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BIOCHEMICAL CHANGES ACCOMPANYING THE INGESTION OF A CARBOXYLIC CATION EXCHANGER IN THE HYDROGEN, AMMONIUM, SODIUM, POTASSIUM, OR CALCIUM FORM

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Preceding studies from this laboratory have defined certain changes in body fluids in dogs (1) and, in preliminary form, in human subjects (2, 3) accompanying the ingestion of carboxylic cation exchangers in the hydrogen cycle. In general, hyperchloremia appeared in both groups, the serum bicarbonate was lowered, and the stool output of sodium and potassium increased whereas chloride and nitrogen excretion did not change. In this paper further studies of the resins in various forms in human subjects are reported as a basis for a more adequate understanding of factors contributing to or limiting the clinical utility of these compounds.

MATERIALS AND METHODS

Carboxylic cation exchangers in the hydrogen, ammonium, potassium, sodium, or calcium form have been tested in children and adults with a variety of diseases. Selection of the patients was based primarily on willingness and ability to cooperate in the study. Edema was present in some. The experimental procedures, analytical techniques, and statistical treatment have been detailed in the animal studies mentioned earlier (1). The patients were usually but not invariably maintained on a milk formula or on a diet not rigidly restricted as to sodium content. Again it should be emphasized that all stools included in the study were formed.

RESULTS

A. Effects of hydrogen or ammonium cycle resin ingestion

From Tables I and II and the summary of mean changes in Figure 1, it is evident that the alterations in serum constituents accompanying comparable average daily intakes of these two agents, 39.7 and 38.3 g. respectively, are essentially indistinguishable. Hyperchloremia, and lowered serum bicarbonate and potassium values developed in both groups of subjects without a statistically significant change in serum sodium. Other measured constituents of serum or blood were not affected. The mean output of sodium and of potassium per day, per unit of stool mass, and per gram of stool nitrogen (Tables III, IV, and Figure 2) rose without alteration in the excretion of chloride or nitrogen via this route.

Ingestion of the hydrogen form resin was accompanied by an increase in the average daily urine volumes without statistically significant variation in the total daily output of the various urinary constituents (Table V). In general the external balances of chloride and of sodium (Table VI) remained positive during resin therapy except in those periods in patients WK, CSc, and GDe, when edema was being delivered and in VG when the body weight was decreasing on a reducing diet. Usually simultaneous declines were recorded in both the chloride space and the extracellular sodium of these subjects. Cell nitrogen balances remained positive during resin therapy save for the obese patient, VG, who was on a limited caloric intake. With but few exceptions losses of potassium from cells coincided with and were induced by hydrogen form resin therapy. The most striking losses occurred in CSc. In the experiments with the ammonium form of the resin it is to be noted that cell potassium balances remained positive during resin therapy (Table VII). Since the stool excretion of this element had increased significantly it is obvious that the intake of this electrolyte had been more than adequate to prevent negative balances.

It is to be noted in addition that in patient SB who received cortisone as well as the ammonium form of the resin a decrease in serum carbon dioxide content and abnormally low serum potassium concentrations occurred (Table II) together with

marked increases in stool sodium and potassium excretion (Table IV and Figure 2).

B. Changes during sodium or potassium cycle resin administration

Neither of these resins produced any statistically significant changes in the mean values for carbon dioxide content, chloride, sodium, potassium, calcium or water, although serum inorganic phosphorus rose slightly when the potassium form of the resin was ingested (Figure 1, Tables VIII and IX). On the other hand in subjects CSt and CSc (Table IX) the serum potassium rose to hyperkaliemic levels, 6.1 meq./l., during therapy with the cation exchanger in the potassium form. In addition in CSc the extracellular potassium increased. Comparable data are not available for the other patient.

TABLE I

Body weight and analyses of blood and serum in subjects receiving the cation exchanger in the H cycle

Subject	Time	Therapy	Body Wgt.	Blood		Serum							
(Age-Sex)	(Days)	(g./d.)	(kg.)	Sugar (mgm%)	NPN (mgm%)	HCO_3 (meq./l.)	Cl (meq./l.)	Na (meq./l.)	K (meq./l.)	Ca (mgm%)	P (mgm%)	H_2O (g./l.)	Protein (g.%)
WW	0	0	32.6	325	34	23.4	97.8	136	4.8	10.2	5.2	928	8.0
12 M	0-3	0	33.0	-	34	25.4	95.4	141	5.0	10.8	5.3	930	7.5
Diabetes	3-6	0	32.6	119	32	25.9	105.6	144	4.4	9.0	6.1	935	6.7
	6-9	25	32.8	288	33	21.9	106.1	142	4.3	9.5	4.9	929	7.2
	9-12	35	33.2	234	32	20.4	104.8	138	4.6	-	-	925	7.9
CAS	0	0	41.6	166	35	25.0	103.4	145	4.5	-	5.7	929	7.4
9 F	0-3	0	41.6	-	31	25.8	102.8	143	4.7	9.8	5.2	926	7.9
Diabetes	3-6	0	40.8	-	34	25.0	104.5	147	3.9	9.2	4.8	929	7.7
	6-9	25	40.6	-	31	22.6	108.3	144	5.3	9.6	5.2	934	7.3
	9-12	35	41.1	131	32	20.7	108.9	141	4.1	-	5.6	923	8.1
VG	0	0	144.0	72	29	19.7	105.2	147	4.5	10.3	3.8	-	7.5
14 F	0-3	0	145.1	68	32	21.8	105.6	156	4.8	10.1	-	-	7.3
Obesity	3-6	0	144.6	75	27	22.9	102.1	142	4.3	9.9	3.5	931	-
	6-9	0	143.1	78	24	22.6	100.8	139	4.3	10.8	3.9	930	7.9
	9-12	32	141.5	80	24	18.7	106.9	135	4.5	-	3.3	-	7.9
	12-15	32	141.0	72	25	17.5	110.2	141	4.2	-	-	-	7.2
	15-18	32	139.8	80	25	19.5	107.7	139	3.9	10.3	3.9	926	8.2
	18-21	0	138.2	-	33	22.8	103.5	145	4.3	10.3	4.1	930	8.4
	21-24	0	136.8	-	30	23.7	101.0	142	4.7	10.8	4.8	926	8.1
	24-27	0	135.5	-	33	21.6	98.5	142	3.9	11.0	-	924	7.8
JMc	0	0	44.0	257	32	22.8	101.4	141	-	-	-	931	7.3
15 M	0-3	0	43.6	231	31	22.9	103.7	143	4.4	-	5.1	932	-
Diabetes	3-6	0	-	266	29	22.9	102.4	136	4.8	-	-	-	6.8
	6-9	40	-	167	33	18.5	105.9	143	3.7	-	-	927	-
	9-12	40	-	249	29	16.1	108.1	138	4.0	10.8	4.8	923	7.2
KMc	0	0	42.0	171	36	25.9	104.7	141	4.4	9.4	4.6	932	7.1
11 F	0-3	0	42.0	150	35	21.7	108.9	145	4.5	-	-	929	-
Diabetes	3-6	0	42.0	207	31	24.1	105.4	145	5.0	9.5	4.5	924	6.8
	6-9	40	42.0	166	31	18.2	111.8	143	3.7	-	-	931	-
	9-12	40	42.2	209	34	16.9	109.2	143	3.7	9.7	4.5	929	7.9
MK	0	0	62.9	70	40	28.3	100.5	142	4.6	11.0	3.8	934	6.5
57 M	0-2	32	61.3	80	49	23.2	106.7	139	4.4	10.6	3.4	934	6.3
Cong.	2-4	32	59.0	84	51	22.4	106.5	138	3.7	9.8	3.3	-	7.0
Failure	4-6	32	58.3	93	48	20.1	104.3	141	4.0	-	4.3	-	7.6
	6-8	32	57.5	83	48	19.3	104.8	142	4.4	-	3.9	934	7.0
	8-9	32	57.3	-	46	20.2	106.4	141	3.9	10.1	-	922	-
	9-13	0	58.2	87	47	25.9	101.8	143	4.1	10.2	4.1	930	7.4
	13-15	0	59.3	-	44	24.7	102.4	142	4.7	-	4.4	934	6.9
CSc	0	0	48.9	87	33	22.2	110.4	142	5.2	11.2	4.8	939	6.3
33 F	0-3	0	49.3	88	32	25.4	104.8	137	5.0	9.7	5.4	941	5.9
C-V Dis.	3-6	0	50.9	-	31	26.4	104.4	144	4.7	9.6	5.8	941	6.2
	6-9	32	49.8	75	29	20.5	107.8	141	4.4	-	6.2	938	-
	9-12	32	49.1	-	29	23.6	106.5	142	4.1	9.6	5.2	939	6.6
	12-15	0	48.5	-	31	23.4	101.9	139	4.9	-	-	928	-
	15-19	0	47.9	-	-	27.0	103.6	142	5.4	-	-	936	-
CDe	0	0	67.7	-	81	21.5	100.6	145	5.2	9.2	6.3	938	5.5
34 M	0-5	30	57.8	-	87	12.2	112.3	139	6.8	9.0	9.1	930	6.3
Chr.	5-10	0	56.4	-	80	14.4	108.6	135	5.4	-	7.3	931	6.2
Nephritis	10-15	21	57.6	-	76	13.7	115.9	142	4.3	9.5	6.2	937	5.9
	15-19	20	56.6	87	73	13.7	113.8	145	4.0	8.7	6.3	936	6.4
	19-25	60	55.8	-	62	13.2	116.3	140	3.5	7.8	5.8	941	5.9

