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THE EFFECT OF DEOXYCORTICOSTERONE ON THE UNIDIRECTIONAL TRANSFERS OF SODIUM AND POTASSIUM INTO AND OUT OF THE DOG INTESTINE

BY E. Y. BERGER, GRACE KANZAKI AND J. M. STEELE

From the New York University Research Service Goldwater Memorial Hospital, Welfare Island, New York 17, *N.Y., U.S.A.*

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The patient with congestive heart failure or cirrhosis of the liver, who gains oedema fluid daily, fails to excrete sodium in the urine in amounts equal to dietary intake. This abnormal conservation of sodium is not limited to the kidney, since the sweat glands, salivary glands, and colons of these patients also conserve sodium (Berger & Steele, 1952). In order to effect this abnormal conservation, in the case of the nephron and colon sodium absorption is increased, while in the case of the salivary gland and sweat gland secretion is decreased.

Although this study is restricted to the intestine, it was launched with the notion that under conditions of sodium retention sodium transfer would be affected in the same manner across all four membranes. Absorption and secretion, that is, net transfer, for these four membranes may be the result of two unidirectional but opposite flows in the same limited area. It is known that this situation exists in the intestinal lumen (Visscher, Varco, Carr, Dean & Erickson, 1944; Visscher, Fetcher, Carr, Gregor, Bushey & Barker, 1944; Curran & Solomon, 1957; Berger, Kanzaki, Homer & Steele, 1959; Berger, Kanzaki & Steele, 1959). Here the addition or removal of sodium (potassium, chloride or water) is not the consequence of a simple one-way passage into or out of the lumen, but the amount appearing in the intestinal lumen is the net result of two simultaneous flows of sodium across the intestinal mucosa. Conservation of sodium may follow either a decrease in the rate at which sodium enters the lumen or an increase in the rate at which sodium leaves the lumen, or both. The object of this study was to determine which of the unidirectional flows was altered under conditions of sodium retention.

In order to determine unidirectional fluxes across a limited area of membrane, it is necessary to sample the contents of the lumen while avoiding contamination from other portions of the tubule or duct. This

poses obvious difficulties for a study of the kidney, the salivary gland or sweat gland, but segments of the intestine may easily be isolated in the dog by preparing a chronic Thiry fistula. This is an isolated segment of intestine fashioned into a pouch with an exteriorized stoma. Such Thiry fistulas were prepared in dogs. Sodium retention was induced with deoxycorticosterone acetate, since the abnormal conservation of sodium by the kidney, colon, salivary gland and sweat gland of the oedematous individual may be simulated in normal men by administration of deoxycorticosterone (Conn, 1949; Berger, Quinn & Homer, 1951; White, Entmacher, Rubin & Leiter, 1955). With the use of radio-isotopes the unidirectional fluxes of sodium and of potassium were measured across the mucosa of various segments of the dog intestine before and after the administration of deoxycorticosterone.

A study of the effects of a drug on the unidirectional fluxes of sodium across the intestine of the normal dog is complicated by a large inherent variability of repeated measurements of sodium flux under presumably the same controlled conditions (Berger, Kanzaki, Homer & Steele, 1959). In order to increase the sensitivity of the statistical evaluation of the measurements, paired experiments were employed. Immediately following 'control' measurements, deoxycorticosterone acetate was administered and a day later the measurements were repeated for the 'treated' experiment. The calculation for a significant effect was based on the difference between each 'control' and its paired 'treated' measurement.

The experiments are further hindered by another factor when deoxycorticosterone acetate is the drug under study. It is well known that the antinatriuretic effect of deoxycorticosterone is difficult to demonstrate in acute experiments on the normal dog (Barger, Berlin & Tulenko, 1958). In the experiments on the normal dog, to be described, one could not be certain that deoxycorticosterone was having an effect every time it was administered. Our solution was to accumulate a sufficient number of paired experiments to demonstrate a difference between the 'control' and 'treated' measurements.

