

ALDOSTERONE ON SODIUM TRANSPORT OF RAT DISTAL COLON IN LONG-TERM ADRENALECTOMY DURING ACUTE AND CHRONIC SUBSTITUTION

BY MICHAEL HORSTER AND ANDREAS LÜCKHOFF

From the Physiologisches Institut der Universität München, Munich, F.R.G.

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SUMMARY

1. The influence of aldosterone upon water and sodium transport properties of the distal colon was studied in long-term adrenalectomy (11–29 days).

2. Six groups of rats were used: I, normal (control); II, adrenalectomized; III, adrenalectomized, acutely substituted with aldosterone (200 $\mu\text{g}/\text{kg}$ 4 h); IV, adrenalectomized rats receiving aldosterone simultaneously with the specific inhibitor spironolactone (40 mg/kg within 4 h); V, adrenalectomized, substituted chronically with aldosterone (2 \times 75 $\mu\text{g}/\text{kg}$ day); VI, adrenalectomized, substituted chronically with dexamethasone (120 $\mu\text{g}/\text{kg}$ day).

3. Distal colon segments were perfused *in vivo* with isotonic Ringer solution. In addition, a hypotonic electrolyte solution (Na^+ 111 mM) was used in groups I and II.

4. In adrenalectomy (group II), net water absorption (J_v) was significantly decreased from (normal) $54.4 \mu\text{l}/\text{h cm}^2 \pm 10.5$ ($n = 9$) to $41.2 \mu\text{l}/\text{h cm}^2 \pm 7.3$ ($n = 4$), and net Na^+ absorption (J_{Na}) was decreased from $13.6 \mu\text{mol}/\text{h cm}^2 + 3.5$ to $8.5 \mu\text{mol}/\text{h cm}^2 \pm 0.9$ (isotonic perfusate). Similarly, J_v was decreased from $54.0 \mu\text{l}/\text{h cm}^2 \pm 8.3$ ($n = 4$) to $37.3 \mu\text{l}/\text{h cm}^2 \pm 4.2$ ($n = 7$), and J_{Na} from $8.6 \mu\text{mol}/\text{h cm}^2 \pm 2.1$ to $4.2 \mu\text{mol}/\text{h cm}^2 \pm 2.1$ (hypotonic perfusate).

5. Acute aldosterone substitution in adrenalectomy (III) had no effect upon J_v ($37.1 \mu\text{l}/\text{h cm}^2 \pm 10.3$; $n = 5$) but increased J_{Na} to $10.3 \mu\text{mol}/\text{h cm}^2 \pm 0.3$.

6. The luminal Na^+ steady-state concentration was higher in group II ($11.2 \text{ mmol l}^{-1} \pm 3.6$; $n = 6$) than in group I ($3.3 \text{ mmol l}^{-1} \pm 1.4$; $n = 29$). Acute aldosterone substitution restored this value to normal ($3.0 \text{ mmol l}^{-1} \pm 1.2$; $n = 4$). The aldosterone effect was partly blocked by spironolactone: the Na^+ steady-state concentration was $6.4 \text{ mmol/l} \pm 0.6$ ($n = 3$) in group IV.

7. At the steady-state luminal Na^+ concentration, the osmotically driven *net water fluxes* were not different in groups I and II, indicating that the hydraulic permeability coefficient is not altered in adrenalectomy.

8. In group V, J_v ($54.9 \mu\text{l}/\text{h cm}^2 \pm 10.9$; $n = 7$) and J_{Na} ($11.9 \mu\text{mol}/\text{h cm}^2 \pm 1.7$; $n = 6$) were not significantly different from normal.

9. In group VI, J_v ($37.3 \mu\text{l}/\text{h cm}^2 \pm 6.0$; $n = 5$) and J_{Na} ($8.0 \mu\text{mol}/\text{h cm}^2 \pm 1.4$) were not significantly different from group II.