TABLE II

Body weight and analyses of blood and serum in subjects receiving cation exchanger in the NH_4 cycle

Subject (Age–Sex)	Time (Days)	Therapy (g./d.)	Body Wgt. (kg.)	Blood		Serum							
				Sugar (mgm. %)	NPN (mgm. %)	HCO_3 (meq./l.)	Cl (meq./l.)	Na (meq./l.)	K (meq./l.)	Ca (mgm. %)	P (mgm. %)	H_2O (g./l.)	Protein (g. %)
JF	0	0	69.5	—	35	25.7	95.9	138	4.5	9.5	3.2	929	7.5
29 M	0–6	40	67.4	124	34	27.5	100.2	150	4.5	9.8	3.5	929	7.8
Diabetes	6–12	0	66.6	—	41	30.1	98.0	149	4.5	10.0	3.6	925	8.1
	12–18	40	67.0	108	38	23.7	104.9	145	5.3	9.7	3.5	925	7.9
	18–24	0	68.9	69	32	28.1	104.0	147	5.0	9.5	4.4	934	7.3
CS	0	0	60.2	—	33	26.3	108.8	144	4.3	8.4	2.6	935	6.6
54 M	0–6	40	—	—	36	14.4	114.5	144	4.1	8.8	2.3	931	7.2
Arthritis	6–7	0	—	—	—	23.0	110.4	144	3.7	—	—	—	—
	7–12	0	—	—	31	27.6	101.7	145	4.4	8.9	2.1	938	—
CSc	0*	*	48.7	—	38	29.4	90.8	142	6.1	8.8	5.0	939	6.3
33 F	0–7	8	48.0	—	39	24.4	97.0	140	4.4	—	—	944	—
C-V dis.	7–13	40	48.4	—	41	22.8	101.2	153	3.8	—	3.8	933	—
	13–19	0	52.7	90	35	26.6	94.5	136	4.3	8.8	4.5	941	6.1
SB†	0	†	28.0	70	36	23.7	106.5	148	4.6	—	—	934	—
7 F	0–3	40	28.3	—	—	28.7	99.9	150	2.4	10.1	3.6	938	—
Rh. Fev.	3–6	40	27.9	65	36	30.2	97.1	144	3.4	9.1	3.5	937	—
	6–9	40	28.1	76	29	28.1	101.4	145	2.8	—	—	934	—
	9–12	40	28.0	78	30	30.1	99.1	145	2.5	—	4.0	—	6.5
	12–15	40	28.5	59	32	—	96.5	144	2.9	—	3.1	—	6.7
	15–18	40	—	61	29	27.8	100.7	150	4.8	—	4.0	936	7.0
	18–21	40	—	92	36	20.3	109.7	148	4.2	—	4.4	—	—
WY	0	0	74.1	—	68	23.2	107.7	138	5.1	9.3	5.0	924	7.0
45 M	0–6	40	71.7	160	63	16.2	108.4	143	3.8	8.5	4.8	921	7.7
Diabetes	6–7	0	—	—	63	17.5	111.5	144	4.4	—	—	—	—
	7–12	0	71.8	172	55	20.4	109.4	140	4.3	9.6	4.7	929	7.3
EMc	0	0	—	—	42	27.2	107.4	144	4.5	9.1	3.3	926	7.3
71 F	0–6	40	—	203	46	11.8	117.2	144	4.0	8.9	3.0	927	8.0
Diabetes	6–7	0	—	—	42	15.2	115.5	145	4.0	—	—	—	—
DY	0‡	‡	30.4	67	44	23.1	108.6	141	3.7	6.7	5.0	936	3.7
12 M	0–4	35	31.4	—	33	19.7	113.7	140	3.1	—	4.2	938	3.5
Nephrosis	4–10	0	31.4	—	36	20.5	110.1	139	4.0	7.3	4.5	933	3.6
WG	0	0	32.4	62	35	25.8	104.1	135	4.5	11.5	5.4	936	6.8
12 M	0–5	0	30.4	80	43	21.7	106.7	—	—	—	5.4	915	—
Gl. Neph.	5–10	0	28.8	—	35	24.9	97.4	140	4.9	—	5.0	921	—
(healed)	10–15	0	30.1	75	36	27.2	100.4	138	5.4	9.9	4.8	927	8.3
	15–20	0	30.1	—	35	26.6	105.1	140	4.4	9.5	4.6	930	7.7
	20–26	38	30.0	—	37	26.6	105.0	141	3.8	—	—	—	—
	26–31	0	29.8	—	44	26.6	101.5	137	4.0	10.0	4.6	925	7.8

* End of K resin period.
† Patient receiving cortisone throughout study, 100 mgm./day for 40 days.
‡ End of K resin period.

Ingestion of the sodium cycle resin increased the stool output of potassium and of sodium (Table X and Figure 2). Similarly, on an intake of the potassium cycle resin, stool potassium and, to a lesser extent, stool sodium increased (Table XI and Figure 2). In each group of experiments, some of the cation, either sodium or potassium, ingested with the resin was released and entered the body fluids. Though daily urinary excretions of the particular cation under scrutiny were quite high, positive external balances were recorded (Tables XII and XIII). In the case of the sodium resin, the absorbed cation, sodium, remained primarily in the extracellular phase (Subjects EB, JV, and VB). Potassium released from the resin on the other hand was retained in the body and entered the cellular phase in patient RC (Table XIII). Patients WG and CSc, however, excreted

this cation in both urine and stool and lost it from cells.

