Effect of Glucose Diuresis on Renal Excretion of Bicarbonate.*† (20999)

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Glucose diuresis in the normal subject greatly augments the urinary excretion of sodium (1-3). Under conditions where the main urinary anion is chloride, the loss of sodium is "covered" chiefly by a corresponding loss of chloride. The fact that there is no significant change in the excretion of bicarbonate (in spite of the fact that this anion makes up about one-sixth of the anions of the glomerular filtrate) might be explained, within the present framework of hypotheses concerning renal function, in several ways: 1) The proximal tubular diuresis does not affect the proximal tubular reabsorption of bicarbonate (*i.e.*, there is no "velocity effect"(4,5) for bicarbonate)—perhaps because of rigid control of this reabsorption by internal regulatory factors such as the serum pCO_2(6). 2) The proximal tubular diuresis increases the delivery of bicarbonate to the distal tubules, but not sufficiently to exceed a proposed distal Tm for bicarbonate(7).

In the present experiments, we studied the effect of glucose diuresis on the excretion of bicarbonate under conditions where bicarbonate made up a large proportion of the urinary anion excretion, and where, therefore, any hypothetical distal Tm for bicarbonate might well have been exceeded.

Procedure. The subjects of this experiment were 3 normal male medical students. Fluids and food were withheld from 10 o'clock on the previous evening. Each study began at approximately 8 A.M. and continued for the next 4½ to 5½ hours. The subjects remained in the recumbent position, except during the collection of urine, which was voided spontaneously in the erect posture. An infusion of 1.4% $NaHCO_3$ was administered at the rate of 1500 cc during the first 1½ hours, followed by 300 cc/hr thereafter. When the excretion of water and chloride had stabilized, (about 2 hr) 750-1000 cc of a 25% solution of glucose in water were infused, in about 30-40 min. Glomerular filtration rates were estimated from the clearance of inulin administered as a constant infusion in one experiment (R. P.), and from the clearance of endogenous creatinine in the others (J. M. and R. K.). Venous blood was drawn anaerobically with minimal stasis at intervals indicated in Table I. Urine was collected by voiding in the erect posture into a specially constructed cup. Urine from the bottom of the cup was collected over mercury, whereas the remainder overflowed into a graduate. In this way exposure to air of the urine collected over mercury was minimized. In 2 experiments, analyses for CO_2 content and pH of urine specimens collected by this method, agreed within 7% with analyses of urine specimens of the same voidings collected directly under oil. *Chemical methods and calculations.* Chemical methods were standard(8,9), or previously defined(10), except that the CO_2 content of the urine was directly determined on urine by the same method used for serum. The pH of serum and urine was determined with a Beckman pH-meter. The pCO_2 of the serum and urine was calculated from the determined values for total CO_2 content and pH, using the Henderson-Hasselbach equation, and the values of 6.1 for pKa′ and of 0.51 for α, for both serum and urine.

Results. Table I summarizes the detailed experimental data of each experiment. Fig. 1 presents the urinary electrolyte patterns of

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TABLE I. Experimental Data. Glucose diuresis during sodium bicarbonate infusions.

