

Regulation of Renal Na-K-ATPase in the Rat

Role of the Natural Mineralo- and Glucocorticoid Hormones

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Abstract. Both mineralo- and glucocorticoids stimulate renal Na-K-ATPase, but their relative role in the regulation of the enzyme remains controversial. In this study we measured Na-K-ATPase activity in the cortical collecting tubule (CCT) of adrenalectomized rats replaced with either the native mineralocorticoid (aldosterone) or glucocorticoid (corticosterone) in doses calculated to yield previously determined physiologic concentrations of these hormones ($5 \text{ ng} \cdot \text{dl}^{-1}$ and $5 \mu\text{g} \cdot \text{dl}^{-1}$, respectively). This was achieved by continuous delivery of aldosterone ($1 \mu\text{g} \cdot 100 \text{ g}^{-1} \cdot \text{d}^{-1}$) from an osmotic minipump or of corticosterone (2 pellets of 20 mg each), implanted subcutaneously either at adrenalectomy or 7 d later, when Na-K-ATPase activity reached its nadir. Adrenalectomized rats not receiving hormone replacement and adrenal-intact animals served as controls. The CCT was chosen because it contains the highest concentration of binding sites for both hormones.

Na-K-ATPase activity declined 52% in the CCT of untreated adrenalectomized rats after 7 d, and remained unchanged thereafter. Physiologic replacement doses of aldosterone prevented this decline and restored the activity of the enzyme after it had been allowed to decrease maximally following adrenal ablation, whereas similar replacement of corticosterone was without effect. These

observations suggest that under physiologic conditions Na-K-ATPase in the CCT, a probable target nephron segment of both hormones, is under mineralocorticoid rather than glucocorticoid control.

Introduction

Both mineralo- and glucocorticoids influence important transport and metabolic functions of the kidney, and among their proposed mechanisms of action is a direct or indirect stimulatory effect on renal sodium- and potassium-activated adenosine triphosphatase (Na-K-ATPase)¹ (1–4). The role of adrenal steroids in the regulation of renal Na-K-ATPase has been amply documented by ablative studies, which invariably show a substantial decline in the activity of the enzyme after adrenalectomy (ADX) (5–17). However, the relative contribution of the two major classes of corticosteroids to this regulation has not been conclusively determined: Whereas some studies stress the importance of the mineralocorticoid effect (1, 2, 9, 10, 14, 17–19), others attribute a predominant role to glucocorticoids (3, 5, 13, 20). This controversy appears largely due to several methodologic or design limitations of previous reports, including determination of enzyme activity in kidney homogenates that are heterogeneous, use of synthetic corticosteroids whose renal actions may differ from that of the native hormones, and administration of supraphysiologic doses of the hormone that could produce non-specific effects because of hemodynamic alterations or receptor cross-occupancy.

The recent development of sensitive methods for measuring Na-K-ATPase activity in discrete nephron segments (21, 22) and for mapping receptor distribution of corticosteroid hormones along the nephron (23, 24), together with a reliable way to maintain chronically plasma aldosterone (Aldo) or corticosterone (CS) of adrenalectomized (ADX) rats at normal endogenous

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1. *Abbreviations used in this paper:* Aldo, aldosterone; ADX, adrenalectomized, adrenalectomy; CBG, corticosterone-binding globulin; CCT, cortical collecting tubule; CS, corticosterone; GFR, glomerular filtration rate; Na-K-ATPase, sodium- and potassium-activated adenosine triphosphatase.

levels (25), prompted us to reevaluate this issue. Combining adrenal ablation with continuous replacement of the individual hormones, we determined in the rat the respective roles of the native mineralocorticoid (Aldo) and glucocorticoid (CS) in the regulation of Na-K-ATPase in the cortical collecting tubule (CCT), a major target nephron segment for both hormones. The results indicate that physiologic replacement doses of Aldo prevent the decline of Na-K-ATPase in the CCT and restore its activity after it had been allowed to decrease maximally following ADX, whereas similar replacement of CS was without effect. These observations suggest that under physiologic conditions renal Na-K-ATPase is under mineralocorticoid, rather than glucocorticoid, control.