C. Studies during calcium cycle resin

Insofar as can be determined by inspection of Table XIV or statistical comparison of mean values (Figure 2) this resin failed to influence either the stool output of chloride, or nitrogen but did raise to a slight extent the stool sodium in all categories and stool potassium in the per day and per gram of nitrogen groupings. It would appear, therefore, that attachment of this divalent cation to the carboxylic exchanger renders it less effective from the point of view of affecting stool excretion of sodium and potassium. Furthermore there is no evidence of any consistent and significant change in either the individual values or the means of most of the measured serum constituents, includ-

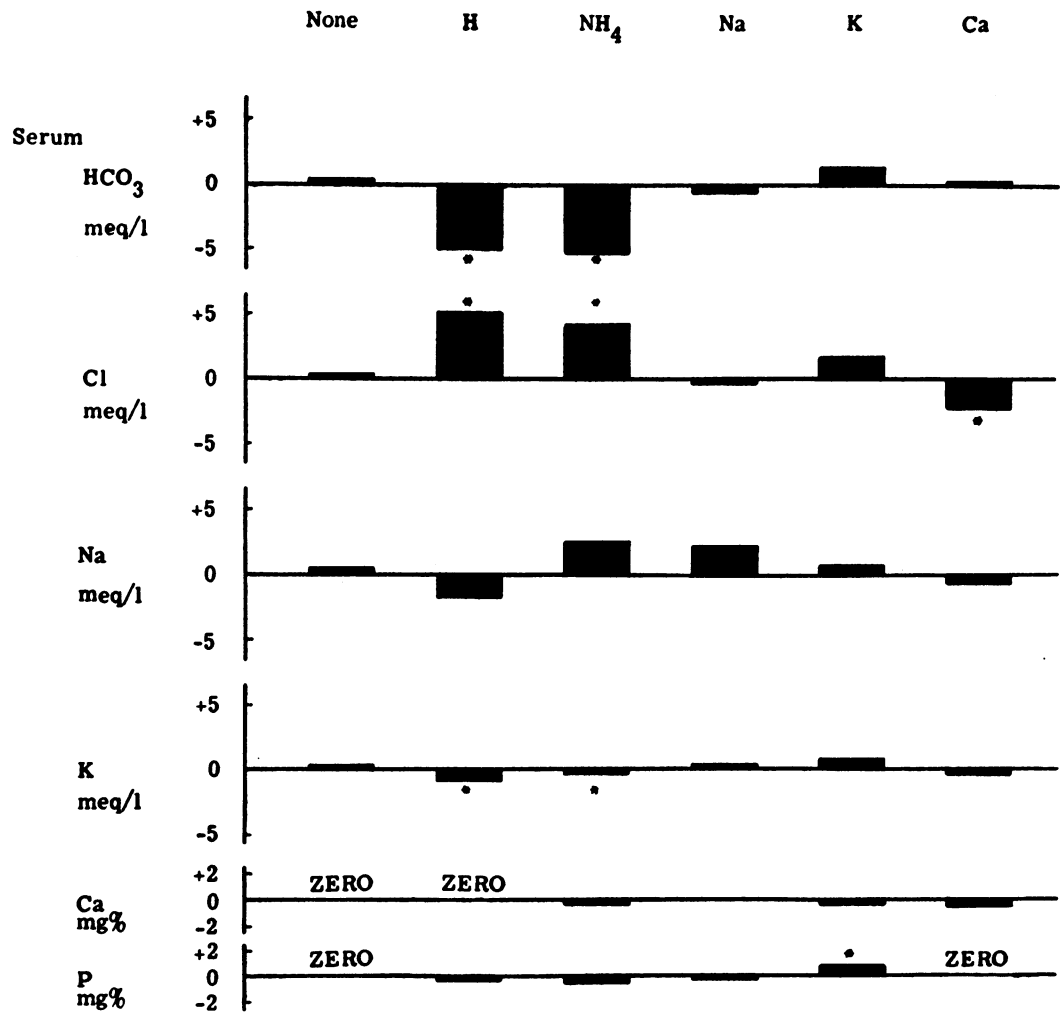

FIG. 1. SERUM ELECTROLYTE CONCENTRATIONS WITH AND WITHOUT RESIN THERAPY

The blocks represent mean alterations in serum constituents between the onset and the end of each of the regimens indicated at the head of the individual columns. The chemical abbreviations stand for the form of resin ingested. Asterisks identify statistically significant differences from the changes in the control values ("p" for the "t" test equals 0.05 or less). Without resin therapy serum constituents listed on the left varied but little. Treatment with H or NH_4 forms produced acidosis and hyperchloremia and lowered serum potassium levels. Ingestion of the Na form did not produce any significant changes. Serum inorganic phosphorus rose during administration of the K cycle, and serum chloride fell when the Ca form was ingested.

TABLE III

Intake data and urine and stool output in subjects receiving the cation exchanger in the H cycle

Subj.	Time	Therapy	Intake					Urine					Stool				
	(days)	(g./d.)	Fluid (l.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	Vol. (l.)	Cl (meq.)	Na (meq.)	K (meq.)	TN (gm.)	Wgt. (gm)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)
WW	0-3	0	7.36	290	259	230	33.5	3.88	253	221	200	27.7					
	3-6	0	7.11	215	180	257	37.4	3.18	115	115	195	28.3	643	7	7	102	5.6
	6-9	25	8.96	215	180	257	37.4	5.91	132	87	189	25.4					
	9-12	35	9.28	215	180	257	37.4	8.30	183	91	91	29.2	563	8	118	319	5.1
CAS	0-3	0	6.84	512	481	230	33.6	3.48	447	470	170	25.0					
	3-6	0	6.80	545	512	245	35.8	2.73	408	459	177	24.9	55	1	3	9	0.8
	6-9	25	7.79	568	534	256	37.3	2.79	389	340	107	23.7					
	9-12	35	7.44	568	534	256	37.3	4.25	509	482	81	29.3	197	3	22	136	1.4
VG	0-3	0	5.55	246	231	111	16.2	1.10	215	188	32	16.2					
	3-6	0	4.58	271	254	122	17.8	0.50	136	139	19	5.6	371	3	140	87	5.0
	6-9	0	3.58	216	203	97	14.2	1.00	233	244	82	11.9					
	9-12	32	4.42	205	193	93	13.5	1.49	204	187	86	13.1					
	12-15	32	4.46	225	192	101	14.8	1.65	240	104	53	14.9	-	0.4	149	104	1.0
	15-18	32	6.12	250	235	113	16.5	4.58	551	280	50	22.7					
	18-21	0	4.40	50	3	120	14.2	2.60	225	98	28	16.2					
	21-24	0	3.40	41	2	99	11.7	3.25	107	36	50	19.4	89	0	28	26	1.0
	24-27	0	4.28	47	3	115	13.5	2.80	50	57	60	15.1					
JMc	0-3	0		Full	diab.	diet		4.25	614	587	193	37.1					
	3-6	0		"	"	"		3.75	515	638	110	34.9	708	5	57	83	10.0
	6-9	40		"	"	"		7.04	716	929	232	43.2					
	9-12	40		"	"	"		3.20	299	173	69	32.0	775	5	174	334	8.8
KMc	0-3	0		Full	diab.	diet		3.76	458	508	140	38.5					
	3-6	0		"	"	"		1.85	249	249	94	22.4	494	5	11	44	7.9
	6-9	40		"	"	"		5.62	516	337	188	42.9					
	9-12	40		"	"	"		4.22	353	146	66	37.0	905	4	351	283	6.6
WK	0-2	32	6.47	83	5	200	23.6	3.96	132	82	84	14.1					
	2-4	32	6.25	89	5	216	25.4	5.38	190	105	93	18.2					
	4-6	32	7.50	89	5	216	25.4	3.57	98	31	51	17.1	451	6	88	147	4.1
	6-8	32	5.79	78	5	189	22.3	4.05	92	24	38	20.0					
	8-9	32	3.02	44	3	108	12.7	1.70	38	5	9	8.6					
	9-13	0	13.48	180	11	437	51.5	5.20	154	50	73	47.1					
	13-15	0	6.71	89	5	216	25.4	0.48	15	3	7	5.7	104	3	9	17	2.6
CSc	0-3	0	8.32	556	525	230	33.6	4.12	446	269	184	26.8					
	3-6	0	10.26	567	532	256	37.3	4.75	442	370	206	26.2	240	5	14	147	2.7
	6-9	32	11.70	567	532	256	37.3	9.70	650	613	247	28.1					
	9-12	32	12.95	649	609	293	42.7	9.80	588	491	138	37.8	1092	9	527	523	9.8
	12-15	0	8.33	112	7	272	32.1	5.80	247	101	163	29.3					
	15-19	0	12.43	166	10	404	47.6	8.40	249	88	300	37.9	288	3	93	129	3.9
DDe	0-5	30	18.63	309	259	369	53.9	5.35	262	317	139	22.1	2466	13	92	94	5.6
	5-10	0	16.76	304	256	364	53.1	4.90	192	162	126	22.5	1443	5	18	42	4.8
	10-15	21		Full	diet			9.25	377	324	365	-	428	1	12	122	4.9
	15-19	20		("Salt-free")		diet		9.50	346	319	137	36.7	317	1	8	98	3.8
	19-25	60		Full	diet			17.40	870	736	197	53.6	548	11	63	230	6.8

ing calcium and phosphorus (Table XV and Figure 1). The chloride concentration, however, fell approximately 2 meq./l. in all patients without other change. Balance data, however, were not consistently altered in VB or JF (Table XVI).

