular cells for fixed base of filtered bicarbonate in the tubular urine.

This $H^+ - B^+$ exchange theory of the renal regulation of bicarbonate excretion however, does not adequately account for the reciprocal changes in the plasma HCO_3^- levels which accompany rises and falls in plasma Cl^- levels. Indeed, it was this phenomenon, together with the observation that increased Cl^- loading facilitated HCO_3^- excretion, which led Pitts and Lotspeich (4) to postulate specific ionic reabsorption of bicarbonate by the proximal tubule. Moreover, although the theory adequately explains the renal compensations in acute and chronic respiratory acidosis and alkalosis, it does not satisfactorily explain the renal compensations for metabolic acidosis and alkalosis, as pointed out by Brazeau and Gilman (2) as well as by Relman, Etsten, and Schwartz (10). One wonders if the main weakness of the theory does not lie in the assumption that HCO_3^- reabsorption can only occur through H^+ ion secretion. If this were so, one would expect that the urine pH would decrease as HCO_3^- reabsorption increases. That this is not the case is apparent from analysis of the data published to date (1–3). In fact, in experiments on dogs with chronic respiratory acidosis (15), it can be seen that as HCO_3^- reabsorption increased with increasing plasma pH levels, the urine became more alkaline and the pCO_2 of the urine declined.

It would appear then, that bicarbonate reabsorption is not entirely due to $H^+ - B^+$ exchange since it is possible to elicit a reciprocal relationship between chloride and bicarbonate reabsorption and to induce an increase in the reabsorption of one of these ions and a decrease in the reabsorption of the other while the pCO_2 remains constant. Furthermore, this reciprocal relationship

was observed in the presence of two factors which have been demonstrated both to reduce chloride reabsorption and to increase bicarbonate reabsorption, *i.e.*, (a) high plasma CO_2 tensions (2, 3), and (b) a probable state of potassium depletion (16, 17) resulting from the infusion of large amounts of sodium bicarbonate, at least as judged by the low plasma potassium levels.

SUMMARY AND CONCLUSIONS

1. In acute experiments performed on anesthetized dogs, it has been observed that:

A. In acute respiratory acidosis, the amount of bicarbonate excreted in the urine decreases and the amount of bicarbonate reabsorbed increases, whereas the amount of chloride excreted decreases and the amount of chloride reabsorbed decreases;

B. The administration of chloride during respiratory acidosis results in an increase in the amount of bicarbonate excreted and a decrease in the amount of bicarbonate reabsorbed.

2. The phenomena observed suggest the possibility that at least part of the reabsorption of bicarbonate is ionic and not dependent upon hydrogen ion secretion by the tubule. This part of the bicarbonate reabsorption is affected by the reabsorption of chloride in such a manner as to suggest competition between the chloride and bicarbonate ions for a common reabsorptive transport mechanism in the tubule.

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