Terminology. The terms 'unidirectional flux', 'influx' and 'efflux' deserve definition. 'Unidirectional flux' will refer to the one-way passage of electrolyte from one side of the intestinal mucosa to the other, which, in the case of sodium (and potassium) occurs concurrently with a one-way passage of sodium (or potassium) in the opposite direction. In this report 'influx' will denote flow into, and 'efflux' flow out of the intestinal lumen, and the direction of flow will be specifically stated, i.e. into or out of the lumen, unless it is otherwise obvious. The terms flux or flow will be reserved for unidirectional movements only. 'Absorption' will be used to indicate a net decrease in the amount of electrolyte or water in the lumen,

resulting from a flux out of the lumen that is greater than the flux into the lumen. Similarly, 'secretion' indicates a net increase in the amount of electrolyte in the lumen resulting from a greater flux into, than out of the lumen. Absorption and secretion will be used where unidirectional fluxes are unknown (for example, secretion of potassium by the distal portion of the nephron). 'Excretion' is reserved for the final excretory product contained in the stool.

METHODS

A chronic Thiry fistula was prepared in the dog by resecting a 20 cm section of proximal jejunum, distal ileum or distal colon with its blood supply intact, and re-establishing the continuity of the intestinal tract. One end of the resected portion was closed, and the other end was exteriorized through the skin of the abdominal wall to form a stoma through which solutions could be placed in the lumen of the isolated segment. After recovery from the operation the animals were trained to lie quietly during the experimental procedures so that anesthesia was unnecessary. The intestinal segment was flushed at the start of an experiment with a modified Ringer's solution containing (m-equiv/l.) Na 144, Cl 109, HCO_3 39, K 4, Mg 2 and SO_4 2. When the returned fluid was clear, 10 or 20 ml. of the same solution, containing in addition methyl-cellulose in concentration of 0·4 %, radiosodium (^{24}Na), and in some experiments radiopotassium (^{42}K) was pipetted into the intestinal segment through a catheter. The volume of fluid in the pouch was calculated from the amount of methyl-cellulose placed in the pouch and its concentration in subsequent samplings. In general, five or more samples were taken at 7–10 min intervals; in some experiments three samples were removed at 20 min intervals. When sampling was done in periods of 7–10 min, transfer rates were calculated for the interval between the first sample and each of the subsequent samples and the reported rate is a mean of these values. Where the samples were removed at 20 min intervals, the reported rate is a mean of the rates calculated from the first to second sample, from second to third, and from first to third.

Sodium and potassium were determined with an internal-standard flame photometer. After precipitating protein with the Somogyi zinc precipitant (Somogyi, 1930), methyl-cellulose was determined by heating 2 ml. of the supernatant fluid with 5 ml. of Harrison's diphenylamine reagent (Harrison, 1942) for 30 min at 108·3° C in an oil bath and measuring the concentration colorimetrically at 645 mμ (Kanzaki & Berger, 1959). Radiosodium (^{24}Na) was determined in the presence of radiopotassium (^{42}K) by Geiger-tube counting with and without a 350 mg/cm^2 aluminum filter (Tait & Williams, 1952). Radiosodium and radio-potassium were added to the modified Ringer's solution in amounts which would yield adequate counting rates and would have a ratio of sodium counts to potassium counts of 2:1 at the time of counting. Corrections were made for radioactive decay during the counting period.

Transfer rates were calculated for two compartment systems not in dynamic equilibrium (Berger & Steele, 1958). The following equations were used:

$$\beta = \frac{A - A_0}{t}\left[\frac{\ln\left[(\theta_A^n - \theta_B^n)/(\theta_{A_1} - \theta_{B_1})\right]}{-\ln\dfrac{[\mathrm{Na}]^n/[\mathrm{MC}]^n}{[\mathrm{Na}]_1/[\mathrm{MC}]_1}}\right] \tag{1}$$

and

$$\alpha = \frac{A - A_0}{t}\left[\frac{\ln\left[(\theta_A^n - \theta_B^n)/(\theta_{A_1} - \theta_{B_1})\right]}{-\ln\dfrac{[\mathrm{Na}]^n/[\mathrm{MC}]^n}{[\mathrm{Na}]_1/[\mathrm{MC}]_1}} - 1\right]. \tag{2}$$