D. Comparison of the efficiency of the various resin forms

Mean stool excretion of sodium and potassium per gram of resin was determined during administration of the hydrogen, ammonium, potassium, sodium, and calcium forms of the cation exchanger in the experiments in which sodium was not rigidly withheld. The few studies in which the diet was almost completely free of sodium are included in the tables, but excluded from the means, to illustrate the decrease in efficiency of the hydrogen and ammonium forms under such circumstances. For simplicity the calculations are omitted, but the findings can be summarized briefly.

The hydrogen, ammonium, and potassium forms of the resin removed equivalent amounts of sodium plus potassium in stools (1.5, 1.9, and 1.9 meq./g. respectively). Mean stool sodium averaged 0.4 to

TABLE IV

Intake data and urine and stool output in subjects receiving cation exchanger in the NH_4 cycle

Subj.	Time	Therapy	Intake					Urine					Stool				
	(*Days*)	(*g./d.*)	Fluid (*l.*)	Cl (*meq.*)	Na (*meq.*)	K (*meq.*)	N (*g.*)	Vol. (*l.*)	Cl (*meq.*)	Na (*meq.*)	K (*meq.*)	TN (*g.*)	Wgt. (*g.*)	Cl (*meq.*)	Na (*meq.*)	K (*meq.*)	N (*g.*)
JF	0–6	40	Full diab. diet					17.60	1442	1045	396	90.6	73	0.3	10	25	2.4
	6–12	0	23.23	521	436	622	90.6	12.15	401	343	274	75.6	286	0.3	30	122	2.6
	12–18	40	20.14	496	416	592	86.3	8.60	156	26	218	86.1	611	4	45	214	3.4
	18–24	0	Full diab. diet					9.24	1850	1862	191	74.1	495	13	44	102	3.3
CS	0–6	40	Full diet					7.00	735	367	189	46.6	704	18	398	130	4.6
	6–12	0						2.50	285	152	54	36.8	782	51	88	67	8.5
CSc	0–7	8	14.92	281	234	336	49.0	8.60	0	0	305	63.0	—	—	—	—	—
	7–13	40	"Salt-free" diet					8.10	26	3	81	—	910	12	48	240	8.1
	13–19	0						8.80	19	0	62	41.9	212	3	9	44	1.9
SB	0–3	40	Full diet					4.00	408	185	81	40.3	1228	21	181	266	9.4
	3–6	40						4.97	434	240	55	34.6					
	6–9	40						4.13	369	224	103	—	—	—	—	—	—
	9–12	40						4.52	460	256	39	33.1	1130	13	293	347	8.4
	12–15	40						4.26	466	318	57	45.7	642	3	195	162	6.2
	15–18	40						5.82	506	640	54	46.0	670	3	192	232	6.9
	18–21	40						4.66	301	—	—	27.7					
	21–23	40						2.02	83	—	—	—	259	3	94	50	2.9
WY	0–6	40	11.89	261	219	311	45.4	6.40	95	85	160	41.4	2109	25	258	134	13.0
	6–12	0	13.02	267	224	318	46.4	7.00	298	186	161	48.4	850	3	17	80	8.0
EMc	0–6	40	Full diab. diet										346	1	118	166	2.4
DY	0–4	35	Full diet					4.10	163	94	189	50.0*	570	3	123	132	5.7
	4–10	0	11.03	146	9	354	65.0	7.05	338	197	270	58.0*	1171	11	26	48	6.3
WG	0–5	0	12.64	223	13	542	64.0	7.88	386	272	259	40.1	470	5	6	96	5.2
	5–10	0	13.58	233	14	566	66.8	7.25	251	54	338	48.9	299	3	9	51	3.7
	10–15	0	13.80	233	14	566	66.8	9.19	275	21	391	52.7	534	6	3	90	5.9
	15–20	0	12.95	233	14	566	103.8	7.72	268	68	363	56.4	475	5	8	77	6.8
	20–26	38	16.72	251	15	608	111.6	12.15	359	85	101	96.6	766	6	28	240	6.7
	26–31	0	14.79	221	13	538	98.6	6.24	204	67	106	57.7	782	5	31	288	7.2

* TN values in this patient include 37.4 and 45.3 g., respectively, of NPN.

1.0 meq./g. for each of these forms. All of these exchangers were more effective in this respect than the calcium cycle. With regard to potassium the hydrogen, ammonium and sodium forms proved to be equally effective in augmenting the loss of this electrolyte via the gastrointestinal tract. They were again superior to the calcium form. More potassium was excreted in the stool during potassium cycle resin administration than during the ingestion of any other form of the exchanger. It does not seem likely that this represents increased removal of endogenous or dietary potassium, since the amounts of this cation recovered in the stools were less than that administered in the resin. The large amount of potassium found in the stool would appear to be best explained by "unchanged resin" or the temporary release of potassium in the acid medium of the stomach and subsequent recovery of large amounts of the cation in the alkaline small intestine by the exchanger. The same reasoning regarding sodium may be applied to the sodium form of the carboxylic resin. Each gram of the potassium and sodium forms of the resin contained 3.8 meq. of their respective cations prior to administration.

E. Clinical concomitants of resin therapy

Ambulatory patients or those without discomfort tolerated the above cation exchangers quite well, whereas those with gastrointestinal symptoms or general malaise experienced varying degrees of difficulty in ingesting and retaining the larger

dosage. In some, emesis was extensive enough to prevent administration of the exchangers; these subjects have been excluded from our studies.

Seven of the studies with the hydrogen or ammonium forms of the resin were conducted in patients with diabetes mellitus. Though the carbohydrate data have been omitted for purposes of brevity the results indicated that the development of acidosis as a result of resin ingestion was not accompanied by ketone bodies in the urine and did not exert any visibly deleterious effect on car-

TABLE V

Statistical expression of urine data during H resin therapy

	Control and post resin*			Resin				
	Mean	No.	S. D.	Mean	No.	S. D.	"t"	"p"
Volume (*ml.*)	1026.1	20	531.2	1873.9 >†	22	775.9	3.99†	0.0025
Cl (*meq./d.*)	89.5	21	54.3	104.4	21	54.6	0.89	0.38
Na (*meq./d.*)	78.9	21	63.2	67.9	20	45.6	0.62	0.52
K (*meq./d.*)	39.5	21	23.1	35.8	21	19.2	0.55	0.62
TN (*g./d.*)	8.0	21	3.1	9.2	21	2.6	1.25	0.22

* Control and post resin periods combined after statistical demonstration that they were indistinguishable.
† Significantly greater than controls

