Na^+-K^+-Activated Adenosine Triphosphatase and Intestinal Electrolyte Transport

EFFECT OF ADRENAL STEROIDS

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ABSTRACT Sodium-potassium-activated adenosine triphosphatase (Na-K-ATPase) is associated with electrolyte transport in many tissues. To help delineate its role in intestinal transport, changes in rat intestinal electrolyte and water transport induced by injecting methylprednisolone acetate 3 mg/100 g or deoxycorticosterone acetate (DOCA) 0.5 mg/100 g per day for 3 days were correlated with changes in Na-K-ATPase activity. Methylprednisolone increased sodium and water absorption, potassium secretion, transmural potential difference, and Na-K-ATPase activity in the jejunum, ileum, and colon. Examination of isolated epithelial cells demonstrated that the jejunal and ileal increase in Na-K-ATPase occurred in both the villus tip and crypt areas. The time-courses of the ileal enzyme and transport changes were identical. Permeability, Mg-ATPase, and adenylate cyclase activities were unchanged by methylprednisolone. DOCA increased sodium and water absorption, potassium secretion, transmural potential difference, and Na-K-ATPase activity in the colon alone. Colonic Mg-ATPase and adenylate cyclase activities were unaffected. Jejunal and ileal enzyme activity, electrolyte transport, and permeability were unchanged by DOCA. Methylprednisolone and DOCA were not additive in their effect on colonic Na-K-ATPase activity. Methylprednisolone and DOCA increased electrolyte and water transport and Na-K-ATPase activity concomitantly in specific segments of small intestine and colon. These data are consistent with an important role for Na-K-ATPase in intestinal electrolyte and water transport.

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INTRODUCTION

Sodium-potassium-activated adenosine triphosphatase (Na-K-ATPase) is associated with sodium and potassium transport in a large number of tissues (1). The relationship between Na-K-ATPase activity and fluid movement across epithelial membranes has been most clearly defined in the kidney (2–4). Adrenocorticosteroids have been shown to increase renal electrolyte transport and Na-K-ATPase activity at identical sites along the tubule (5–8). Whether a similar relationship between Na-K-ATPase and electrolyte transport exists in the intestine is not known. Adrenocorticosteroids have been shown to enhance colonic sodium absorption, potassium secretion, and transmural potential difference (PD)[1] (9–13). Except for a single report (14), however, effects on colonic Na-K-ATPase have not been studied.

To further delineate the role of Na-K-ATPase in intestinal fluid transport, increases in electrolyte and water transport induced by gluco and mineralocorticoids were correlated with changes in Na-K-ATPase activity in the small intestine and colon of the rat.

METHODS

Normal male albino Walter Reed rats[2] weighing 200–300 g were maintained on a standard diet with free access to water. Methylprednisolone acetate (Depo-Medrol, Upjohn Co., Kalamazoo, Mich.) was injected subcutaneously as an

[1] *Abbreviations used in this paper:* cAMP, adenosine 3′,5′-cyclic monophosphate; DOCA, deoxycorticosterone acetate; PD, potential difference; ΔPD, change in potential difference; Pi, inorganic phosphate.

[2] In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Research Council.

aqueous suspension in a dose of 3 mg/100 g per day for 1 or 3 days to one group of animals. Deoxycorticosterone acetate (Percorten, Ciba Corp., Summit, N. J.) was injected subcutaneously as a suspension in sesame oil in a dose of 0.5 mg/100 g per day for 3 days to another group of rats. A severalfold higher dose or longer period of injection of either steroid did not affect the results obtained with the above protocol. Untreated normal littermates of similar weight served as controls for each group. 24 h after the last steroid injection, the small intestine and colon of experimental rats were perfused in vivo. After perfusion, mucosa obtained from the perfused segments of jejunum, ileum, and colon was assayed for ATPase and adenylate cyclase activities. In preliminary studies, injection of sesame oil did not affect electrolyte or water transport, and neither the sesame oil injections nor the perfusion studies affected ATPase or adenylate cyclase activities.