The transfer rate of sodium (or potassium) into the bowel in micro-equivalents per minute is β, the rate out of the bowel, α. The micro-equivalents of sodium (or potassium) in the

intestine, corrected for that previously removed in sampling, is A_0 at the beginning and A at the end of a period of t min. θ_{A_1}, $[Na]_1$ and $[MC]_1$, are respectively the specific activity (counts/min/μequiv), sodium (or potassium) concentration (μequiv/ml.) and methylcellulose concentration (mg/ml.) in the first sample and θ_A^n, $[Na]^n$, and $[MC]^n$ are their values at any subsequent sampling. Plasma specific activity is denoted by θ_{B_1}, for the first and θ_B^n for any subsequent sampling. The specific activity of the plasma may be neglected for potassium ($\theta_A \gg \theta_B$) and, except where radiosodium was administered intravenously, for most experiments specific activity of plasma sodium may also be neglected (Berger, Kanzaki, Homer & Steele, 1959). Further details of the method are described in previously published work (Berger & Steele, 1958; Berger, Kanzaki, Homer & Steele, 1959; Berger, Kanzaki & Steele, 1959).

The experiments were conducted in pairs, a control experiment and one in which the drug was used. The statistical evaluation of the results was based on the difference between the experiments of each pair. Once the control experiment was completed, deoxycorticosterone acetate 2 mg/kg in sesame oil was administered intramuscularly to the dog and measurements were repeated the following day (19–21 hr after deoxycorticosterone administration). Mean values are expressed $\pm$ the standard error ($\sigma_{\bar{x}}$) where $\sigma_{\bar{x}} = \frac{\sigma}{\sqrt{N}}$ and σ, the standard deviation, $= \sqrt{\left(\left[\frac{\Sigma x^2}{N} - \bar{x}^2\right]\left[\frac{N}{N-1}\right]\right)}$. The coefficient of correlation (r) was calculated from $\sqrt{bb'}$ where b is the slope of the regression line of x on y, and b' is the slope of the regression line of y on x. The coefficient of correlation was considered significant if $3\sigma z$ did not exceed the z transformation of r.

RESULTS

Effects of deoxycorticosterone on the dog small intestine

Two animals were studied, one with a jejunal, the other with an ileal fistula. In fifteen paired experiments on these dogs, one experiment a control the other 20 hr after intramuscular administration of deoxycorticosterone, sodium transfers were not altered. In six of these pairs, where potassium transfers were measured in addition to sodium, the administration of deoxycorticosterone did not alter transfer rates of potassium (Table 1).

Effects of deoxycorticosterone on the dog large intestine

Absorption and secretion. Four animals were studied, each with a Thiry fistula prepared from the colon. Twenty-nine pairs of experiments were conducted where sodium transfer was measured, and in thirteen of these potassium was measured in addition. Deoxycorticosterone increases the absorption of sodium from the colon and increases the secretion of potassium into the colon (Table 2). Those experiments which had the largest absorption of sodium from the lumen were not the same experiments as those which had the largest secretion of potassium (the correlation coefficient for net sodium difference between control and treated against net potassium difference was +0·48).

Unidirectional fluxes. Sodium decreased in the colonic lumen in consequence of an increase in the rate of transfer out of the colon; whereas the

TABLE 1. The effect of deoxycorticosterone on the unidirectional fluxes of sodium and potassium across the dog small intestine (μequiv/min/20 cm length of intestine)