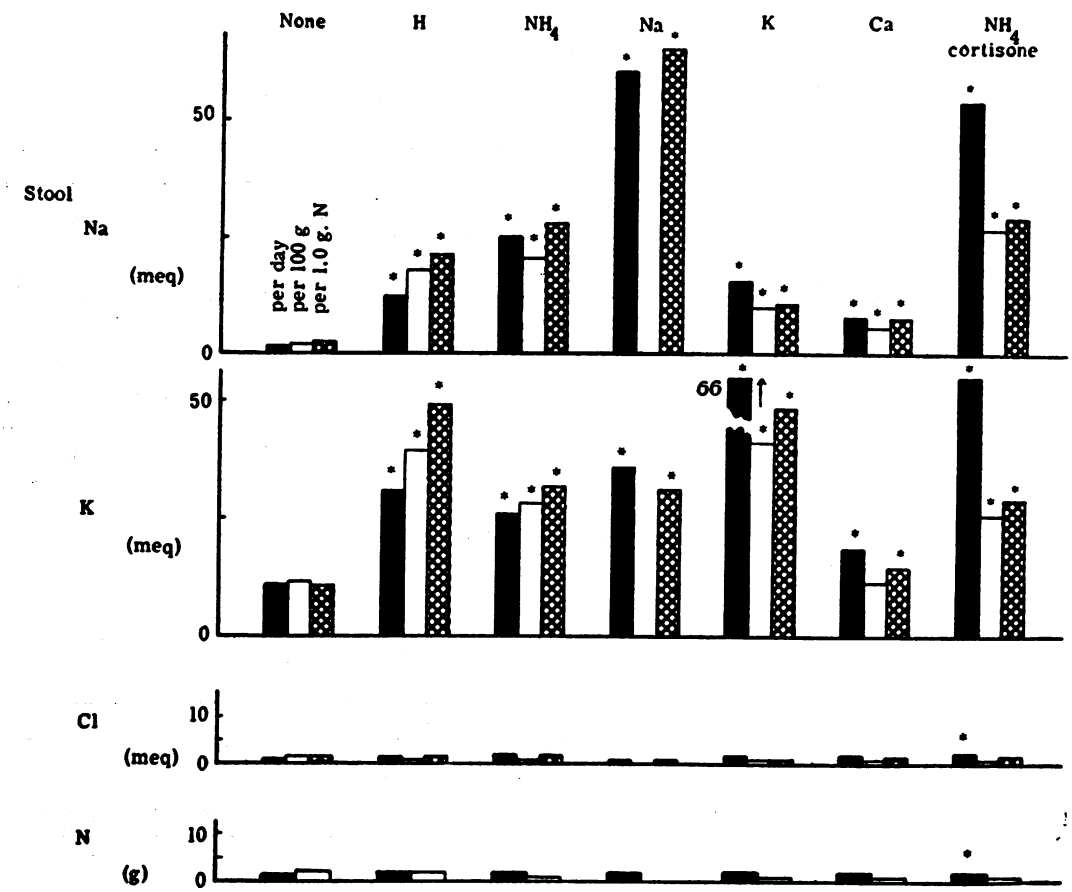

FIG. 2. STOOL DATA

The columns represent stool excretion of Na, K, Cl, and N per day, per 100 g. of wet stool, and per 1.0 g. of nitrogen during therapy indicated at the head of each group of columns. Again the chemical abbreviations indicate the form of the resin ingested, and the asterisks stand for values significantly different from the control column entitled "none." The column headed "NH_4 cortisone" indicates the patient receiving the NH_4 form of the resin together with cortisone. Stool excretion of sodium and of potassium increased to a variable degree irrespective of the particular form of the resin administered, or of cortisone therapy. Mean stool chloride and nitrogen values were not changed during the ingestion of any of the exchangers, but did increase slightly when cortisone was given during NH_4 form therapy in one patient.

TABLE VI

External, extracellular, and cell balances in subjects receiving the cation exchanger in the H cycle

Subject	Time	Therapy	Ext. Bal.				Extracell. Bal.			Cell Bal.			
	(Days)	(g./d.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	H_2O (l.)	Na (meq.)	K (meq.)	Na (gm.)	Na (meq.)	K (meq.)	K** (meq.)
WW	0-3	0	+ 31	+ 31	- 21	+ 2.7	+0.5	+101	+ 4	+ 2.7	- 70	- 25	- 31
	3-6	0	+ 94	+ 59	+ 11	+ 6.0	+0.1	+ 29	- 4	+ 6.4	+ 30	+ 15	0
	6-9	25	+ 77	+ 30	- 92	+ 9.1	+0.6	+ 85	+ 2	+ 8.9	- 55	- 94	-115
	9-12	35	+ 25	+ 27	+ 7	+ 5.3	+0.3	+ 12	+ 5	+ 5.5	+ 15	+ 2	- 11
CAS	0-3	0	+ 62	+ 6	+ 55	+ 7.9	+0.6	+ 79	+ 5	+ 9.0	- 73	+ 50	+ 29
	3-6	0	+133	+ 48	+ 64	+10.2	+1.0	+182	- 4	+ 9.4	-134	+ 68	+ 46
	6-9	25	+175	+180	+ 81	+12.6	+1.1	+124	+20	+13.4	+ 56	+ 61	+ 29
	9-12	35	+ 55	+ 37	+107	+ 7.0	+0.3	+ 26	-12	+ 6.7	+ 11	+119	+103
VG	0-3	0	+ 28	- 7	+ 50	- 1.9	+0.1	+272	+ 9	- 4.7	-279	+ 41	+ 52
	3-6	0	+132	+ 66	+ 74	+10.3	+2.1	-116	- 5	+15.0	+182	+ 79	+ 43
	6-9	0	- 20	- 91	- 14	+ 0.4	+0.2	- 65	+ 1	+ 3.2	- 26	- 15	- 23
	9-12	32	- 1	- 46	- 28	- 0.1	-1.8	-366	- 2	- 0.1	+320	- 26	- 26
	12-15	32	- 17	+ 76	+ 13	- 0.6	-1.0	+ 36	-13	- 1.5	+ 40	+ 26	+ 30
	15-18	32	-303	- 19	+ 28	+ 6.7	-1.9	-318	-16	+ 6.7	+299	+ 44	+ 28
	18-21	0	-177	-107	+ 83	- 2.5	-0.3	+104	+ 9	- 9.8	-211	+ 74	+ 97
	21-24	0	- 68	- 46	+ 40	- 8.2	-0.1	- 80	+13	- 5.5	+ 34	+ 27	+ 40
	24-27	0	- 5	- 66	+ 46	- 2.1	+0.6	+117	-21	- 4.8	-183	+ 67	+ 78
MK	0-2	32	- 53	-100	+ 83	+ 8.3	-1.2	-198	- 8	+ 4.6	+ 98	+ 91	+ 80
	2-4	32	-105	-123	+ 90	+ 6.0	-0.9	-145	-12	+ 5.2	+ 22	+102	+ 90
	4-6	32	- 12	- 48	+133	+ 7.2	+0.1	+ 51	+ 5	+ 8.4	- 99	+128	+108
	6-8	32	- 20	- 44	+118	+ 0.9	-0.2	- 16	+ 3	+ 0.9	- 28	+115	+113
	8-9	32	+ 2	- 15	+ 83	+ 3.3	-0.3	- 41	- 6	+ 4.0	+ 26	+ 89	+ 79
	9-13	0	+ 22	- 48	+354	+ 2.6	+0.7	+113	+ 5	+ 2.2	-161	+349	+344
	13-15	0	+ 71	- 5	+204	+18.7	+0.6	+ 64	+ 9	+19.8	- 69	+195	+148
CSc	0-3	0	+105	+245	- 29	+ 5.1	+1.4	+147	+ 6	+ 5.4	+ 98	- 35	- 48
	3-6	0	+119	+152	- 23	+ 9.5	+1.1	+237	+ 2	+ 9.8	- 85	- 25	- 48
	6-9	32	- 90	-349	-254	+ 4.0	-1.2	-205	- 9	+ 4.7	-144	-245	-256
	9-12	32	+ 54	-149	-106	- 0.3	+0.6	+103	- 1	- 0.3	-252	-105	-104
	12-15	0	-139	-102	+ 44	+ 0.5	-0.8	-139	+ 7	- 0.1	+ 37	+ 37	+ 37
	15-19	0	- 87	- 86	+ 40	+ 7.5	-0.8	- 94	- 1	+ 7.5	+ 8	+ 41	+ 23
CDe	0-5	30	+ 31	-153	+136	+25.9	-1.3	-249	+15	+23.3	+ 96	+121	+ 65
	5-10	0	+108	+ 83	+195	+25.5	+1.3	+123	-11	+28.1	+206	+206	+139

* Value has been corrected for external balances of NPN
** K represents transfers of K in excess of protein metabolism

TABLE VII

External, extracellular, and cell balances in subjects receiving the cation exchanger in the NH_4 cycle