Transport studies. Under sodium pentobarbital anesthesia (5 mg/100 g), 15 cm segments of jejunum, ileum, and colon were perfused in vivo. Jejunal and ileal segments began 1 cm distal to the ligament of Treitz and 16 cm proximal to the ileocecal valve, respectively. After rinsing each segment with warm perfusate, either jejunum and colon or ileum and colon were perfused simultaneously with an isotonic (305 mosmol/liter) saline solution at 37°C at 0.5 ml/min by a Harvard infusion pump (Model 954, Harvard Apparatus Co., Inc., Millis, Mass.). The perfusion solution (Solution A) contained 130 mM Na^+, 100 mM Cl^-, 5.0 mM K^+, 30 mM HCO^-_3, 56 mM glucose, and 6 g/liter polyethylene glycol. [^{14}C]polyethylene glycol (New England Nuclear, Boston, Mass.) was added as a nonabsorbable water marker. After a 30-min equilibration period, two 30-min collections were obtained and measured to the nearest 0.1 ml. After the perfusions, the intestinal segments were measured by the same observer in a uniform manner and assayed for enzyme activity.

[^{14}C]polyethylene glycol was measured in a Beckman Liquid Scintillation System LS-345 (Beckman Instruments, Inc., Fullerton, Calif.). Sodium and potassium were measured by flame photometry and osmolality by freezing point depression. Glucose was measured by a standard *o*-toluidine method (15). Water, sodium, potassium, and glucose transport rates were calculated by standard formulae (16). For uniformity, the results were expressed as μl, μeq, or mmol per 30 min per 15 cm intestinal length. Net lumen to blood flux was termed absorption (negative sign), whereas net blood to lumen flux was termed secretion (positive sign).

PD and permeability studies. Deoxycorticosterone acetate (DOCA) and methylprednisolone-treated and control rats were cannulated as above, but polyethylene tubing (PE 190) containing 2.5% agar in Solution A was inserted distally into each segment as a bridge for determination of PD. A bridge to the peritoneal cavity served as a reference, and both bridges were then inserted into half cells containing saturated KCl and balanced calomel electrodes. PD was measured by a high impedence direct current potentiometer (Orion Research Model 801A, Orion Research Inc., Cambridge, Mass.) and was recorded every 5 min for 30 min after a 30-min steady-state period. The perfusion solution was then changed from Solution A to a hyperosmolar solution (405 mosmol/liter) containing 100 mM mannitol in Solution A. The change in PD (ΔPD) induced by this hyperosmolar solution in treated and untreated rats was compared and used as an estimate of small intestinal permeability (17–19).

Morphological and isolated cell studies. In several methylprednisolone-treated and control rats, coded sections of jejunum and ileum were fixed in formalin, embedded in paraffin, stained with hematoxylin and eosin, and examined by light microscopy. Villus height and crypt depth were measured by eyepiece micrometry. In others, separated villus tip and crypt cells were collected, as previously described (20). Jejunal and ileal segments were incubated in a solution containing 27 mM sodium citrate, 96 mM NaCl, 1.5 mM KCl, 8 mM KH_2PO_4, and 5.6 mM Na_2HPO_4 (pH 7.3) at 37°C for 15 min. Succeeding incubation periods with a solution containing 130 mM NaCl, 5 mM Na_2EDTA, and 30 mM imidazole (pH 6.8) resulted in villus tip cells in early collections and crypt cells in late collections. After washing, these isolated cells were assayed for alkaline phosphatase by the method of Weiser (21), thymidine kinase by the method of Breitman (22), and ATPase activity (20).

Enzyme assays. Mucosa obtained from intestinal segments of perfused rats by scraping with a glass slide and the isolated villus tip and crypt cell collections were homogenized with a Teflon pestle and iced glass homogenizer in a solution containing 130 mM NaCl, 5 mM Na_2 EDTA, 30 mM imidazole, and 2.4 mM sodium deoxycholate (pH 6.8). The membrane-rich pellet obtained after successive centrifugations at 770 × *g* and 10,000 × *g* for 10 min at 0°C was incubated at 37°C for 15 min in a solution containing 100 mM NaCl, 20 mM KCl, 10 mM imidazole, 5.6 mM $MgCl_2$, 5.6 mM disodium ATP, and 5–30 μg/ml protein. Details of the pellet preparation, the distribution of ATPase activities among the fractions obtained by centrifugation, and the ATPase assay have been described (20, 23). Results were expressed as micromoles of inorganic phosphate (Pi) liberated per millgram protein per hour.