Date of control measurement	Sodium									Potassium								
	Rate into lumen			Rate out of lumen			Net change in lumen			Rate into lumen			Rate out of lumen			Net change in lumen		
	CONT*	DOCA†	R_x–C‡	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C
Dog MAR, jejunum operation 23. x. 52																		
3. ii. 53§	65·4	84·0	+18·6	79·9	94·8	+14·9	−14·5	−10·8	+3·7									
10. iii. 53	78·4	113·9	+35·5	101·4	110·3	+8·9	−23·0	+3·6	+26·6									
7. iv. 53§	70·0	93·3	+23·3	62·9	99·7	+36·8	+7·1	−6·4	−13·5									
16. x. 56	65·5	83·2	+17·7	56·9	66·8	+9·9	+8·6	+16·4	+7·8									
30. x. 56	66·6	105·2	+38·6	55·3	77·4	+22·1	+11·3	+27·8	+16·5									
7. v. 57	80·5	64·7	−15·8	46·9	42·6	−4·3	+33·6	+22·1	−11·5	2·80	2·05	−0·75	1·59	1·25	−0·34	+1·21	+0·80	−0·41
30. vii. 57	71·4	70·7	−0·7	65·8	60·4	−5·4	+5·6	+10·3	+4·7	5·62	2·21	−3·41	5·24	1·89	−3·35	+0·38	+0·32	−0·06
Dog BRN, ileum operation 6. vi. 52																		
21. x. 52**	81·7	105·4	+23·7	95·4	89·2	−6·2	−13·7	+16·2	+29·9									
17. iii. 53	72·9	81·1	+8·2	65·3	67·7	+2·4	+7·6	+13·4	+5·8									
14. iv. 53§	79·9	78·1	−1·8	80·3	60·7	−19·6	−0·4	+17·4	+17·8									
16. x. 56	52·8	59·2	+6·4	44·7	51·9	+7·2	+8·1	+7·3	−0·8									
18. vi. 57	98·2	82·1	−16·1	42·3	30·8	−11·5	+55·9	+51·3	−4·6	2·66	3·87	+1·21	1·05	1·67	+0·62	+1·61	+2·20	+0·59
23. vii. 57	82·1	74·6	−7·5	49·7	52·3	+2·6	+32·4	+22·3	−10·1	2·98	2·84	−0·14	1·78	1·60	−0·18	+1·20	+1·24	+0·04
6. viii. 57	94·3	70·0	−24·3	32·8	39·2	+6·4	+61·5	+30·8	−30·7	3·65	2·75	−0·90	1·53	1·78	+0·25	+2·12	+0·97	−1·15
3. xii. 57	51·0	75·4	+24·4	40·6	52·3	+11·7	+10·4	+23·1	+12·7	1·88	2·41	+0·53	1·71	1·88	+0·17	+0·17	+0·53	+0·36
Mean	74·0	82·7	+8·7	61·3	66·4	+5·1	+12·7	+16·3	+3·6	3·26	2·69	−0·58	2·15	1·68	−0·47	+1·12	+1·01	−0·10
σ	13·2	15·7		20·3	23·5		24·1	15·2		1·29	0·65		1·54	0·24		0·74	0·67	
$\sigma_{\bar{x}}$	3·4	4·0	5·0	5·2	6·1	3·6	6·2	3·9	4·2	0·52	0·27	0·65	0·63	0·10	0·59	0·30	0·27	0·25
t			1·7			1·4			0·9			0·88			0·80			0·42

* CONT control measurements; † DOCA measurements ~ 20 hr after an intramuscular injection of deoxycorticosterone acetate in sesame oil, 2·0 mg/kg body weight; ‡ R_x–C change in flux rate following deoxycorticosterone; § Dog on high-salt diet by adding salt to drinking water (150–250 m-equiv/l.). Usual diet contained up to 6 m-equiv kg body weight/day; the high-salt diet 7–15 m-equiv/kg/day; ** Measurements made with radiosodium administered intravenously.

TABLE 2. The effect of deoxycorticosterone on the unidirectional fluxes of sodium and potassium across the dog large intestine (μequiv/min/20 cm length of intestine)