10. The mineralocorticoid effects of aldosterone in long-term adrenalectomy appear to represent the principal determining factors of colonic J_v and J_{Na} .

INTRODUCTION

Adrenalectomy establishes an altered state of transporting epithelia in which aldosterone-independent functions of ion and water transport and their stimulation by specific, dose-dependent substitution of corticosteroids can be evaluated. The colon, one of the corticoid target organs, has served this purpose in a variety of studies.

Distal colon Na^+ absorption was not significantly depressed after adrenalectomy, although it was somewhat lower than control (Dolman & Edmonds, 1975); by contrast, J_{Na} of the proximal colon was clearly decreased (Dolman & Edmonds, 1975), and J_{Na} as well as J_v of the entire colon were lower after adrenalectomy (Bastl, Binder & Hayslett, 1980). Aldosterone in physiological amounts increased both J_{Na} and J_v in adrenalectomized rats (Edmonds & Marriott, 1967). Aldosterone substitution, corresponding to the endogenous secretion rate in rats on a low Na^+ diet, restored J_v to values of normal animals whereas J_{Na} remained below control (Bastl *et al.* 1980). Dexamethasone substitution, by contrast, maintained both J_v and J_{Na} at normal level (Bastl *et al.* 1980). This effect of the glucocorticoid is puzzling in view of the well established role of aldosterone in salt and fluid absorption, particularly since chronic spironolactone application decreased J_{Na} and J_v (Bastl *et al.* 1980). It may be relevant for the interpretation of these data (Bastl *et al.* 1980; Dolman & Edmonds, 1975; Edmonds & Marriott, 1967) that adrenalectomy was maintained for short-term periods only. The time elapsed after adrenalectomy was either 24–26 h (Bastl *et al.* 1980), or 'at least 2 days' (Dolman & Edmonds, 1975), or '2 days' and 'not less than 3 days' (Edmonds & Marriott, 1967). We believe, as do others (Chignell & Titus, 1966; Landon, Jazab & Forte, 1966), that this period is too short to reach an aldosterone-independent state of basal transport functions.

The aim of the present work, therefore, was a study in long-term adrenalectomy of colonic water and Na^+ absorption. The influence of acute *vs.* long-term substitution of aldosterone was evaluated. Mineralo- and glucocorticoid effects on transport functions were defined by application of the specific aldosterone inhibitor spironolactone and by continuous substitution of dexamethasone. Parts of the work have been reported in abstract form (Horster & Lückhoff, 1981).

METHODS

Six groups of rats (Wistar, 160–220 g body wt.) of either sex were studied: I, normal rats, kept on a standard diet (Altromin, Na content 2.5 g/kg, K content 6 g/kg) and tap water; II, adrenalectomized rats; III, adrenalectomized rats, substituted acutely with aldosterone; IV, adrenalectomized rats, substituted acutely with aldosterone and simultaneous administration of spironolactone; V, adrenalectomized rats, substituted chronically with aldosterone; VI, adrenalectomized rats, substituted chronically with dexamethasone.

Adrenalectomy. This was performed under pentobarbitone (Nembutal, 30 mg/kg) and ether anaesthesia. The adrenal glands were removed within their capsules via lateral incisions. After the operation, rats in groups II–IV received a single dose of dexamethasone (100 $\mu\text{g}/\text{kg}$, i.m.) and were kept on normal food and saline (0.7%). Rats in group V, following the operation, were injected with aldosterone (Aldocorten, Ciba), 75 $\mu\text{g}/\text{kg}$ s.c., every 12 h, and kept on tap water. Animals in group VI received dexamethasone (Fortecortin, Merck) in crystalline suspension, 120 $\mu\text{g}/\text{kg}$ day, and were kept on the saline solution. The amount of hormone substitution was chosen according to the endogenous production rate of corticosterone, measured in anaesthetized rats (Singer & Stack-Dunne,