Subject	Time	Therapy	Ext. Bal.				Extracell. Bal.			Cell Bal.			
	(days)	(g./d.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	H_2O (l.)	Na (meq.)	K (meq.)	Na (gm.)	Na (meq.)	K (meq.)	K** (meq.)
JF	6-12	0	+117	+ 59	+226	+12.1	+1.3	+195	+ 6	+ 9.0	-136	+220	+199
	12-18	40	+334	+342	+160	- 3.5	+1.8	+208	+22	- 2.2	+134	+138	+143
CBc	0-7	34	+279	+230	+ 31	-14.3	+1.9	+243	-12	-14.6	- 13	+ 43	+ 78
WY	0-6	40	+139	-128	+ 17	- 9.3	+1.0	+231	-15	- 6.9	-359	+ 32	+ 48
	6-12	0	- 36	+ 17	+ 76	-10.3	-0.3	-103	+ 7	- 6.6	+180	- 69	- 53
DY	4-10	0	-206	-217	+ 36	+ 0.5	-1.4	-201	+ 4	- 0.1	- 16	+ 32	+ 32
WG	0-5	0	-171	-269	+188	+18.4	-1.8	-206	- 6	+16.7	- 63	+194	+154
	5-10	0	- 24	- 52	+177	+13.9	+0.6	+100	+ 5	+15.5	-152	+172	+135
	10-15	0	- 51	- 13	+ 86	+ 7.9	-0.6	-110	0	+ 7.7	+ 97	+ 86	+ 68
	15-20	0	- 42	- 65	+126	+10.3	-0.7	- 84	-11	+10.5	- 19	+137	+ 41
	20-26	38	-117	-101	+267	+ 8.0	-1.0	-135	- 8	+ 7.6	+ 34	+275	+257
	26-31	0	+ 10	- 89	+144	+33.4	+0.3	+ 20	+ 3	+32.0	-109	+142	+ 66

* Value has been corrected for external balance of NPN
** K represents transfers of K in excess of protein metabolism

TABLE VIII

Body weight and analyses of blood and serum in subjects receiving the cation exchanger in the Na cycle

Subject	Time	Therapy	Body Wgt.	Blood		Serum							
(Age-Sex)	(Days)	(g./d.)	(kg.)	Sugar (mgm%)	NPN (mgm%)	HCO_3 (meq./l.)	Cl (meq./l.)	Na (meq./l.)	K (meq./l.)	Ca (mgm%)	P (mgm%)	H_2O (g./l.)	Protein (g.%)
EB	0	0	51.0	172	31	23.9	99.4	140	4.3	10.3	5.0	937	6.7
14 M	0-3	0	50.8	240	34	24.8	99.5	149	4.6	-	-	-	-
Diab.	3-6	0	51.0	273	33	25.4	100.8	144	5.3	9.8	5.0	-	7.2
	6-7	0	51.4	-	38	26.2	104.7	142	4.2	10.2	4.6	932	7.6
	7-10	40	51.8	226	33	27.0	101.0	138	4.3	-	-	-	-
	10-13	40	51.8	-	33	23.6	102.1	143	4.6	-	4.7	936	6.8
JV	0	0	54.2	173	32	25.7	96.7	139	3.8	10.2	3.8	932	6.5
15 M	0-3	0	54.4	318	36	25.4	97.7	147	4.5	-	-	-	-
Diab.	3-6	0	54.6	249	33	25.9	98.7	142	4.3	10.0	4.1	930	6.8
	6-7	0	54.0	-	35	26.3	98.7	-	5.3	10.2	4.6	-	7.0
	7-10	40	55.4	222	33	27.2	98.9	142	4.3	-	-	-	-
	10-13	40	55.4	-	34	25.3	99.1	143	4.8	-	4.0	928	6.7
VB	0	*	36.6	75	35	24.0	100.0	139	3.5	-	4.9	923	8.0
11 M	0-8	40	37.4	91	30	26.0	97.4	144	4.3	-	4.9	931	7.3
Rh. Fev.													

* End of Ca cycle resin

TABLE IX

Body weight and analyses of blood and serum in subjects receiving cation exchanger in the K cycle

Subject	Time	Therapy	Body Wgt.	Blood		Serum							
(Age-Sex)	(Days)	(g./d.)	(kg.)	Sugar (mgm%)	NPN (mgm%)	HCO_3 (meq./l.)	Cl (meq./l.)	Na (meq./l.)	K (meq./l.)	Ca (mgm%)	P (mgm%)	H_2O (g./l.)	Protein (g.%)
RC	0	0	48.4	-	31	24.4	97.0	150	5.2	10.0	3.8	-	-
13 M	0-4	60	47.4	-	37	22.7	100.7	140	4.2	-	-	934	-
Diabetes	4-6	60	47.2	311	35	25.1	99.7	142	4.2	10.0	4.4	936	7.0
	6-9	60	48.0	286	33	23.3	99.4	143	4.5	9.4	4.5	937	6.8
	9-12	60	48.8	288	33	25.0	101.0	148	4.6	9.1	4.1	931	-
EMc	0*	*	-	209	34	16.9	109.2	143	3.7	9.6	4.5	929	7.9
11 F	0-3	40	-	255	32	27.3	101.4	137	4.2	-	-	935	-
Diabetes													
CSt	0	0	60.2	-	31	27.6	101.7	145	4.4	8.9	2.1	938	-
54 M	0-6	40	-	-	34#	28.7	100.5	145	6.1	8.8	2.9	936	6.7
Arthritis	6-12	0	-	-	35	26.0	106.1	147	4.0	9.2	2.7	930	7.0
WG	0**	**	30.0	-	37	26.6	105.0	141	3.8	-	-	-	-
12 M	0-5	0	29.8	-	44	26.6	101.5	137	4.0	10.0	4.6	925	7.8
Cl. Nephr.	5-10	40	29.8	-	40	28.1	99.6	145	4.4	10.1	5.5	-	8.1
(healed)													
CSc	0	0	47.5	-	39	28.9	86.7	137	4.3	8.8	4.1	-	6.6
33 F	0-5	32	48.7	-	38	29.4	90.8	142	6.1	8.8	5.0	939	6.3
C-V dis.													

* End of H cycle resin # Drawn on seventh day ** End of NH_4 cycle

TABLE X

Intake data and urine and stool output in subjects receiving the cation exchanger in the Na cycle

Subj.	Time	Therapy	Intake					Urine					Stool				
	(days)	(g./d.)	Fluid (l.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	Vol. (l.)	Cl (meq.)	Na (meq.)	K (meq.)	TN (gm.)	Wgt. (gm)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm)
EB	0-3	0	9.52	268	225	320	46.7	5.80	312	330	212	35.4					
	3-6	0	9.54	268	225	320	46.7	4.35	157	167	224	36.1	816	11	19	103	6.6
	6-7	0	3.23	89	75	107	15.6	1.70	64	49	81	13.1					
	7-10	40	9.97	282	681	337	49.1	4.32	169	332	130	33.1					
	10-13	40	9.52	279	678	333	48.6	5.55	264	-	-	42.7	-	1	466	236	4.9
JV	0-3	0	10.56	268	225	320	46.7	5.60	303	213	261	34.6					
	3-6	0	10.05	279	234	333	48.6	3.76	123	77	184	27.9	774	5	27	103	9.6
	6-7	0	3.23	89	75	107	15.6	1.51	74	54	83	11.0					
	7-10	40	9.83	272	672	325	47.4	2.99	84	344	144	27.0					
	10-13	40	9.71	274	674	327	47.7	4.61	-	-	-	32.0	-	4	192	74	2.9
VB	0-8	40	22.45	295	1201	716	123.5	16.70	233	411	180	106.2	2021	12	605	446	16.2

TABLE XI

Intake data and urine and stool output in subjects receiving cation exchanger in the K cycle

