ELECTROLYTE EXCRETION IN RESPIRATORY FAILURE

BY

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Patients with chronic emphysema and pulmonary insufficiency commonly arrive at a new steady state in which the carbon dioxide pressure in the blood is increased and the pH lowered; this situation can be prolonged for months during which these patients must be in acid-base balance. This equilibrated state of mild respiratory acidosis is, at times, upset by complicating pneumonitis which aggravates the acidosis; this later returns to its previous mild degree, and observations have been made in patients recovering from an acute episode superimposed on chronic lung disease. It was hoped that changes in renal function would be more easily apparent when the degree of acidosis was changing than when it was in equilibrium. In some of these patients the effect of a mild superimposed metabolic acidosis induced by ammonium chloride was observed.

Methods

The 10 patients studied were all men, suffering from chronic bronchitis. Their ages are listed in Table I. Cases 1-7 and 10 were admitted in congestive heart failure, Case 8 in status asthmaticus, and Case 9 with an acute pneumothorax. Cases 1, 4, 5, 6, 8, and 9 had obvious bronchospasm. Case 1 was also hypertensive (blood pressure 220/115 mm. Hg). Most of the patients were being given antibiotics for superimposed pneumonitis and were receiving treatment for congestive heart failure which included low sodium diet and in all but one (Case 8) mercurial diuretics. The general treatment of these patients with antibiotics and with diuretic agents was not altered, and some of the observations may be confused by these facts. Another difficulty has been that of accurately collecting specimens in ill patients, so the results have been "corrected" on the assumption that creatinin excretion did not change in periods of a few hours.

All the patients were judged to be retaining carbon dioxide, with plasma bicarbonate levels either frankly elevated or in the upper normal range (see Table I), and most of them were cyanotic on admission. At the time when observations were made, all patients were improving clinically, but the plasma electrolytes were

still abnormal. Cases 3-10 were given ammonium chloride (NH_4Cl) by mouth in a dose of 0.1 g./kg. body weight. An hour later the bladder was emptied, and thereafter, from four to five hours, urine was collected for analysis (Davies and Wrong, 1957). In one patient (Case 7), because of difficulty in emptying the bladder, the period of observation after NH_4Cl had been given had to be extended to 16 hours. In Case 9 the NH_4Cl load was given on two occasions. Plasma and urine samples were analysed in all patients by standard methods in this laboratory (Black and Mills, 1954); the sum of titratable acidity (T.A.), plus ammonium (NH_4^+) less bicarbonate (HCO_3^-), i.e., hydron (H^+) excretion was calculated as $(\text{NH}_4^+ + \text{T.A.}) - \text{HCO}_3^-$ (Albright and Reifstein, 1948). Blood pH was measured in Cases 6-10 by an electrometric method at room temperature and corrected to 37°.

Results

Table I shows base line plasma electrolytes. Plasma Na concentrations are generally rather low, K concentrations normal, Cl definitely low, and bicarbonate increased. Possible factors in

TABLE I
BASE LINE PLASMA ELECTROLYTE CONCENTRATION
IN PATIENTS WITH CHRONIC RESPIRATORY
INSUFFICIENCY

No.	Name	Age	Na	K	Cl	Total CO_2	Urea	Blood pH	Diuretics
1	A.W.	56	139	4.4	88	29	44	—	M
2	D.M.	53	146	4.7	92	33	32	—	M
3	O.M.	55	134	6.5	88	31	24	—	M
4	F.H.	58	131	6.1	76	37.3	44	—	M
5	S.B.	78	131	4.8	88	33	42	7.37	M
6	A.H.	33	136	5.2	84	37.9	23	7.30	M
7	W.B.	75	132	3.5	88.5	32.4	66	7.43	M
8	J.S.	65	143	3.8	101	30.8	—	7.32	—
9	J.B.	59	140	4.7	94.5	36.2	34	7.31	M
9a	J.B.	59	140	4.7	94.5	36.8	34	7.31	M
10	R.H.	54	137	4.6	86	33	47	7.31	M

M=mercurial diuretic.

producing hyponatraemia are the state of the congestive heart failure, the treatment with diuretics and the presence of pneumonitis; the relative importance of these cannot be assessed. The hypochloraemia which is usual in patients

with respiratory acidosis may have been aggravated by similar factors.