1955). This dose is similar to that previously applied in a study on colonic transport in adrenalectomized rats (Bastl *et al.* 1980). In the acutely substituted groups (III and IV), the amount of aldosterone given during the experiment (4 h) corresponds to the secretion of the steroid in salt-depleted rats during a period of 24 h (190–360 $\mu\text{g}/\text{kg}$). (It is of interest that even a 10-fold lower dose of aldosterone (22.5 $\mu\text{g}/\text{kg}$) produced the same colonic transport changes as reported here for the higher dose, although with a considerable delay. Time-dependent effects, however, cannot be demonstrated in this preparation.) The colon perfusion studies (see below) were done 11–29 days after adrenalectomy and 4 h after the last injection in groups V and VI. Experiments were discontinued if one of the following criteria was apparent: (i) arterial blood pressure (A.B.P.) fell more than 20 mmHg below the initial value; (ii) A.B.P. fell below 85 mmHg; (iii) respiration was irregular; (v) peripheral skin became cyanotic. The aldosterone-substituted rats (group III) received a bolus injection of aldosterone (100 $\mu\text{g}/\text{kg}$ i.v.) followed by an aldosterone infusion (25 $\mu\text{g}/\text{kg}$ h). The animals of group IV were given spironolactone (Aldactone) simultaneously with aldosterone at doses of 20 mg/kg and 5 mg/kg h. Results reported here were obtained 150–400 min after the first injection.

Distal colon perfusion. The experimental procedure for distal colon perfusion has been described in detail (Lückhoff & Horster, 1981). In brief, rats were anaesthetized with Inactin (100 mg/kg) and placed on a heated table. Tracheotomy was performed, a Ringer–glucose infusion was given at a rate of 10 ml/kg h via the jugular vein, whereby plasma Na^+ concentration was restituted to normal value within the first hour. Urine concentrations of Na^+ and K^+ were measured in groups V and VI at the beginning of the perfusion experiment. Arterial blood pressure was recorded via a catheter in the femoral artery. The distal colon was reached through a subcostal incision, ligated twice at the level of the inferior mesenteric artery, incised between the ligations, and the perfusion pipette was tied in. The sample pipette was advanced through the anus and was fixed in the suprapubic region with a further ligation. The cannulated segment was then perfused with the aid of a pump (Unita, Braun Melsungen) at a rate of 1.0 ml/h. Every 15 min (sample period), the accumulated fluid was removed by a thin polythene tube, transferred into a plastic vial and weighed for volume determination. After an equilibrium time of not more than 105 min the effluent fluid had reached constant concentrations of salt and of the volume marker; at least four samples obtained during this plateau phase were considered necessary for any experiment reported here.

The measurement of the *perfused area* becomes an important determinant of the accuracy and relevance of the statistical differentiation since the differences of net absorptive rates (J_{Na} and J_v) are small. The size of the perfused area was always assessed after the end of an experiment prior to analysis of the effluent according to the standard protocol. The perfused segment was excised from the pipettes and opened along the mesenteric border. It was placed as a tissue sheet on paper and adrenaline (0.5 mm) was dripped on the surface. The ensuing relaxation allowed the tissue to be stretched without injury almost to a square. Length and width were measured with a scale to the millimetre. The measured areas ranged from 2.40 to 4.14 cm^2 . The relation of area to dry weight for the distal colon segments ($n = 34$) was 94 ± 13 (s.d.) cm^2/g dry weight (control).