Another part of the mucosal scrapings from perfused rats was homogenized with an iced sintered glass homogenizer in a solution containing 75 mM Tris-(hydroxymethyl) aminomethane and 25 mM $MgCl_2$ (pH 7.6). The whole homogenate was assayed for adenylate cyclase by the method of Krishna, Weiss, and Brodie (24) with minor modifications. The final incubation volume of 0.05 ml contained 1.5 mM ATP, 1 μCi [α-^{32}P]ATP (New England Nuclear), 10 mM $MgCl_2$, 10 mM theophylline, 30 mM Tris-(hydroxymethyl) aminomethane, 20–50 μg protein, and an ATP-regenerating system including 5 mM phospho(enol)-pyruvate, 50 μg/ml pyruvate kinase, and 20 μg/ml myokinase. Incubation for 5 min at 37°C was terminated by addition of 0.5 ml of a solution containing 0.15 μmol adenosine 3′,5′-cyclic monophosphate (cAMP), 4 nCi [^{3}H]cAMP and 0.15 μmol ATP, and immersion in boiling water for 3 min. The reaction mixture was then passed over a 0.5 × 4.0-cm column containing Dowex 50W-X4 resin, hydrogen form, 200–400 mesh (Bio-Rad Laboratories, Richmond, Calif.). After addition of 0.2 ml of 1.5 M imidazole (pH 7.2) to the eluate, it was passed over a 0.5 × 1.0-cm column containing neutral alumina, activity grade 1 (Sigma Chemical Company, St. Louis, Mo.) and washed with 2 ml of 0.1 M imidazole (pH 7.07). Radioactivity in the eluate was measured in a Beckman Liquid Scintillation System LS-345 (Beckman Instruments, Inc.). Appropriate corrections were made for incubations run without enzyme and for the incomplete recovery of [^{3}H]cAMP. Results were expressed as picomoles cAMP formed per mg protein per 5-min incubation.

Protein concentrations were determined by the method of Lowry, Rosebrough, Farr, and Randall (25) using standards of bovine albumin. All statistical analyses were performed by Student's *t* test for paired and unpaired data.

RESULTS

Effect of DOCA on intestinal transport and enzyme activity. The administration of DOCA resulted in increased absorption of sodium and water and secretion of potassium in the colon. As shown in Fig. 1, both sodium and water absorption increased approximately 100% in the colon. Sodium, potassium, and water transport were not significantly altered in the jejunum and ileum. Concomitant with these transport alterations,