Methods

The purpose of this study was to assess the role of corticosteroid hormones in maintaining renal Na-K-ATPase if given at ADX, and in restoring its activity after it was allowed to reach a nadir after adrenal ablation. The two components of this work are accordingly labeled the "maintenance" (A) and "restoration" (B) study, respectively. Duration of the experimental protocol was 1 wk in the former (groups I–IV, see below), and 2 wk in the latter (groups V–VII). All animals were fed a normal chow diet (Teklad 4%, Harlan Sprague Dawley, Inc., M. A. Laboratory Animals & Teklad Diets, Madison, WI) that contained 1% NaCl by weight, and were given 0.3% NaCl to drink ad lib. Doses of hormones administered in this study were shown to generate in ADX rats circulating levels similar to those of intact, nonstressed animals and to restore colonic potential difference to normal (25).

Male, albino Sprague-Dawley rats (Lab Supply, Indianapolis, IN) weighing 190–220 g were distributed into seven groups:

Study A

Group I. Animals from this group underwent a sham-ADX, and constituted the adrenal-intact controls. Animals in groups II–VII were bilaterally ADX under pentobarbital anesthesia (25 mg/kg i.p.) using a lumbar approach.

Group II. These rats received no hormonal replacement (ADX-control).

Group III. In this group two pellets containing 20 mg CS each were implanted subcutaneously in the interscapular region at the time of ADX.

Group IV. In these rats, osmotic minipumps (Alzet model 2001, Alza Corp., Palo Alto, CA) containing Aldo in concentrations calculated to deliver 1 μ g/100 g body wt per d at the rate of 1 μ l/h, were implanted subcutaneously in the interscapular region at ADX.

Study B

Group V. These animals, like those in group II, received no hormone replacement.

Group VI. In this group of rats, CS pellets as described above were implanted 7 d following ADX.

Group VII. In these animals, Aldo-containing osmotic minipumps were implanted 7 d after ADX and delivered 1 μ g Aldo/100 g body wt per d. In this group, experiments aimed at determining the time sequence of Na-K-ATPase restoration included enzyme measurements 1, 3, and 7 d after beginning Aldo replacement (or 8, 10, and 14 d after ADX).

Metabolic balance study

Animals of groups I–IV (study A) were individually placed in metabolic cages (Nalge Co., Rochester, NY) for two separate periods of 24 h (5th and 6th d after ADX). On the first, they were allowed to acclimate to the cage; food and fluid intake and the urinary excretion of sodium and potassium were determined during the 2nd d (6th d post-ADX).

Renal function

Clearance experiments were performed in rats from groups I–IV on the 7th d post-ADX. The animals were anesthetized with 100 mg/kg i.p. sodium 5-ethyl-5-(1'-methylpropyl)-2-malonylthiourea (Inactin, Promonta, Hamburg, FRG). The trachea, bladder, and one jugular vein and carotid artery were cannulated. During surgery, 1 ml isotonic saline (~0.5% body wt) was infused to replace estimated fluid losses. The rats were placed on heated boards and their rectal temperature was monitored with a thermistor probe (Yellow Springs Instrument Co., Yellow Springs, OH) and maintained between 37° and 38°C. All solutions were administered with constant-infusion pumps (model 975, Harvard Apparatus Co. Inc., S. Natick, MA). Glomerular filtration rate (GFR) was measured as the clearance of radioactive inulin. The priming dose of [*methoxy*-³H]inulin (100 μ Ci/kg body wt) was followed by a sustaining infusion of isotonic saline in a volume (0.11 ml/min) sufficient to ensure adequate urine flow that delivered appropriate amounts of inulin (50 μ Ci/kg per h) to maintain constant plasma concentrations. After an equilibration period of 45 min, three urine specimens were collected in preweighed plastic tubes and four arterial blood samples were obtained for clearance measurements. At the end of the experiments the right kidney was removed and weighed, and the left kidney was perfused in situ with a collagenase-containing solution (type I, 400 U/ml, Sigma Chemical Co., St. Louis, MO) in preparation for microdissection (see below). Concentrations of radioactive inulin (New England Nuclear, Boston, MA) in urine and serum were determined using a liquid scintillation counter (Packard Instrument Co., Inc., Downers Grove, IL). The clearance of inulin was calculated by standard formulas using urine/plasma concentration ratios and urine flows. Sodium and potassium were measured by flame photometry with lithium as the internal standard (model IL 343, Instrumentation Laboratory, Inc., Lexington, MA).

Hormone assays

Methods for the determination of plasma Aldo and CS have been described in detail elsewhere (25). In brief, plasma CS levels were determined by the competitive protein-binding method described by Murphy (26). Two ethanol extractions of rat plasma (0.1 ml plasma/1.0 ml ethanol) were combined, dried under nitrogen, and allowed to compete with tritiated CS (New England Nuclear) for binding sites on human corticosterone-binding globulin (CBG) at 4°C. After equilibration, CBG-bound CS was separated from the unbound fraction by the addition of dextran-coated charcoal, followed by centrifugation. The supernatant was decanted into scintillation fluid and the activity of [³H]CS was determined in a Packard Tri-Carb scintillation counter (Packard Instrument Co., Inc.). The concentration of CS was calculated by comparing the percent CS bound to unknowns with standards processed in the same way.