Solutions. Three different types of solutions were used as perfusates. (1) An isotonic electrolyte solution containing (mm): Na, 141; K, 5; Ca, 1; Mg, 1.2; Cl, 121; HCO_3 , 25; H_2PO_4 , 1; SO_4 , 1.2; glucose 5.5. (2) A hypotonic electrolyte solution containing (mm): Na, 111; K, 10; Ca, 1; Mg, 1.2; Cl, 96; HCO_3 , 25; H_2PO_4 , 1; SO_4 , 1.2; glucose 5.5. (3) Solutions containing electrolytes near the distal colon steady-state concentrations plus dialysed polyethylene-glycol 4000 (PEG). The concentrations (mm) for groups II–IV were: Na, 8; K, 15; Ca, 1; Cl, 10; HCO_3 , 15; glucose, 5.5. PEG had been added to isosmolarity (290 mosm) for groups III and IV; the osmotic activities of the solutions used for group II were varied from 125 to 725 mosm to relate the net water flux to the luminal osmotic activity.

The *luminal steady-state Na^+ concentration* represents the maximal Na^+ gradient between lumen and blood established and maintained by the epithelium. The steady-state Na^+ values in normal rats have been reported (Lückhoff & Horster, 1981). Values for groups II–IV were obtained by perfusing the above PEG solutions at a rate of 1 ml/h. In this situation, Na^+ concentration of the effluent is the Na^+ steady-state concentration (Lückhoff & Horster, 1981).

Dialysed [^{14}C]PEG (Amersham) was used as volume marker. Net water absorption (J_v) was calculated according to

$$J_v = \dot{V}_0 \left(1 - \frac{^*C_0}{^*C_1} \right) A^{-1},$$

TABLE 1. Distal colon water and Na^+ absorptive rates for isotonic perfusate (145 mM- Na^+). Group I was normal and group II was adrenalectomized. The other groups were all adrenalectomized and either substituted with aldosterone acutely (III) or chronically (V), or substituted with dexamethasone chronically (VI)

Group	<i>n</i>	J_v ($\mu\text{l}/\text{h cm}^2$)	S.d. ^a	J_{Na} ($\mu\text{mol}/\text{h cm}^2$)	S.d. ^a	J_{Na}/J_v (mM)	S.d. ^a
I	9	54.4 ± 10.5	II*, III*, VI†	13.6 ± 3.5	II***, VI† ^b	265 ± 45	II*, VI***
II	4	41.2 ± 7.3	I*, V*	8.5 ± 0.9	I***, III†	203 ± 31	I*, III**, V*
III	5	37.1 ± 8.7	I*, V***	10.3 ± 0.3	III†, V*, VI†	287 ± 51	II**, VI† ^c
V	7/6	54.9 ± 10.9	II*, III***, VI†	11.9 ± 1.7	III†, III*, VI†	242 ± 24	II*, VI* ^c
VI	6	37.3 ± 6.0	I†, V†	8.0 ± 1.4	I†, III†, V†	215 ± 12	I***, III†, V*

^a Significantly different (s.d.) from group; ^b group I not s.d. from III (0.05 < *P* < 0.1); ^c group III not s.d. from V (0.05 < *P* < 0.1).

* *P* < 0.05; ** *P* < 0.025; *** *P* < 0.02.

† *P* < 0.01; ‡ *P* < 0.005.

where \dot{V}_0 is the perfusion rate, $*C$ is the activity of the [^{14}C]PEG of the perfusate ($*C_0$) and effluent ($*C_1$), A is the absorbing area. The net sodium absorption (J_{Na}) was calculated according to

$$J_{\text{Na}} = \dot{V}_0 \left(\text{Na}^+{}_0 - \text{Na}^+{}_1 \frac{*C_0}{*C_1} \right) A^{-1},$$

where Na^+ is the sodium concentration of the perfusate ($\text{Na}^+{}_0$) and effluent ($\text{Na}^+{}_1$).

For any experiment reported here, J_v and J_{Na} are given as the mean of all sample periods.

Data are presented as mean \pm s.d. Student's t test was used to compare mean values between groups.