Date of control measurement	Sodium									Potassium								
	Rate into lumen			Rate out of lumen			Net change in lumen			Rate into lumen			Rate out of lumen			Net change in lumen		
	CONT*	DOCA†	R_x–C‡	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C	CONT	DOCA	R_x–C
Dog JIT, colon operation 7. ii. 57																		
2. iv. 57	22·0	16·2	−5·8	68·0	52·4	−15·6	−46·0	−36·2	+9·8	4·18	18·47	+14·29	2·95	6·73	+3·78	+1·23	+11·74	+10·51
11. iii. 58	31·4	17·3	−14·1	63·5	50·9	−12·6	−32·1	−33·6	−1·5	4·48	4·05	−0·43	1·16	1·10	−0·06	+3·32	+2·95	−0·37
Dog MAM, colon operation 27. ii. 57																		
9. iv. 57	21·3	25·4	+4·1	73·9	75·0	+1·1	−52·6	−49·6	+3·0	5·61	7·04	+1·43	4·34	3·82	−0·52	+1·27	+3·22	+1·95
6. viii. 57	22·0	23·2	+1·2	70·1	86·8	+16·7	−48·1	−63·6	−15·5	2·05	7·89	+5·84	2·30	5·34	+3·04	−0·25	+2·55	+2·80
11. iii. 58	26·7	33·9	+7·2	64·5	69·8	+5·3	−37·8	−35·9	+1·9	6·19	8·31	+2·12	3·72	5·01	+1·29	+2·47	+3·30	+0·83
8. vii. 58	29·0	33·6	+4·6	66·1	89·1	+23·0	−37·1	−55·5	−18·4	5·68	6·95	+1·27	3·01	4·37	+1·36	+2·67	+2·58	−0·09
Dog LDY, colon operation 2. iv. 52																		
5. xi. 52§	27·2	37·2	+10·0	75·3	85·7	+10·4	−48·1	−48·5	−0·4									
27. i. 53§	39·2	24·1	−15·1	57·6	64·5	+6·9	−18·4	−40·4	−22·0									
17. ii. 53§	21·4	25·4	+4·0	50·0	61·1	+11·1	−28·6	−35·7	−7·1									
3. iii. 53	29·8	33·8	+4·0	72·5	88·9	+16·4	−42·7	−55·1	−12·4									
31. iii. 53§	30·1	22·9	−7·2	65·8	52·1	−13·7	−35·7	−29·2	+6·5									
9. x. 56	17·7	16·9	−0·8	45·0	44·9	−0·1	−27·3	−28·0	−0·7									
30. x. 56	26·7	39·8	+13·1	48·3	59·6	+11·3	−21·6	−19·8	+1·8									
13. xi. 56	22·6	12·6	−10·0	49·6	37·8	−11·8	−27·0	−25·2	+1·8									
23. iv. 57	26·5	20·7	−5·8	44·5	50·7	+6·2	−18·0	−30·0	−12·0	0·78	3·58	+2·80	0·96	1·32	+0·36	−0·18	+2·26	+2·44
Dog SKP, colon operation 4. vi. 52																		
15. x. 52	31·1	29·4	−1·7	53·3	96·7	+43·4	−22·2	−67·3	−45·1									
28. x. 52§	63·0	17·4	−45·6	35·8	75·4	+39·6	+27·2	−58·0	−85·2									
5. xi. 52§	16·4	22·6	+6·2	55·8	75·0	+19·2	−39·4	−52·4	−13·0									
10. ii. 53§	28·4	45·6	+17·2	69·4	103·5	+34·1	−41·0	−57·9	−16·9									
25. ii. 53	53·5	39·3	−14·2	70·6	80·5	+9·9	−17·1	−41·2	−24·1									
24. iii. 53	28·3	36·8	+8·5	51·6	79·5	+27·9	−23·3	−42·7	−19·4									
28. iv. 53§	22·1	37·9	+15·8	55·4	85·5	+30·1	−33·3	−47·6	−14·3									
9. x. 56	17·0	19·3	+2·3	45·3	49·1	+3·8	−28·3	−29·8	−1·5									
22. i. 57	15·2	32·4	+17·2	43·7	64·8	+21·1	−28·5	−32·4	−3·9	2·21	6·12	+3·91	1·83	2·50	+0·67	+0·38	+3·62	+3·24
5. ii. 57	22·6	12·7	−9·9	50·7	44·4	−6·3	−28·1	−31·7	−3·6	1·84	4·40	+2·56	1·80	2·05	+0·25	+0·04	+2·35	+2·31
16. iv. 57	24·0	22·9	−1·1	58·8	54·3	−4·5	−34·8	−31·4	+3·4	1·41	4·08	+2·67	1·42	1·73	+0·31	−0·01	+2·35	+2·36
30. vii. 57	23·0	15·1	−7·9	39·0	53·8	+14·8	−16·0	−38·7	−22·7	1·51	4·72	+3·21	0·92	2·65	+1·73	+0·59	+2·07	+1·48
8. vii. 58	44·6	21·6	−23·0	28·6	60·9	+32·3	+16·0	−39·3	−55·3	4·85	4·35	−0·50	0·72	1·63	+0·91	+4·13	+2·72	−1·41
15. vii. 58	29·3	35·5	+6·2	27·1	41·5	+14·4	+2·2	−6·0	−8·2	3·02	13·26	+10·24	1·11	2·68	+1·57	+1·91	+10·58	+8·67
Mean	28·0	26·6	−1·4	55·2	66·7	+11·5	−27·2	−40·1	−12·9	3·37	7·17	+3·80	2·02	3·15	+1·13	+1·35	+4·02	+2·67
σ	10·6	9·2		13·4	18·0		17·9	13·8		1·87	4·30		1·16	1·76		1·44	3·21	
$\sigma_{\bar{x}}$	2·0	1·7	2·5	2·5	3·3	3·0	3·3	2·6	3·7	0·52	1·19	1·16	0·32	0·49	0·34	0·40	0·89	0·94
t			0·6			3·9			3·5			3·27			3·35			2·85