	Period*	Time, min.	Excretion rates, urine: H_2O, cc/min.	Na, μeq./min.	Cl, μeq./min.	K, μeq./min.	HCO_3, μeq./min.	pCO_2, mmHg	Glucose, μm/min.	Concentrations in serum†: Na, meq./l	Cl, meq./l	K, meq./l	CO_2, meq./l	Glucose, mm/l	pCO_2, mmHg	GFR,‡ cc/min.
(1) J.M.	A	68	7.9	713	212	221	670	96		(141)	(103)	(4.1)	(27.2)		(48)	186
91.8 K	B	30	4.4	504	97	178	537	103								194
	C**	35	4.9	477	122	131	382	111	558	142	97.1	4.1	33.7	4.8	47	214
	D	35	11.1	600	268	71	302	77	2020	140	93.4	4.1	32.8	23.9	47	258
	E	35	6.2	628	214	50	350	85	818	141	97.3	3.4	33.2	7.7	48	220
	F	41	3.7	582	84	103	503	95	115	143	93.7	3.8	35.1	1.4	51	195
(2) R.P.	A	41	3.8	982	282	177	760	86		(144)	(105)	(3.8)	(27.6)		(41)	167
73 K	B	35	4.0	1052	306	155	770	107								
	C**	28	16.9	1790	895	135	728	98	2930	144	101	3.5	33.9	4.7	42	203
	D	18	21.0	1615	1112	63	483	54	4710	130	86.6	3.1	32.3	56.1	46	175
	E	14	17.6	1565	915	70	440	50	3540	137	94.6	3.4	33.0	28.7	44	
	F	42	8.3	1270	514	90	730	89	1230	139	97.4	3.4	33.8	12.5	42	223
(3) R.K.	A	90	3.5	743	221	22	665	147		(147)	(107)	(4.2)	(28.2)		(48)	153
93.6 K	B	43	3.2	745	181	19	695	137								168
	C**	33	13.2	905	526	127	420	52	3170	148	103	3.7	33.7	4.5	47	207
	D	37	19.6	1190	827	61	350	73	4350	130	91.6	3.9	31.3	59.6	51	224
	E	24	8.3	832	414	55	391	88	1770	141	97.2	3.7	32.1	28.2	52	186
	F	26	4.0	640	203	82	436	108	548	146	100	3.7	34.5	10.2	52	162

* Each period is composed of 1-2 consecutive sub-periods corresponding to individual periods of urine collection. Period A followed 2-4 periods during which urine flow and rate of chloride excretion were being stabilized under influence of maintenance infusion of sodium bicarbonate (see Procedure). Glucose infusions were administered during periods designated by (**). 1000 cc of 25% sol. were given to R.P. and R.K.; 750 cc of 25% sol. to J.M.

† Serum values at *beginning* of corresponding urinary periods, except that *underlined values* were at *end* of corresponding urinary periods, and *values in parentheses* were before infusions of sodium bicarbonate.

‡ Values of glomerular filtration are based on clearance of endogenous creatinine in subjects J.M. and R.K., and of inulin in subject R.P. Simultaneous values for inulin clearance in periods C and D of exp. No. 3 (subject R.K.) were 193 cc/min. and 232 cc/min. respectively.

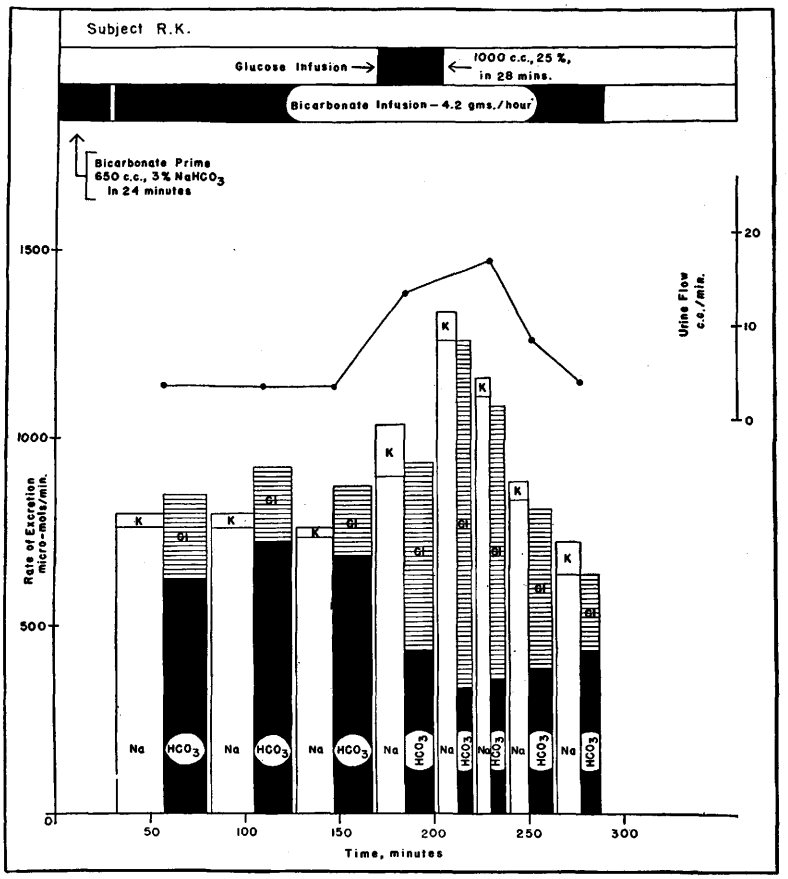

FIG. 1. Urine flows and rates of excretion of individual ions in consecutive periods of urine collection. Rate of excretion of potassium is *added* to that of sodium, rate of excretion of chloride, to that of bicarbonate.

consecutive periods of one representative experiment.