TABLE 2. Distal colon water and Na^+ absorptive rates for hypotonic perfusate (110 mM- Na^+)

Group	n	J_v ($\mu\text{l/h cm}^2$)	J_{Na} ($\mu\text{mol/h cm}^2$)	J_{Na}/J_v (mM)
I. Normal	4	54.0 \pm 8.3 \dagger	8.6 \pm 2.1 ^a	157 \pm 19 ^c
II Adrenalectomized	7	37.3 \pm 12.5* \S	4.2 \pm 2.1 \dagger^b	125 \pm 18* ^b

^a S.d. from isotonic perfusate $P < 0.025$.

^b S.d. from isotonic perfusate ($P < 0.005$).

^c S.d. from isotonic perfusate ($P < 0.001$).

* Significantly different (s.d.) from normal ($P < 0.05$).

\dagger S.d. from normal ($P < 0.01$).

\ddagger Not s.d. from values at isotonic perfusate (Table 1) ($P > 0.95$).

\S Not s.d. from isotonic perfusate ($P > 0.5$).

RESULTS

Adrenalectomy

Net absorptive rates for water as well as for Na^+ are listed in Table 1 (isotonic perfusate) and Table 2 (hypotonic perfusate) for all groups studied. For groups I and II, water absorption from the isotonic perfusate was the same as from the hypotonic perfusate, although Na^+ absorption was different. In two normal rats, isotonic and hypotonic perfusates were used sequentially. Net water absorption was identical, indicating that the measurement of area itself did not artifactually influence absorptive rate. This protocol, however, could not be applied to adrenalectomized rats. Absorptive rates for both, J_v and J_{Na} , were significantly decreased in adrenalectomy. The decrease, however, was higher for Na^+ than for water, as expressed by the altered ratio of Na^+ to water absorption.

The steady-state Na concentration (Table 3) for the distal colon of adrenalectomized rats was evaluated by perfusing PEG solutions containing 8 mM- Na^+ . At the low perfusion rate of 1 ml/h, the effluent Na^+ represents the steady-state value. It was significantly higher than the value for normal rats, reported previously (Lückhoff & Horster, 1981).

The transmural hydraulic conductivity (L_p) of the distal colon has been derived in normal rats from the relation of the transmural net water flux (J_v) and the effective luminal osmotic activity, π_{eff} (the logarithmic mean between the perfusate and effluent osmotic activity), at Na^+ steady state (Lückhoff & Horster, 1981). This type of experiment was performed in adrenalectomized rats. At Na^+ steady state, luminal osmotic activity was varied by addition of different amounts of PEG to the perfusate. J_v and π_{eff} are depicted in Fig. 1 and compared with the regression line calculated from the results obtained in normal rats. These two sets of data indicate that an

increased transmural L_p in adrenalectomy can be excluded as the cause of the altered J_{Na}/J_v ratio. The close fit of the two data sets in Fig. 1, furthermore, suggests that the ability to absorb water from an hyperosmotic luminal fluid in the absence of transmural net Na^+ flux is maintained in adrenalectomy.

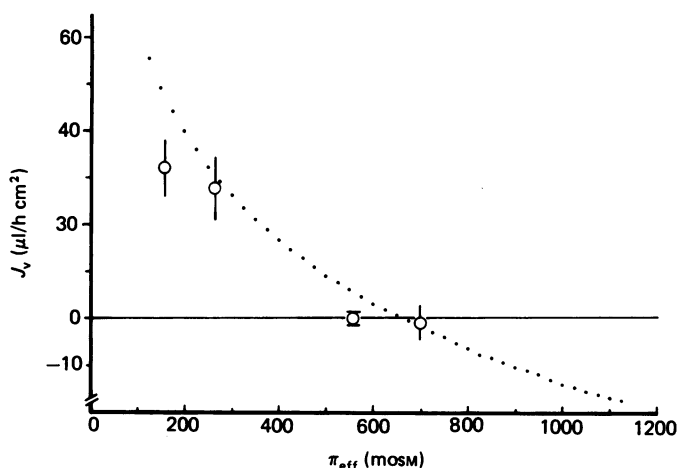


Fig. 1. Transmural net water flux (J_v) at Na^+ steady state and the effective luminal osmotic activity (π_{eff}) in the distal colon of adrenalectomized rats (O). Comparison with the regression line (···) of the J_v/π_{eff} relation in normal rats (Lückhoff & Horster, 1981).