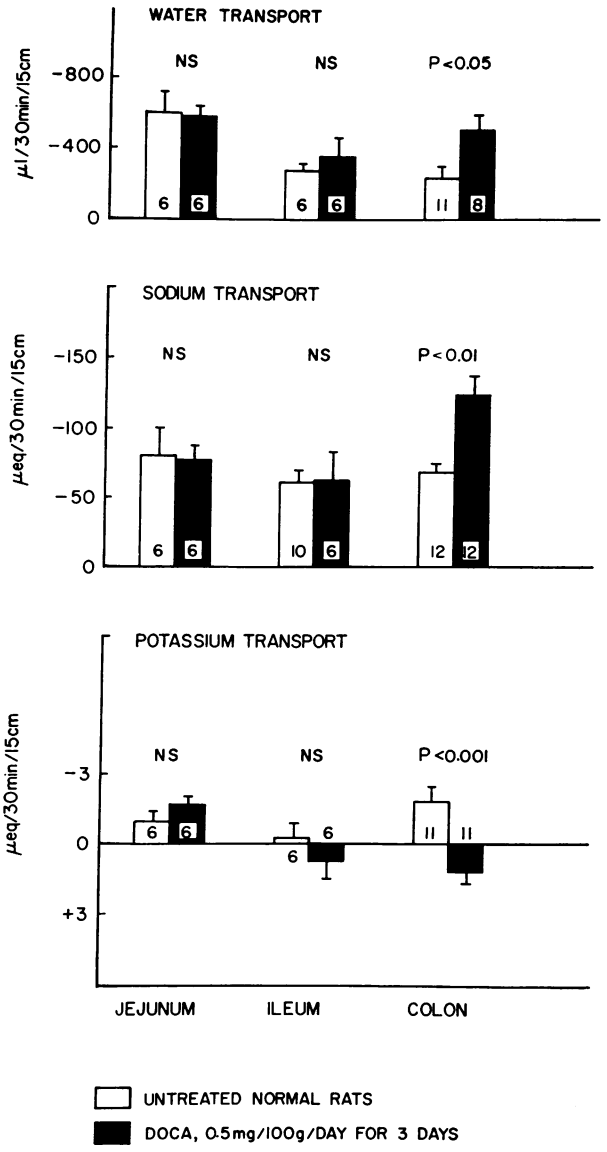

FIGURE 1 Effect of DOCA on net intestinal electrolyte and water transport. Values were obtained with an isotonic glucose-saline perfusate (Solution A). Values (mean±SE) above the abscissa indicate net absorption; values below indicate net secretion. Number in bar indicates the number of animals studied.

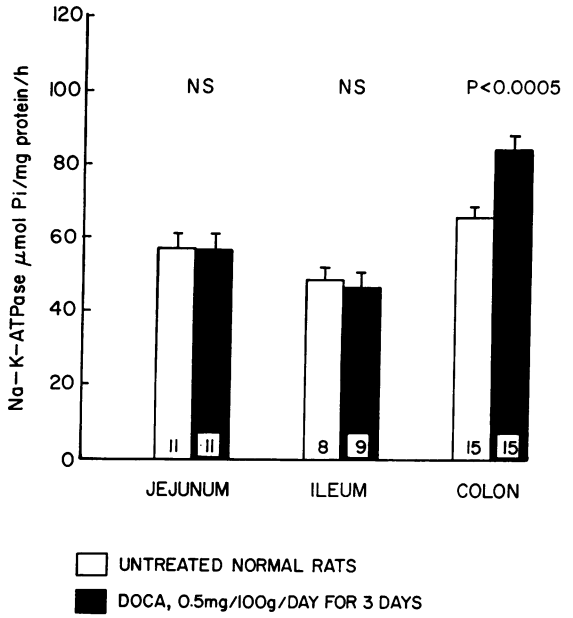

FIGURE 2 Effect of DOCA on intestinal Na-K-ATPase activity. Values are mean±SE. Number in bar indicates the number of animals studied.

DOCA treatment resulted in a significant increase in colonic Na-K-ATPase activity (Fig. 2). Na-K-ATPase activity in the jejunum and ileum was unchanged. DOCA treatment did not affect Mg-ATPase or adenylate cyclase activity (Table I) in any segment.

Effect of methylprednisolone on intestinal transport and enzyme activity. The administration of methylprednisolone for 3 days resulted in increased absorption of sodium and water and secretion of potassium in the jejunum, ileum, and colon (Fig. 3). These changes were accompanied by marked increases in Na-K-ATPase activity in each intestinal segment (Fig. 4). The specific activities of Mg-ATPase and adenylate cyclase

TABLE I

Effect of DOCA and Methylprednisolone on Intestinal Adenylate Cyclase Activity

	Adenylate cyclase activity		
	Jejunum	Ileum	Colon
	pmol cAMP/mg protein/5 min		
Untreated normal rats	259±29 (8)	269±45 (8)	221±43 (7)
DOCA*	257±28 (8)	299±49 (8)	212±34 (7)
	NS	NS	NS
Untreated normal rats	289±52 (8)	286±41 (8)	197±36 (8)
Methylprednisolone‡	286±51 (8)	294±37 (8)	210±19 (8)
	NS	NS	NS

All values are mean±SE. Number of animals are in parentheses.
* Deoxycorticosterone acetate, 0.5 mg/100 g per day for 3 days.
‡ Methylprednisolone acetate, 3 mg/100 g per day for 3 days.