Changes in serum electrolytes. The infusions of sodium bicarbonate increased the serum bicarbonate, decreased the serum chloride, but did not change significantly the serum sodium or potassium. In the 2 experiments in which 250 g of glucose was infused (R.P. and R.K.) the serum sodium and chloride decreased as a result of the cellular dehydration caused by hypertonic glucose(3). The serum bicarbonate and pH also fell and the serum pCO_2 increased slightly. Changes in these serum values were not clearly significant in subject J. M. in whom only 188 g of glucose was infused. The serum potassium was essentially unchanged in all experiments.

Changes of urine flow and of excretion of sodium, chloride and bicarbonate during and following glucose infusion are indicated in Fig. 1 for experiment R. K. They were closely similar in the 2 other experiments (Table I). In all experiments, the excretion of chloride was increased out of proportion to that of sodium. Changes of urinary pCO_2 followed those of total CO_2 content (or bicarbonate). The excretion of potassium decreased with glycosuria in 2 experiments (in which it was initially high) and increased in the third (in which it was initially low).

Glomerular filtration was transiently increased by the glucose infusions in the two experiments in which it was measured. As a result, the filtered bicarbonate was either unchanged (subject R. P.), or increased (R. K.) at the time when the excretion of bicarbonate declined.

Discussion. In the present experiments, the

excretion of bicarbonate decreased during osmotic (glucose) diuresis, even though, in 2 cases, the filtered bicarbonate was increased or unchanged, and although the increased excretion of water, sodium and chloride in all cases indicated the probable occurrence of proximal tubular diuresis(1-3). The results do not indicate whether proximal tubular diuresis may have decreased the proximal reabsorption of bicarbonate. If this occurred, however, it was superseded by other factors tending to increase the net tubular reabsorption of bicarbonate, since the urinary bicarbonate was diminished, while the filtered bicarbonate was increased or unchanged. One such factor may have been the slight (barely significant) increase in the serum pCO_2 which occurred in the two most definitive experiments (R. P. and R. K.). Recent workers have offered convincing evidence of a direct relationship between bicarbonate reabsorption and the serum pCO_2(6).

Summary. Under conditions favoring the excretion of bicarbonate, the rate of excretion of bicarbonate decreased, while the rates of excretion of other electrolytes increased, during an osmotic (glucose) diuresis. Possible explanations for this observation are discussed in relation to present concepts of osmotic diuresis and of the excretion of bicarbonate.

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Prevention of Innominate Bone Separation During Pregnancy in the Mouse.* (21000)

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Gardner and Van Heuverswyn(1) injected large amounts of testosterone propionate into pregnant mice and found that it inhibited pregnancy pelvic changes such as the formation of an interpubic ligament and increased flexibility of the sacroiliac joints. Since the interpubic ligament did not form, the separation of the innominate bones at the symphysis failed to occur. This prevented the marked increase in size of the birth canal which normally occurs during pregnancy. Two mice died with macerated fetuses in the cervix and upper vagina, 4 gave birth to macerated fetuses, and 4 gave birth to living young. These results indicate that in some mice one or more of the pregnancy pelvic changes are necessary for normal parturition to occur. In a previous experiment(2) the interpubic tissue in Brown-belt strain, virgin mice consisted chiefly of cartilage. During the first pregnancy this cartilage was replaced by an interpubic ligament. The latter produced a 4.3 mm average separation of the innominate bones at the symphysis. The present experiment was performed to determine the necessity of innominate bone separation at the symphysis during pregnancy.

Materials and methods. Twenty virgin mice of the Brown-belt strain were used. At puberty their innominate bones were tied together at the pubic symphysis in order to prevent their separation during pregnancy.

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