Measurement of plasma Aldo was accomplished by combining the chromatographic purification method of Bühler et al. (27) with a commercial Aldo radioimmunoassay kit (Kald-2, Diagnostic Products Corp., Los Angeles, CA). Purification of the samples before radioimmunoassays was necessary because of the relatively high cross-reactivity of the commercial Aldo antiserum with CS (manufacturer's information), and possibly with other substances occurring naturally in rat plasma. Using

Table I. Study A: Metabolic Balance Study

Group	n	Body wt		Food intake	Fluid intake	Na intake	U · V	U _{Na} · V	U _K · V	P _{Na}	P _K
		Day 1	Day 8								
		g	g	g · 24h ⁻¹	ml · 24 h ⁻¹	μeq · 24 h ⁻¹	ml · 24 h ⁻¹	μeq · 24 h ⁻¹	μeq · 24 h ⁻¹	meq · liter ⁻¹	meq · liter ⁻¹
I Sham	11	208±8	249±10	22.7±1.6	47.3±3.1	6,308±395	24.5±2.5	5,683±389	4,570±312	144±1	3.7±0.2
II ADX	7	218±6	234±7	19.4±0.5	59.8±3.9*	6,380±214	38.5±3.7*	5,312±149*	4,104±189	142±3	5.3±0.6*
III ADX plus CS	9	205±8	214±9	18.3±0.7	62.1±6.3	6,359±389	40.2±6.0*	5,783±420	4,060±194	144±1	3.8±0.1‡
IV ADX plus ALDO	8	211±7	249±7§	20.2±1.0	36.0±2.8‡§	5,296±278‡	15.7±1.1*‡	4,363±237*‡	3,640±183	142±2	3.2±0.2‡§

Results are mean±SE. UV, urine volume; U_{Na} · V, urinary sodium excretion; U_K · V, urinary potassium excretion.

* Significantly ($P < 0.0125$) different from group I.

‡ Significantly different from group II.

§ Significantly different from group III.

these methods, Aldo and CS levels in ADX rats treated with the protocol outlined above averaged 5 ng/dl and 5 μg/dl, respectively, in our laboratory (25).

ATPase assay

Na-K-ATPase was determined in CCT obtained on the 7th d post-ADX in groups I–IV (study A), and on the 14th d post-ADX in groups V–VII (study B). In group VII, additional measurements were done on the 8th and 10th d post-ADX. The procedures for tubule microdissection and Na-K-ATPase assay have been reported in detail before (21, 22), and will be described only briefly here: The animals were killed by exsanguination from the abdominal aorta, and the left kidney was perfused as indicated above. CCT were dissected in the cold under stereomicroscopic observation in a medium containing (in mM): NaCl, 137; KCl, 5; MgSO₄, 0.8; Na₂HPO₄, 0.44; MgCl₂, 1; CaCl₂, 0.25; Tris-HCl, 10; pH 7.4. The tubules were individually transferred to a concave bacteriological slide and photographed to determine their length. ATPase activity was measured after a two-step permeabilization procedure, by incubation of tubule segments for 15 min at 37°C in a 1-μl droplet of the following solutions: For determination of total ATPase activity the incubation medium contained (in mM): NaCl, 50; KCl, 5; MgCl₂, 10; EGTA, 1; Tris-HCl, 100; Na₂ATP (grade II, vanadate-free, Sigma Chemical Co.), 10; and [γ-³²P]ATP (Amersham Corp., Arlington Heights, IL) in tracer amounts (~5 nCi/μl). For determination of Mg-dependent ATPase activity, NaCl and KCl were omitted, Tris-HCl was 150 mM and 1 mM ouabain was added. Phosphate liberated by the hydrolysis of [γ-³²P]ATP was separated by filtration through a Millipore filter (Millipore Continental Water Systems, Bedford, MA) after absorption of the unhydrolyzed nucleotide on activated charcoal, and the radioactivity was counted in a liquid scintillation spectrophotometer (Packard Instrument Co., Inc.).