(Table I) were unchanged in all segments. The largest increases in both Na-K-ATPase activity and electrolyte and water transport occurred in the ileum, resulting in a reversal of the normal jejunal-ileal gradients for

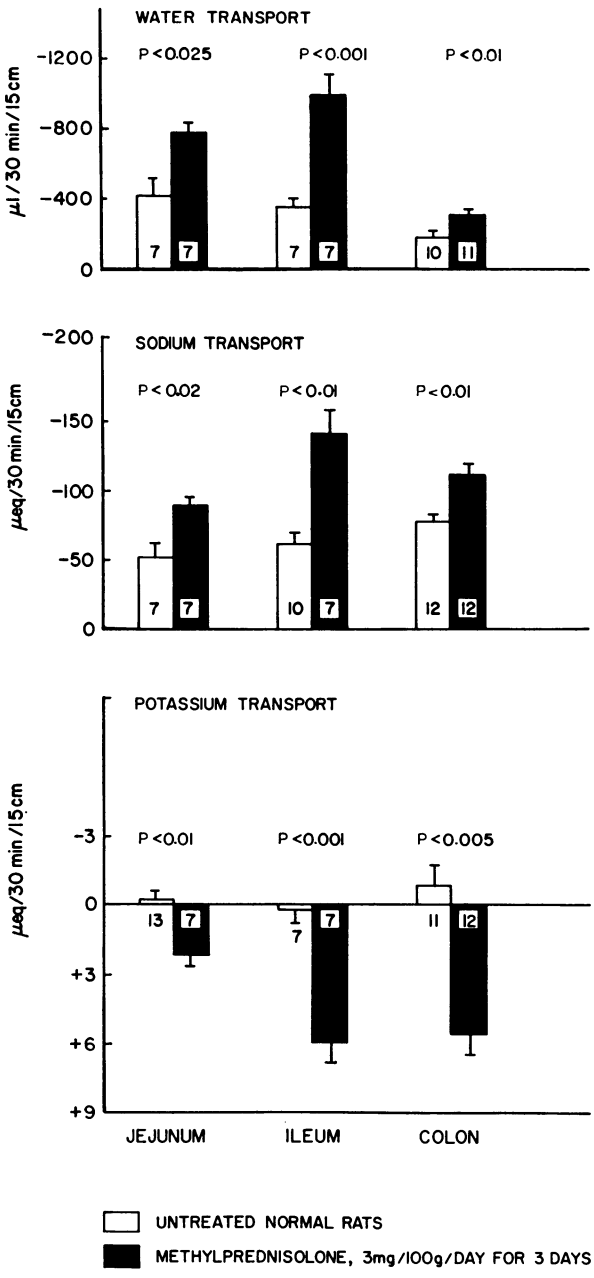

FIGURE 3 Effect of methylprednisolone on net intestinal electrolyte and water transport. Values were obtained with an isotonic glucose-saline perfusate (Solution A). Values (mean±SE) above the abscissa indicate net absorption; values below indicate net secretion. Number in bar indicates the number of animals studied.

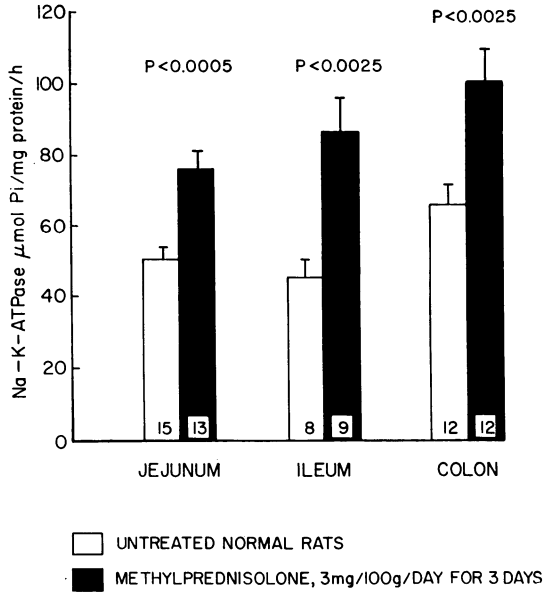

FIGURE 4 Effect of methylprednisolone on intestinal Na-K-ATPase activity. Values are mean±SE. Number in bar indicates the number of animals studied.