Subj.	Time	Therapy	Intake					Urine					Stool				
	(days)	(g./d.)	Fluid (l.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	Vol. (l.)	Cl (meq.)	Na (meq.)	K (meq.)	TN (gm.)	Wgt. (gm)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm)
RC	0-4	60	13.72	353	297	1334	95.1	12.70	440	318	492	-	1248	12	5	546	12.7
	4-6	60	6.96	183	154	675	49.2	5.25	204	236	157	45.2					
	6-9	60		Full	diab.	diet		7.72	473	563	742	46.6	745	3	27	299	8.7
	9-12	60		"	"	"		8.50	777	1020	450	-					
RKc	0-3	40		Full	diab.	diet		4.24	512	36	394	38.4	745	4	165	189	6.7
CSt	0-6	40		Full	diet			8.00	873	980	864	52.8	460	1	105	260	3.6
	6-12	0		"	"			6.40	705	752	284	41.6	386	3	28	108	4.6
WG	0-5	0	12.75	221	13	538	98.6	6.25	204	67	106	57.7	782	5	31	288	7.2
	5-10	40	12.52	227	14	552	101.2	5.75	227	71	504	46.3	799	6	10	133	8.7
CSc	0-5	32	11.26	225	189	877	39.2	2.45	0	7	515	33.0	1047	4	25	402	6.4

TABLE XII

External, extracellular, and cell balances in subjects receiving the cation exchanger in the Na cycle

Subject	Time	Therapy	Ext. Bal.				Extracell. Bal.			Cell Bal.			
	(Days)	(g./d.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	H_2O (l.)	Na (meq.)	K (meq.)	N (gm.)	Na e (meq.)	K (meq.)	K** (meq.)
EB	0-3	0	- 51	-117	+ 64	+ 8.3	-0.5	+ 18	+ 1	+ 7.3	-135	+ 63	+46
	3-6	0	+104	+ 46	+ 52	+ 7.6	+0.8	+ 69	+10	+ 7.9	- 23	+ 42	+23
	6-7	0	+ 21	+ 20	+ 11	+ 1.0	-0.3	- 58	-12	- 0.7	+ 78	+ 23	+25
	7-10	40	+110	+112	+ 88	+13.2	+1.4	+153	+ 7	+14.9	- 41	+ 81	+45
	10-13	40	+ 12	-	-	+ 3.2	0	+ 59	+ 4	+ 3.2	-	-	-
JV	0-3	0	- 40	- 3	+ 15	+ 7.6	-0.5	+ 14	+ 5	+ 6.2	- 17	+ 10	- 5
	3-6	0	+151	+142	+105	+16.2	+1.2	+123	+ 3	+17.3	+ 19	+102	+61
	6-7	0	+ 12	+ 14	+ 9	+ 2.9	+0.1	+ 15	+12	+ 2.2	- 1	- 3	- 8
	7-10	40	+183	+314	+145	+18.6	+1.6	+234	- 5	+19.3	+ 80	+140	+94
VB	0-8	40	+ 48	+182	+ 89	+ 0.8	+0.7	+134	+ 9	+ 2.0	+ 48	+ 80	+75

* Corrected for balance of NPN
** Represents transfers of K in excess of the anabolism and catabolism of protein

TABLE XIII

External, extracellular, and cell balances in subjects receiving cation exchanger in the K cycle

Subject	Time	Therapy	Ext. Bal.				Extracell. Bal.			Cell Bal.			
	(days)	(g./d.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	H_2O (l.)	Na (meq.)	K (meq.)	N (gm.)	Na (meq.)	K (meq.)	K** (meq.)
RC	0-4	60	- 99	- 28	+478	-	-1.2	-270	-14	-	+242	+492	-
	4-6	60	- 27	- 87	+336	- 0.5	-0.1	0	- 1	+0.1	- 87	+337	+337
WG	0-5	0	+ 10	- 89	+144	+33.4	+0.3	+ 20	+ 2	+32.0	-109	+142	+ 66
	5-10	40	- 8	- 71	- 85	+35.9	+0.1	+ 68	+ 3	+36.7	-139	- 88	-199
CSc	0-5	32	+217	+152	- 40	- 0.8	+1.7	+288	+28	- 0.5	-136	- 68	- 67

* Value has been corrected for external balance of NPN
** Represents transfers of K in excess of protein metabolism

bohydrate metabolism. In view of the inherent variations in carbohydrate utilization from day to day, even in well-regulated diabetic patients, only this general statement is justified. The possibility of some influence of the acidosis, such as that described in dogs receiving ammonium chloride (4), cannot therefore be excluded.

Several of the studies were conducted in patients with edema. WK in Tables I, III, and VI is of particular interest in this respect because on a combination of marked sodium restriction and resin therapy his body weight dropped 5.6 kg. in nine days. The stool sodium excretion during this interval totaled 88 meq. It is obvious that this de-

TABLE XIV

Intake data and urine and stool output in subjects receiving the cation exchanger in the Ca cycle

Subj.	Time	Therapy	Intake					Urine						Stool				
	(days)	(g./d.)	Fluid (l.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)	Vol. (l.)	Cl (meq.)	Na (meq.)	K (meq.)	TN (gm.)	NPN (gm.)	Wgt. (gm)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm.)
VB	0-2	0	4.77	74	4	179	21.2	1.71	44	-	-	13.5	-	1183	11	32	237	11.7
	2-8	40	15.14	221	13	537	92.6	11.20	242	110	226	90.5	-					
JF	0-5	0		Full	diab.	diet		8.25	480	1258	349	63.2	-	1457	6	61	153	9.0
	5-11	40		"	"	"		14.95	1809	1742	468	-	-					
	11-17	0	15.57	365	306	436	97.7	9.15	380	345	390	72.5	-	472	5	12	61	-
	17-23	40	26.69	709	595	847	123.6	11.50	430	309	421	97.3	-	647	6	8	99	5.5
CSt	0-6	0		Full	diet			7.40	936	907	335	45.1	-	291	2	105	83	2.0
	6-12	40		"	"			6.50	778	681	246	38.2	-	463	3	46	81	4.4
DY	0-6	50		("Salt-	free")	diet		12.50	421	413	249	59.5	53.5	1229	11	108	54	6.8
	6-11	60		"	"	"		10.40	219	201	251	55.6	44.8	1003	14	58	82	8.8
	11-16	60		"	"	"		11.00	0	117	298	54.8	47.6	961	7	46	94	9.0
BF	0-5	40		("Salt-	free")	diet		4.60	4	20	116	28.2	26.9	1049	11	56	121	7.7
	5-10	40		"	"	"		4.00	75	84	92	32.4	30.5	-	8	55	96	5.4
	10-16	33		"	"	"		4.80	140	115	93	40.3	35.5	1849	4	-	183	11.5

TABLE XV

Body weight and analyses of blood and serum in subjects receiving the cation exchanger in the Ca cycle

Subject	Time	Therapy	Body Wgt.	Blood		Serum							
(Age-Sex)	(Days)	(g./d.)	(kg.)	Sugar (mgm%)	NPN (mgm%)	HCO. (meq./l.)	Cl (meq./l.)	Na (meq./l.)	K (meq./l.)	Ca (mgm%)	P (mgm%)	H_2O (g./l.)	Protein (g.%)
VB	0	0	37.1	91	29	25.7	101.5	-	-	-	4.6	924	8.0
11 M	0-2	0	36.9	102	38	24.7	102.0	145	4.2	-	5.4	920	8.9
Rh.Fev.	2-8	40	36.6	75	35	24.0	100.0	139	3.5	-	4.9	923	8.0
JF	0*	*	68.5	45	39	28.3	101.2	146	5.1	10.1	4.0	927	-
29 M	0-5	0	69.5	98	41	26.9	98.6	145	5.3	9.9	3.0	925	7.3
Diab.	5-11	40	67.6	168	37	28.9	96.7	149	4.8	-	-	928	7.0
	11-17	0	67.6	37	32	29.3	96.8	140	3.4	10.9	3.9	926	6.8
	17-23	40	67.6	-	37	27.8	93.6	134	3.3	9.9	-	928	7.2
CSt	0**	**	-	-	32	26.3	104.9	143	5.0	9.3	3.2	934	6.8
54 M	0-6	0	-	105	30	27.2	102.0	143	4.5	9.2	2.7	931	6.9
Arthr.	6-12	40	-	77	28	27.2	100.3	144	3.9	9.2	3.4	937	6.5
DY	0*	*	-	89	45	17.3	108.0	135	3.9	7.8	4.5	921	4.3
12 M	0-6	50	28.4	-	39	21.5	104.6	136	4.1	8.2	4.5	925	4.3
Nephro.	6-11	60	29.6	-	38	21.3	104.1	143	4.1	8.4	4.8	933	3.8
	11-16	60	30.6	-	38	23.1	101.7	141	3.9	7.6	4.6	929	3.8
BF	0*	*	21.0	-	28	24.1	102.3	139	3.8	8.6	5.3	-	3.9
5 M	0-5	40	-	-	36	22.6	99.8	135	4.1	7.5	5.7	928	3.7
Nephro.	5-10	40	-	-	32	20.9	103.7	138	4.4	-	-	935	4.0
	10-16	33	-	87	31	20.7	102.7	134	4.0	-	5.0	935	3.9