Table II shows the urinary pH and the average excretion of NH_4^+ , titratable acidity, H^+ , and other electrolytes in the control periods, and Table III in the periods after NH_4Cl had been given.

TABLE II
URINARY EXCRETION OF ELECTROLYTES, AMMONIUM, TITRATABLE ACIDITY, AND HYDROGEN ION IN CONTROL PERIOD

No.	Av. Periods	Na ($\mu\text{Eq./min.}$)	K ($\mu\text{Eq./min.}$)	Cl ($\mu\text{Eq./min.}$)	TA ($\mu\text{Eq./min.}$)	NH_4 ($\mu\text{Eq./min.}$)	P ($\mu\text{Mol./min.}$)	H^+ ($\mu\text{Eq./min.}$)	pH
1	4	33.3	44.7	29.3	27.5	16.2	—	43.7	5.63
2	2	44.8	34.7	58.8	17.1	24.6	—	41.7	5.60
3	3	44.3	33.0	67.9	20.3	30.5	15.4	50.8	5.84
4	3	16.6	31.4	8.5	29	28.3	25.8	57.3	5.50
5	3	62.6	50.0	51.6	8.8	13.5	18.3	22.3	6.20
6	4	59.1	54.1	53.0	5.3	26.6	28.3	21.3	6.65
7	4	99.3	16.6	87.6	12.8	39.6	8.2	52.4	5.47
8	4	21.8	21.5	38.1	19.2	28.7	12.2	47.9	5.56
9	4	95.4	53.2	91.9	12.8	16.4	25.4	29.2	6.27
9a	1	91.5	40.5	93.9	3.1	13.0	—	16.1	6.5
10	4	44.5	97	64.6	3.6	18.1	—	21.7	6.57

TABLE III
URINARY EXCRETION OF ELECTROLYTES, AMMONIUM, TITRATABLE ACIDITY, AND HYDROGEN ION DURING PERIOD AFTER AMMONIUM CHLORIDE ADMINISTRATION

No.	Na ($\mu\text{Eq./min.}$)	K ($\mu\text{Eq./min.}$)	Cl ($\mu\text{Eq./min.}$)	TA ($\mu\text{Eq./min.}$)	NH_4 ($\mu\text{Eq./min.}$)	P ($\mu\text{Mol./min.}$)	H^+ ($\mu\text{Eq./min.}$)	pH
3	142	97.1	244	26.3	46.5	22.6	72.8	5.3
4	39.4	42	50.5	32	49	27.6	81	5.25
5	98	52	89	33.5	24.2	46.6	57.7	5.36
6	168	85	240	27.7	68.5	28.6	96.2	6.06
7	158	17.8	156	13.8	20.5	6.1	34.3	5.21
8	63.7	20.2	80.5	34.6	44.6	27.9	79.2	5.1
9	160	55.2	178	38.5	41.7	29.1	80.2	4.88
9a	178	52	179	39	41.3	—	80.3	5.03
10	48.6	77.5	91.5	46	55	—	101	5.37

There is a striking increase in the excretion of Na, Cl, a less striking increase of P, but not of K. H^+ excretion increased by 130%: titratable activity accounts for 78.8% and NH_4^+ for 51.2% of the increase in H^+ . This proportion of NH_4^+ comes within the range found in normal subjects by Wrong and Davies (personal communication).

The relation NH_4^+/pH in all patients but one (Case 6) fell within the normal range (Fig. 1) observed by Davies and Wrong (1957) and Clarke, Evans, MacIntyre, and Milne (1955), a rather surprising result in view of the observed increase in the NH_4 excretion in relation to pH in chronic metabolic acidosis (Gamble, Blackfan, and Hamilton, 1924; Sartorius, Roemmelt, and Pitts, 1949; Wood, 1955).

Tables IV and V show the change in the excretion of Na (ΔNa), K (ΔK), and K/Cl

FIG. 1.—Relationship between urinary pH and ammonium output in the patients with respiratory acidosis compared with the same relationship in 10 normal controls. The regression line and 95% limits are taken from Davies and Wrong (1957).

relationship ($\Delta\text{K}/\text{Cl}$) in 10 normals and in the patients with respiratory failure after NH_4Cl load. There is in relation to normals a significantly decreased Na and K excretion ($t=2.8$, $P\approx 0.02$, and $t=2.7$, $0.05>P>0.02$ respectively) but a decrease that is not significant in the K/Cl relationship ($t=1.7$, $P>0.1$).