TABLE 3. The luminal Na^+ steady-state concentration (Na^+_1) in the distal colon of groups I–IV. Group I was normal; the other groups were all adrenalectomized. III was acutely substituted with aldosterone and IV with aldosterone and spironolactone

Group	<i>n</i>	Na^+_1 (mM)	S.d. ^a
I§	29	3.3 ± 1.4	II†, IV‡
II	6	11.2 ± 3.6	I†, III†, IV*
III	4	3.0 ± 1.2	II†, IV‡
IV	3	6.4 ± 0.6	I†, II*, III†

^a Significantly different (s.d.) from group.

* $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$.

§ Data from Lückhoff & Horster, 1981.

Acute substitution of aldosterone

The luminal Na^+ steady-state concentration in adrenalectomy was restituted to normal by an acute aldosterone substitution (Table 3). The restitution was complete since there was no significant difference between group III and I. The aldosterone effect was partly blocked by spironolactone as evidenced by the Na^+ steady-state concentration of group IV. The value of this group was significantly different from those of all other groups.

Similarly, net Na^+ absorption from an isotonic Ringer solution was increased by aldosterone in chronic adrenalectomy (Table 1). The J_{Na} of group III was significantly higher than that of group II; it was lower, albeit not significantly, than the J_{Na} of

normal rats. Statistical analysis of the data (groups I and III) does not prove that the restoration of J_{Na} is complete.

Acute aldosterone substitution in chronic adrenalectomy had no effect on net water absorption (Table 1). Therefore, the J_{Na}/J_v ratio was maximal in group III; it was, however, not significantly higher than in group I.

Chronic substitution of aldosterone

Colonic fluxes of water and Na^+ in group V (Table 1) were not statistically different from normal (group I). The value of J_v in group V was greatly elevated in comparison to group III, and even J_{Na} showed a small, but significant increase. Urinary Na^+ concentration in group V was below 35 mM and urinary K^+ was higher than 200 mM, indicating adequate mineralocorticoid substitution.

Chronic substitution of dexamethasone

Absorptive rates of water and Na^+ in group VI (Table 1) were not statistically different from untreated, long-term adrenalectomized animals (group II). Dexamethasone, when given at a dose of 2 mg/kg day in three animals, restored J_v ($57.6 \pm 6.3 \mu\text{l/h cm}^2$) and J_{Na} ($12.8 \pm 0.4 \mu\text{mol/h cm}^2$) to normal values (group I), suggesting non-specific effects of this excessive dose on colonic water and Na^+ absorption.

DISCUSSION

Methods. The state of the adrenalectomized rats before the experiment was not evaluated in a detailed way. The animals were gaining some weight during the intake of 0.7% saline and standard diet. The urinary Na^+ concentrations in groups II and VI were above 120 mM and the Na/K ratio was always higher than 0.9.

The ratio of J_{Na} to J_v also deserves some consideration in relation to the methods. The luminal Na^+ concentration decreased along the perfused segment since the Na^+ concentration of the absorbate was very much higher than that of the perfusate. This decrease was between 12 and 28 mM. Further, J_{Na} , but not J_v , has been shown to depend upon the luminal Na^+ concentration; therefore J_{Na} must fall along the perfused segment. Hence, the J_{Na} will vary with different J_v values, as the latter result in different luminal Na^+ concentrations. This process, then, could explain the fact that no differences were observed in the J_{Na}/J_v ratio between I and III, as well as the finding that J_{Na} was lower (although not significantly) in III when compared with I. These considerations, in turn, may be used to predict identical J_{Na} but different J_v values between I and III at those colonic sites where the perfusate is still isotonic.