Na-K-ATPase activity (20, 26) and sodium and water absorption (27). When ileal transport and enzyme activity were measured 24 h after a single injection of methylprednisolone 3 mg/100 g, similar increases in sodium and water absorption, potassium secretion, and Na-K-ATPase activity (59.3±2.7 (4) vs. 35.0±1.7 (6) μmol Pi/mg protein per h, $P < 0.0005$) were found.

Since the presence of glucose in the perfusion solution (Solution A) might have affected these findings, the effect of methylprednisolone on glucose absorption was examined. As shown in Table II, methylprednisolone treatment did not affect jejunal glucose transport, but markedly increased glucose absorption in the ileum. To determine the relationship of ileal glucose absorption

TABLE II
Effect of Methylprednisolone on Intestinal Glucose Absorption

	Glucose absorption*	
	Jejunum	Ileum
	μmol/30 min/15 cm	
Untreated normal rats	157±26 (8)	75±13 (8)
Methylprednisolone‡	142±11 (8)	133±19 (8)
	NS	$P < 0.02$

All values are mean±SE. Number of animals are in parentheses.

* All values were obtained with an isotonic saline perfusate containing 56 mM glucose (Solution A).

‡ Methylprednisolone acetate, 3 mg/100 g per day for 3 days.

TABLE III

Effect of Methylprednisolone on Na-K-ATPase Activity in Isolated Intestinal Villus Tip and Crypt Cells

	Na-K-ATPase activity			
	Jejunum		Ileum	
	Villus tip	Crypt	Villus tip	Crypt
	μmol Pi/mg protein/h			
Untreated normal rats	74.7±3.3 (8)	33.7±3.4 (8)	60.2±2.3 (11)	29.7±2.1 (11)
Methylprednisolone*	108.0±3.6 (8) $P < 0.0005$	52.1±5.2 (9) $P < 0.01$	101.0±7.1 (6) $P < 0.0005$	59.6±6.8 (6) $P < 0.0005$

All values are mean±SE. Number of animals are in parentheses.

* Methylprednisolone acetate, 3 mg/100 g per day for 3 days.

to electrolyte transport (after methylprednisolone), ileal sodium and water transport were measured with a glucose-free perfusion solution of identical osmolality in which glucose was replaced by mannitol. Substitution of this glucose-free perfusate for Solution A did not alter the percent increases in ileal sodium and water absorption observed when rats were treated with methylprednisolone. Sodium absorption increased from −49.2±5.9 to −104.2±7.5 μeq/30 min per 15 cm, $P < 0.001$, and water absorption increased from −232±25 to −486±39 μl/30 min per 15 cm, $P < 0.001$.

To determine whether DOCA 0.5 mg/100 g and methylprednisolone 3 mg/100 g administration were additive in their effects on colonic Na-K-ATPase activity, rats were injected with both agents each day for 3 days. Colonic Na-K-ATPase activity was no higher in rats treated with both agents than in rats treated with methylprednisolone alone.

Effect of methylprednisolone on Na-K-ATPase in isolated cells. Isolated small intestinal villus tip and crypt cells from methylprednisolone-treated rats were assayed to determine the site of the Na-K-ATPase increase. The Na-K-ATPase activity in villus tip and crypt cells in the untreated control rats was similar to our previous findings (20). As shown in Table III, after methylprednisolone treatment for 3 days, Na-K-ATPase activity was increased in both villus tip and crypt cells in the jejunum and ileum. Mg-ATPase activity was similar in jejunal and ileal villus tip and crypt cells in normal rats, as previously reported (20), and was unchanged by methylprednisolone treatment. The origin of these isolated cell collections was documented by assay of alkaline phosphatase and thymidine kinase, enzymatic markers for villus tip, and crypt cells, respectively (20, 21, 28). The specific activities of alkaline phosphatase and thymidine kinase were unaltered by methylprednisolone treatment.

Effect of DOCA and methylprednisolone on transmural electrical PD. The transmural electrical PD was significantly higher in the colon of DOCA-treated rats as compared to control rats (Table IV). There was no difference, however, between our glucose-dependent potentials in the jejunum or ileum of DOCA-treated rats as compared to controls. These findings are consistent with a previous report (14).