TABLE IV
URINARY SODIUM, POTASSIUM, AND POTASSIUM CHLORIDE RATIO CHANGES AFTER AMMONIUM CHLORIDE ADMINISTRATION IN NORMALS (UNPUBLISHED DATA BY WRONG AND DAVIES)

Case No.	ΔNa	ΔK	$\Delta\text{K}/\text{Cl}$
1	142	114	0.38
2	392	44	0.14
3	198	62	0.21
4	139	65	0.23
5	119	—9	0.00
6	88	44	0.38
7	90	62	0.24
8	77	28	0.24
9	76	3	0.00
10	107	54	0.35

TABLE V

URINARY SODIUM, POTASSIUM, AND POTASSIUM/CHLORIDE RATIO CHANGES AFTER AMMONIUM CHLORIDE ADMINISTRATION IN PATIENTS WITH CHRONIC RESPIRATORY INSUFFICIENCY

Case No.	Na	K	K/Cl
3	98	64	0.38
4	23	11	0.26
5	35	2	0.07
6	109	31	0.17
7	17	1	0.01
8	22	-1	-0.02
9	74	3	0.04
9a	86	11	0.14
10	4	-19	-0.70

Discussion

As would be expected, the results show an increase in H^+ , Na, Cl, and P excretion after NH_4Cl loading. A logarithmic relationship between the rate of ammonium excretion and the urinary pH has already been shown (Clarke *et al.*, 1955). The present results show that all but one of the patients with chronic respiratory insufficiency have an NH_4^+/pH relationship in the normal range (Clarke *et al.*, 1955; Davies and Wrong, 1957) even after NH_4Cl loading. The ammonium excretion in chronic metabolic acidosis is high in relation to the urinary pH (Gamble *et al.*, 1924; Sartorius *et al.*, 1949; Wood, 1955) and this has been attributed to a high glutaminase activity in the renal cortex induced by chronic acidosis (Davies and Yudkin, 1952). It seemed likely that in chronic respiratory acidosis the same renal response might occur, but in fact a normal NH_4^+/pH relationship has been found in almost all the patients. In the light of the recent work published by Carter, Seldin, and Teng (1958), these results can be interpreted as a consequence of the lack of increase in renal glutaminase activity in respiratory acidosis.

It has been shown in normal subjects that there is a rapid fall of urinary pH after NH_4Cl (Clarke *et al.*, 1955; Davies and Wrong, 1957); values higher than 5.3 after NH_4Cl are commonly interpreted as caused by renal tubular acidosis or K deficiency (Davies and Wrong, 1957). The average urinary pH in the patients after NH_4Cl had been given was 5.28, which is near the upper limit of the normal range given by Davies and Wrong (1957) and Clarke *et al.* (1955).

In the patients with respiratory failure the excretion rate of urinary K and Na after NH_4Cl increased less than it did in normal subjects given NH_4Cl . In respect of Na this can be attributed partly to low salt intake and partly to congestive heart failure. The K intake, however, was normal,

and congestive heart failure is not usually associated with low excretion of K.

Clarke *et al.* (1955) have shown that, when normal persons are made K-deficient, their K output falls, Na increases, and K/Cl after NH_4Cl is low; and the low K output in these patients may well be due to K depletion. Potassium depletion has not been generally recognized as a complication of congestive heart failure secondary to respiratory insufficiency, but Black and Davies (unpublished observations) found K retention in two patients recovering from acute respiratory failure. More recently Levitin, Jockers, and Epstein (1958) and Carter *et al.* (1958) have shown a decrease in muscle K in rats exposed to high CO_2 tension for a long time. Although the present results may suggest K depletion they do not indicate whether this is due to the acidosis, to the state of heart failure, or to the effect of treatment with a low salt diet and diuretics. The determination of the changes in K and Na excretion after NH_4Cl might be of interest in other types of congestive heart failure in which K depletion may coexist with a normal level of plasma K, and urinary output of K within the wide normal range.

Summary

The urinary excretion of ammonium, titratable acidity, and electrolyte has been estimated in 10 patients with respiratory failure. In eight an NH_4Cl load was given. In all cases but one, ammonium excretion bore the normal relationship to urinary pH. After ammonium chloride administration, the increase of sodium and potassium excretion was significantly smaller in these patients than in normal subjects; this finding is discussed.

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