The specificity of aldosterone effects was tested by spironolactone at a dose which was 200-fold higher than that of aldosterone. However, the effect of aldosterone could not be blocked completely (see Results). This fact is in general agreement with observations in renal epithelia where even an 800-fold higher dose of spironolactone did not completely inhibit the effect of aldosterone on electrolyte transport (Kagawa, 1960).

Colonic transmural conductivity. The differences of the ratio J_{Na}/J_v between groups I and II (Tables 1 and 2) might have resulted from an altered transmural

hydraulic permeability coefficient (L_p), since the transmural water movement (J_v), driven by the net Na^+ movement (J_{Na}), depends on the relative ion and water conductivities of the epithelium. However, the *transmural* hydraulic conductivity (L_p) is not altered in adrenalectomy. The change, then, of the J_{Na}/J_v ratio must be attributed to effects of the hormone on parameters which either have not been assessed or are not accessible in the perfused epithelium. These include the possibility that the local cellular water permeability changes despite constant transmural conductance. Alternatively, aldosterone affects the major determinants of transmural Na net flux, i.e. transmural Na^+ permeability and active Na^+ transport which have been demonstrated in the colon (Dolman & Edmonds, 1975; Edmonds & Marriott, 1967, 1970) and in other epithelia to depend on the corticosteroid.

Colonic transmural fluxes of Na^+ and water have previously been studied during *in vivo* perfusion of the entire proximal and distal epithelium in adrenalectomized rats (Bastl *et al.* 1980). J_v and J_{Na} were measured 24–26 h after adrenalectomy and were found to be decreased by 60 and 53 %, respectively. When adrenalectomized rats were given aldosterone (300 $\mu\text{g}/\text{kg}$ per day), J_v was found to be normal whereas transmural J_{Na} reached only 70 % of control. However, dexamethasone (100 $\mu\text{g}/\text{kg}$ per day), when given in the adrenalectomized state, maintained both J_{Na} and J_v . It was concluded that glucocorticoid hormones exert regulatory functions on colonic fluid and ion absorption. Similarly, when aldosterone ($2 \times 5 \mu\text{g}/\text{kg}$ within 3 h) was injected in 2-day adrenalectomized rats (Edmonds & Marriott, 1967), J_v of the distal colon increased from 22.6 ± 9.0 to $45.5 \pm 6.0 \mu\text{l}/\text{h cm}$ and J_{Na} from 8.22 ± 1.0 to $13.0 \pm 1.4 \mu\text{mol}/\text{h cm}$. Another study (Fromm & Hegel, 1979) in long-term (1–2 weeks) adrenalectomized rats has demonstrated that a single dose of aldosterone (40 $\mu\text{g}/\text{kg}$) restores the transmural electric potential difference of the rectum to normal. (It is likely that the definition of the term ‘rectum’ includes a part of the distal colon, as defined in the present work.) The present study has demonstrated a complete restoration of the luminal steady-state Na^+ concentration and a significant increase of J_{Na} in the distal colon under the influence of aldosterone when substituted acutely in chronically adrenalectomized rats. The acute aldosterone substitution did not alter J_v . By contrast, chronic substitution of aldosterone in long-term adrenalectomized rats, as shown in the present study, maintained water and Na^+ absorption.

Furthermore, the chronic substitution of dexamethasone in long-term adrenalectomized rats failed to sustain water and Na^+ transport rates, whereas in short-term adrenalectomy the same dose of dexamethasone was shown to preserve water and electrolyte movement.

The differing data and conclusions reached on the basis of steroid substitution in acute *vs.* long-term adrenalectomy suggest that these may represent two functionally different states. The mineralocorticoid effects of aldosterone in long-term adrenalectomized rats appear to represent the main determining factors in the regulation of colonic electrolyte and water absorption.

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