* Abbreviations as for Table 1.

mean control value was $55{\cdot}2 \pm 2{\cdot}5$ μequiv/min, after deoxycorticosterone it increased to $66{\cdot}7 \pm 3{\cdot}3$ μequiv/min. Sodium transfer into the colonic lumen was unaffected by deoxycorticosterone, $28{\cdot}0 \pm 2{\cdot}0$ in the control as compared with $26{\cdot}6 \pm 1{\cdot}7$ μequiv/min after deoxycorticosterone.

Potassium transfer rates into and out of the colonic lumen were both increased by deoxycorticosterone; the influx into the lumen increased to a greater degree than the efflux, with a resultant net increase in the potassium in the lumen. The mean potassium influx into the lumen was $3{\cdot}37 \pm 0{\cdot}52$ in the control experiments against $7{\cdot}17 \pm 1{\cdot}19$ μequiv/min after deoxycorticosterone. The mean potassium efflux from the colonic lumen was $2{\cdot}02 \pm 0{\cdot}32$ in the control and $3{\cdot}15 \pm 0{\cdot}49$ μequiv/min after deoxycorticosterone.

Those experiments where sodium efflux from the colonic lumen was largest were not the same experiments as those where potassium influx was largest ($r = +0{\cdot}18$) neither was the potassium efflux correlated with sodium influx ($r = -0{\cdot}07$).

DISCUSSION

Intestinal absorption and secretion of sodium and potassium

Small intestine. The data fail to demonstrate an effect of intramuscularly administered deoxycorticosterone acetate on the absorption or secretion of sodium or potassium by the small intestine. However, by other techniques, possible hormonal influences on the small intestine have been shown. Field, Swell, Dailey, Trout & Boyd (1955) have demonstrated that the sodium concentration decreased and potassium concentration increased in the terminal ileum of the dog when the daily dietary sodium was changed from 85 to 1 μequiv. Clark (1939) found that following the administration of sodium chloride by mouth, more chloride was found in the intestine of the adrenalectomized rat than in the normal control. Dennis & Wood (1940), observing two adrenalectomized dogs, found a decrease in the absorption of sodium, potassium and chloride from chronic lower ileal Thiry fistulas when adrenal cortical extract was withheld. The difference between the present observations and those of Clark (1939), Dennis & Wood (1940) and Field *et al.* (1955) is in all probability a consequence of the type of experiment performed.

Large intestine. There is a considerable body of evidence to indicate that the large intestine, as opposed to the small intestine, does alter the absorption or secretion of electrolyte in response to hormonal factors. The administration of deoxycorticosterone to the rat decreases faecal sodium excretion (Berger *et al.* 1951). The administration of 9-α-fluorohydrocortisone to the dog decreases faecal sodium and increases faecal potassium (Poutsiaka, Thomas & Linegar, 1957). In the dog, during the development

of ascites following constriction of the thoracic inferior vena cava, there is a decrease in faecal sodium and an increase in faecal potassium (Davis & Howell, 1953). This reduced ratio of sodium:potassium in the faeces returns toward normal after bilateral adrenalectomy (Davis, Howell & Southworth, 1953) and the reduced ratio has been correlated with increased aldosterone excretion in the urine (Davis, Ball, Bahn & Goodkind, 1959).