The PD in methylprednisolone-treated rats perfused with Solution A was significantly higher than in controls in all three intestinal segments. The colonic PD in methylprednisolone-treated rats was comparable to the PD seen after DOCA treatment. As was the case for ileal sodium and water absorption, substitution of mannitol for glucose in the perfusion solution decreased the jejunal and ileal PD in control rats, but did not blunt the increase in PD produced by methylprednisolone (Table IV).

Effect of methylprednisolone on intestinal permeability. The effect of methylprednisolone on permeability in the jejunum and ileum was assessed by comparing the streaming potentials generated by a mixture of Solution A and mannitol (100 mM) in untreated and methylprednisolone-treated rats. An increase in permeability in the treated group would be reflected by a smaller ΔPD (17, 18). The ΔPD induced by the hyperosmolar solution was no smaller in the jejunum (4.7± 0.2 [8]) or ileum (7.2±0.7 [5]) of methylprednisolone-treated rats than in the jejunum (4.5±0.4 [3]) or ileum (4.1±0.4 [5]) of normal controls.

Effect of methylprednisolone on intestinal histology. To reduce the likelihood that histological alterations in methylprednisolone-treated animals affected small intestinal electrolyte transport, coded sections of jejunum and ileum were examined by light microscopy. Gross histology and eyepiece micrometric measurements of villus height and crypt depth of control and experimental animals were recorded. No pathologic changes or changes in gross histology were found. Villus height and crypt depth in the jejunum were similar in methylprednisolone treated and control animals (villus height:

TABLE IV

Effect of DOCA and Methylprednisolone on Transmural Electrical PD

	PD*				
	Jejunum		Ileum		Colon
	Glucose‡	Glucose-free§	Glucose‡	Glucose-free§	Glucose‡
	mV		*mV*		*mV*
Untreated normal rats	6.8±0.4 (11)	3.0±0.2 (6)	4.2±0.7 (12)	1.7±0.4 (6)	14.6±1.6 (11)
Methylprednisolone‖	10.1±0.5 (15) $P < 0.001$	5.1±0.6 (6) $P < 0.02$	16.5±0.9 (13) $P < 0.001$	7.3±0.6 (6) $P < 0.001$	43.9±4.7 (7) $P < 0.001$
DOCA¶	6.5±0.1 (4) NS	—	4.7±0.8 (5) NS	—	38.7±4.1 (8) $P < 0.001$

All values are mean±SE. Number of animals are in parentheses.

* Lumen in electronegative.

‡ Isotonic saline perfusate containing 56 mM glucose (Solution A).

§ Isotonic saline perfusate containing 56 mM mannitol.

‖ Methylprednisolone acetate, 3 mg/100 g per day for 3 days.

¶ Deoxycorticosterone acetate, 0.5 mg/100 g per day for 3 days.

407±34 [5] vs. 448±27 [5] μm, crypt depth: 192±15 [5] vs. 192±18 [5] μm). Ileal villi also were similar in methylprednisolone-treated and control animals (villus height: 213±11 [5] vs. 249±16 [5] μm, crypt depth: 142±0 [5] vs. 156±9 [5] μm). These values are consistent with the values usually observed in untreated normal rats in our laboratory.

DISCUSSION

Our results demonstrate a striking association between intestinal electrolyte transport and mucosal Na-K-ATPase activity. Where increased electrolyte and water transport was induced by gluco or mineralocorticoid treatment, Na-K-ATPase activity was significantly increased; in those segments in which no increases in transport occurred, Na-K-ATPase activity remained unchanged. Several explanations for this association are possible. Activation of Na-K-ATPase may precede and be required for transport changes to occur. Alternatively, the alterations in Na-K-ATPase activity may be adaptive, occurring in response to enhanced sodium absorption or potassium secretion initiated by other mechanisms. It is most unlikely that the increases in intestinal Na-K-ATPase and electrolyte transport we observed were entirely unrelated. Na-K-ATPase is believed to play a role in sodium and potassium transport in many other tissues (1, 4). Furthermore, strophanthin G (ouabain) in serosal surface concentrations known to inhibit Na-K-ATPase activity (29) markedly diminished short circuit current and mucosal to serosal sodium flux in the isolated rabbit ileum studies of Schultz and Zalusky (30). Their hypothetical model of intestinal sodium transport, derived in part from these studies, suggested the presence of a ouabain-sensitive sodium pump along the serosal cell membrane (31). The location of this pump (Na-K-ATPase) along the basolateral cell membrane, in fact, has now been established (23, 32, 33). Schultz and Zalusky proposed that the rate of sodium transfer across the serosal cell membrane (by Na-K-ATPase) is a function of the intracellular sodium concentration which in turn is responsive to the rate of sodium entry across the luminal cell surface. We are suggesting that either a primary effect on Na-K-ATPase activity or enhancement of sodium entry by the gluco and mineralocorticoids could account for the changes in sodium and water transport observed. Augmented small intestinal and colonic potassium secretion, following an increased electrical gradient (34, 35), would be expected in either case.