* End of H and K resin period

** End of NH_4 and K resin period

TABLE XVI

External, extracellular, and cell balances in subjects receiving the cation exchanger in the Ca cycle

Subject	Time	Therapy	Ext. Bal.				Extracell. Bal.			Cell Bal.			
	(Days)	(g./d.)	Cl (meq.)	Na (meq.)	K (meq.)	N (gm)	H_2O (l.)	Na (meq.)	K (meq.)	N* (gm.)	Na (meq.)	K (meq.)	K** (meq.)
VB	0-2	0	+ 24	-	-	+ 4.5	-	-	-	-	-	-	-
	2-8	40	- 31	-124	+133	- 7.0	-0.1	- 69	- 6	- 6.3	- 55	+139	+154
JF	11-17	0	- 22	- 55	- 15	-	-0.2	-150	-21	-	+ 95	+ 6	-
	17-23	40	+271	+274	+327	+20.5	+3.0	+327	+ 7	+16.3	+181	+320	+276

* Value has been corrected for external balance of NPN

** Represents transfers of K in excess of protein metabolism

crease in endogenous sodium as a result of stool losses could not by itself account for the extensive decrease of edema. The bulk of the sodium was lost in urine. It seems probable that the additive effect of the acidosis should be listed among other factors contributory to this diuresis.

On the other hand in patient CSc in the same tables much larger amounts of sodium were excreted in stools during the administration of the exchanger together with a milk diet unrestricted as to sodium. It is reasonable to suggest that without resin to interfere with the absorption of the ingested sodium this patient would not have lost edema fluid. Patient GDe demonstrates the degree to which the efficacy of the resin in augmenting stool sodium can vary not only from patient to patient, but also in the same subject. In the 10 to 15 day period he lost much less sodium per day in stool than in the somewhat longer 19 to 25 day interval. In this patient it is again worth pointing out that his initial huge diuresis with a body weight loss of 9.9 kg. cannot be attributed to stool losses of sodium, but that the marked acidosis which appeared during resin therapy may have hastened the delivery of the edema fluid.

Finally it should be pointed out that these exchangers have been administered to patients with renal failure. These can be most readily identified by the elevated blood nonprotein nitrogen values in the various tables of serum and blood data. The fact that in this series no complications developed such as clinical acidosis or potassium intoxication does not mean that these exchangers can be used with impunity in all forms of renal disease. The risks and benefits have been described in greater detail in another paper in this series (5). Insofar as the current studies are concerned it should be emphasized that they were of limited duration and interrupted short of undesirable or dangerous changes when certain trends had become well established, as with the acidosis in GDe, Table I. Incidentally, the ammonium released from the ammonium form of the resin apparently does not raise whole blood nonprotein nitrogen, but it may have, in some patients, as in WG, Table IV, raised the output of nitrogen in urine.

DISCUSSION

The data which have been presented indicate that the hydrogen and the ammonium forms of the resin produce effects which are indistinguishable, including essentially equal tendencies to induce acidosis and to increase the excretion of sodium and potassium in the stool. Furthermore, neither influences the output of nitrogen and chloride via this route. Although the efficiency of these resins is relatively low *in vivo,* it is clear that they may be useful in reducing the absorption of sodium from the diet so that a patient requiring low sodium therapy could ingest food seasoned with more of this cation. That he could not ingest much larger amounts of salt should be clear from the data indicating that each gram of the hydrogen or ammonium forms will remove only up to 1 meq. of sodium.

These studies also support an interpretation voiced elsewhere (1), *i.e.,* that the acidifying resins produce certain serum effects similar to those which follow the use of diuretics such as ammonium chloride, potassium nitrate, et cetera. This suggests that the diuresis accompanying hydrogen or ammonium cycle resin therapy of patients cannot be augmented by the use of acidifying diuretics. On the other hand it is reasonable to predict that mercurial diuretics used in conjunction with these two acidifying resins will exert their maximal effects without the aid of ammonium chloride. There is, however, probably an increased danger of producing potassium depletion under these circumstances which may be counteracted by administration of extra potassium.

Certain extrapolations seem justified with respect to possible clinical application of the sodium and potassium cycle resin findings. The relatively high efficiency of the sodium cycle resin in augmenting the stool output of potassium suggests its possible application in renal insufficiency of the salt-wastage and potassium accumulation type. This agent under such circumstances should augment the external losses of potassium and simultaneously cancel the negative balances of sodium which characterize this disorder (6–8).

The effects of the potassium cycle exchanger suggest that it may be beneficially employed in combination with the hydrogen or ammonium cycle congeners. It is obvious that upon exchange with sodium and hydrogen present in the intestinal tract the released potassium becomes available for absorption and is, as the data indicate, in great measure retained. This effect should serve to cancel

the deficits of potassium accompanying prolonged use of the hydrogen or ammonium cycle resins without adding to their acidifying effects; although the same purpose may more efficiently be served by increasing dietary potassium intake by means of a salt such as $KHCO_3$ or KCl. The clinical practicality of such combinations has been evaluated elsewhere (9). In addition, the danger of producing potassium intoxication in patients with oliguria and renal disease must be recognized (10–12).

It is possible that certain features of these resins may be utilized in cancelling some of the side effects of prolonged cortisone or ACTH therapy such as alkalosis, sodium retention, and potassium depletion (13–16). For example, combinations of hydrogen and potassium exchangers may be effective in this regard. Potassium depletion, however, may be enhanced under these circumstances unless the intake of potassium is large enough to counteract the combined effects of the resin and ACTH or cortisone on this ion. This problem has been studied in some detail in a subsequent paper (17).

Finally, the lack of any marked effects upon ingestion of the calcium cycle resin is both a disappointment and a reassurance. From the theoretical point of view the resin in this cycle should be useful in far-advanced renal insufficiency: release of the calcium ion from the exchanger should *a*) increase stool losses of sodium and of potassium which accumulate in kidney failure, and *b*) provide calcium to accelerate phosphate losses as insoluble salts via the bowel and alternatively replace the deficits characteristically present in serum and extracellular fluid of such patients. Unfortunately, neither of these predictions is substantiated by our data. These studies, however, provide a highly satisfactory control for a number of the other reports in this series. The following conclusion is inescapable, if such support be needed: the effects of the ammonium, hydrogen, sodium, and potassium forms of the carboxylic cation exchanger under investigation in this series of studies are attributable to the attached cation and not to the resin itself. If the cation with which the resin is charged is not displaced in sufficient quantity the resin has no detectable effect.

SUMMARY

1. The ammonium cycle resin produces effects quite comparable to those seen with hydrogen cycle resin ingestion, *i.e.*, hyperchloremia develops, and serum carbon dioxide content falls while the stool sodium and potassium excretion rises.

2. The stool changes seen with either the ammonium or the hydrogen cycle resins are also observed in subjects receiving the exchanger in either the potassium or sodium cycle. In the use of the latter the efficiency in removing potassium is less. Neither consistently affects the serum constituents but occasionally hyperkaliemia appears during potassium resin therapy. With the sodium form of the resin, sodium balances become positive with extracellular retention of this cation. With potassium resin, the intracellular stores of potassium may rise during therapy.

3. In a series of studies on one patient concomitant administration of cortisone did not interfere with the ability of the ammonium resin to raise stool sodium and potassium but hypokaliemia appeared.

4. The calcium cycle of the carboxylic cation exchanger in the form used was relatively inert and produced much smaller changes in stool sodium and potassium. These findings, however, do add support to the view that the cycle of the resin and not the resin *per se* is the determinative factor in the observed results.

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