In man on a high-salt diet, measurements suggest that the administration of deoxycorticosterone decreases stool sodium and increases stool potassium (Relman & Schwartz, 1952), whereas on a normal salt intake, and receiving cation exchange resin by mouth, the administration of deoxycorticosterone acetate reduces the amount of sodium appearing with the resin in the stool (Berger *et al.* 1951). More sodium is removed by the resin from the normal individual than from the oedematous patient, who fails to excrete sodium in the urine in amounts equal to the dietary intake (Berger & Steele, 1952). Administration of resin to individuals who lack the sodium-retaining hormone (e.g. in Addison's disease or after bilateral adrenalectomy) results in a large excretion of sodium in the stool, which again may be reduced by the administration of deoxycorticosterone (Emerson, Kahn & Jenkins, 1953). Duncan, Liddle & Bartter (1956) demonstrated that when large amounts of sodium were removed in the stool by resin, the urinary aldosterone was diminished, and conversely the faecal excretion of small amounts of sodium was associated with large amounts of urinary aldosterone. The evidence cited indicates that the faecal excretion of sodium in rat, dog and man is in part regulated by the presence or absence of mineralocorticoids.

Unidirectional fluxes of sodium and potassium

Small intestine. Turning our attention to the unidirectional fluxes which determine absorption or secretion of sodium or potassium, these fluxes across the small intestine were not altered by deoxycorticosterone. Similarly, Barnett, Turner & Hardy (1958) found that when radiosodium was placed in a chronic Thiry ileal loop, the subsequent blood levels of radiosodium were the same in six dogs, four serving as controls and two receiving 20 mg of ACTH intravenously.

Large intestine. As would be expected from the observations of faecal electrolyte excretion, there were changes in the unidirectional transfer rates of sodium and potassium across the colon after deoxycorticosterone. Sodium transfer into the lumen of the colon was unchanged, while transfer out of the lumen was increased. The unidirectional potassium flux into the colon increased after deoxycorticosterone to a greater extent than the increase in potassium flux out of the colon, with a resultant net increase in the amount of potassium in the colon lumen. Although the efflux of

sodium from the colonic lumen and the influx of potassium into the lumen are increased after deoxycorticosterone, the experiments with the largest sodium efflux were not the same experiments as those with the largest potassium influx ($r = +0{\cdot}18$). The data do not support an exchange of sodium for potassium across the intestinal mucosa after deoxycorticosterone, such as has been considered (from observations of the effects of acetazoleamide and mercury) to occur across the distal portion of the kidney tubule (Berliner, Kennedy & Orloff, 1951; Mudge, 1953).

Sweat gland, salivary gland and kidney

From necessarily indirect evidence, sodium is considered to be secreted by the proximal portion of the sweat gland, parotid gland and submaxillary gland and then reabsorbed distally (White *et al.* 1955; Schwartz & Thaysen, 1956). If deoxycorticosterone has an effect on the sweat and salivary glands similar to that on the intestine, where it increases the rate of sodium transfer from lumen to blood, then a movement of sodium from lumen to blood exists in the sweat and salivary glands and this would add further indirect evidence that sodium absorption occurs in these glands.

As yet little can be said about the existence of two opposite unidirectional fluxes occurring proximally and again distally across the sweat and salivary glands. With regard to the kidney, Solomon, Hanenson, Shipp, Windhager & Schatzmann (1957) and Oken, Whittembury, Windhager, Schatzmann & Solomon (1959) have reported unidirectional movements of sodium into and out of the proximal tubule of Necturus kidney. Tosteson & White (1959), using tritiated water and stop-flow urine samples, have indicated that in the dog kidney water moves into and out of both the proximal and distal tubules. The intestine allows for direct measurement of such unidirectional flows occurring within an area of histologically similar intestinal mucosa and permits the *in vivo* study of the effect of various drugs on such fluxes.

SUMMARY

1. Measurements of the unidirectional flux rates of sodium and potassium across the dog colon demonstrated the manner in which deoxycorticosterone increased sodium absorption and potassium secretion.

2. Deoxycorticosterone increased the rate at which sodium left the colon, with little effect on the influx of sodium into the colon.

3. In the case of potassium, deoxycorticosterone increased potassium flux both into and out of the intestine; the rate of potassium influx into the colon increased to a greater degree than that of efflux, resulting in a net increase of potassium in the colon.

4. In contrast to the colon, no effect of deoxycorticosterone on the transfer rates of sodium or potassium across the dog small intestine was demonstrated.

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