Although we did not observe a temporal dissociation of Na-K-ATPase from electrolyte transport in the small intestine after methylprednisolone, Thompson and Edmonds (14) have found that a 20-h infusion of aldosterone increased rat colonic PD and short-circuit current in the absence of Na-K-ATPase changes. This may indicate that Na-K-ATPase activation is not the initial event in mineralocorticoid and possibly glucocorticoid-induced electrolyte transport changes. However, temporal-dissociation alone does not eliminate the possibility of a primary role for the increased Na-K-ATPase activity since functional or technical considerations may be important. For example, early changes in Na-K-ATPase activity may involve increases in turnover rate and enzyme velocity rather than new enzyme synthesis. These increases in functional activity,

of critical significance in vivo, would not be measured under the usual in vitro assay conditions. Secondly, the ability to measure alterations in transport and enzyme activity may be of different orders of sensitivity. Transport changes, then, might be detected before enzyme changes.

To explore the possibility that Na-K-ATPase changed adaptively, and the initial changes in transport were due to mechanisms unrelated to Na-K-ATPase, a number of phenomena known to influence intestinal electrolyte transport were studied. No alterations were observed in mucosal permeability, adenylate cyclase activity, or intestinal histology (and villus height/crypt depth measurements) after corticosteroid treatment. Ileal glucose absorption, however, was increased by methylprednisolone treatment. Inasmuch as jejunal glucose absorption was unaffected, this may account for the greater increment in electrolyte transport and PD in the ileum than in the jejunum after methylprednisolone. Nevertheless, methylprednisolone induced a similar increment in ileal sodium and water absorption when glucose was omitted from the perfusion solution, although the absolute level of sodium and water transport was lower. A primary effect of this steroid on sodium-coupled glucose absorption (31) in either jejenum or ileum, therefore, was very unlikely.

There have been several reports in which increased colonic sodium and water absorption (11, 36) and PD (10, 12) and reduced ratios of sodium to potassium in fecal dialysates (10, 37, 38) were recorded in patients with primary or secondary aldosteronism or in patients injected with mineralocorticoids. However, as suggested by an earlier observation of Richards (38) and corroborated by our current findings, these increases in colonic PD and reductions in fecal dialysate sodium potassium ratios are not specific for hyperaldosteronism because glucocorticoids produce similar changes. In addition, our findings may help explain the beneficial effects of glucocorticoid treatment in many patients with inflammatory bowel disease, such as ulcerative colitis (39, 40). Although the glucocorticoids have numerous effects (41), Na-K-ATPase activation and enhanced electrolyte and water transport in the small and large intestine may contribute to the reduction in diarrhea and electrolyte disturbances in these patients.

To define the mechanisms of normal intestinal fluid transport, the production of transport alterations by specific and atraumatic means is essential. Recently, models of intestinal secretion involving adenylate cyclase stimulation and accumulation of intracellular cAMP have received much attention (42). Models exhibiting enhanced intestinal absorption, however, are limited (43, 44). The production of compensatory intestinal hypertrophy, for example, requires surgical intervention and altered intestinal histology (45–47). Gluco and mineralocorticoids offer useful tools whereby intestinal sodium, water, and potassium transport can be altered in concert with changes in the activity of the transporting enzyme Na-K-ATPase. These adrenal steroid models should contribute to our understanding of the mechanisms of physiological and pathological transport processes in the small and large intestine.

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