Total and Mg-dependent ATPase activities were each determined on five replicate samples from individual animals, and were expressed as picomoles inorganic phosphate liberated per millimeter of tubule length per hour. Sodium- and potassium-dependent, ouabain-inhibitable ATPase was taken as the difference between the means of each group of measurements, and thus represents a single data point in each animal; the results show mean values of these determinations in all animals within a given experimental group. To minimize the variability between experiments, one appropriate control and one animal from each experimental group were studied simultaneously.

Statistical analysis

The statistical analysis was done using Student's *t* test for paired and nonpaired samples. When more than two groups were compared, Bonferroni inequalities were considered and a level of significance of 0.05/*n* was used, *n* being the number of groups (28).

Results

Maintenance study (A)

Metabolic balance study (Table I). Adrenal-intact animals gained on average 6 g/d and Aldo-replaced animals (group IV) had a similar weight gain. In contrast, ADX controls (group II) and CS-replaced (group III) rats gained only a modest amount. Sodium intake and excretion were comparable in groups I–III, and somewhat lower in group IV. Plasma Na was similar in all experimental groups. ADX, untreated animals were hyperkalemic, and both CS and Aldo replacement normalized serum potassium. Daily K excretion did not differ between the groups.

Renal function (Table II). GFR was significantly lower in all ADX animals (groups II–IV) compared with sham-operated controls, regardless of steroid replacement; this finding persisted whether GFR was calculated in relation to body weight or kidney weight. Although GFR was slightly higher in Aldo-replaced than in ADX, untreated rats, the difference was not significant when factored by body or kidney weight. Both net tubular sodium reabsorption (*T*_{Na}) and potassium excretion were decreased by ADX and only partially restored towards control levels by Aldo replacement, while CS replacement had only a minimal effect on these measurements.

ATPase activity (Fig. 1). ADX led to a 52% decrease in Na-K-ATPase activity in CCT, and CS replacement (group III) failed to prevent this decrease; the enzyme activity in this group was similar to that measured in untreated ADX animals. In contrast, Aldo replacement (group IV) maintained Na-K-ATPase activity at a level not different from sham-operated controls.

Restoration study (B)

Body weight, plasma electrolytes, and hormone levels (Table III). Weight gain was minimal in ADX animals between the seventh and fourteenth postoperative days, but both CS and

Table II. Study A: Kidney Function

Group	n	Body wt	Kidney wt	Inulin clearance			Net T _{Na}	U _K · V
		g	g	ml/min	ml/min · 100 g body wt ⁻¹	ml/min · g kidney wt ⁻¹	μeq · min ⁻¹	μeq · min ⁻¹
I Sham	7	256±7	1.04±0.03	4.13±0.15	1.60±0.03	2.05±0.13	638±30	3.33±0.07
II ADX	7	215±9*	0.92±0.03	2.06±0.13*	0.95±0.03*	1.12±0.06*	297±14*	1.43±0.23*
III ADX plus CS	8	220±7*	0.88±0.03*	2.28±0.15*	1.02±0.05*	1.29±0.06*	348±25*	1.70±0.21*
IV ADX plus Aldo	6	257±9‡§	1.03±0.02§	2.73±0.17*‡	1.05±0.04*	1.31±0.07*	423±29*‡	2.06±0.18*

Results are mean±SE. T_{Na}, tubular sodium reabsorption; U_K · V, urinary potassium excretion.

* Significantly ($P < 0.0125$) different from group I.

‡ Significantly different from group II.

§ Significantly different from group III.

Aldo replacement led to significant weight gains. Hyponatremia and severe hyperkalemia were observed on the 14th d postadrenalectomy in untreated animals. These changes were much less pronounced, but still present in CS-replaced animals (group VI), whereas Aldo-replaced animals (group VIII) exhibited a normal serum electrolyte profile. Both Aldo and CS were vanishingly low, and not significantly different from zero in ADX animals. Aldo and CS levels averaged 5.0 ± 0.6 ng/dl and 7.4 ± 0.4 μg/dl in animals receiving replacement doses of the respective hormone, which are comparable to the values measured in intact, unstressed animals (25).

ATPase activity (Fig. 2). Na-K-ATPase activity in ADX rats (group V) decreased at 14 d to a level not different from that observed at 7 d (group II). CS replacement (group VI) failed to restore Na-K-ATPase activity, as it failed to maintain it when given at ADX: the level of enzyme activity in these animals was not different from that measured in untreated ADX controls. In contrast, Aldo replacement (group VII) led to a marked in-

crease in Na-K-ATPase activity to levels higher than those measured in all other groups.

The time course of the restoration of enzyme activity by Aldo replacement is illustrated in Fig. 3. Partial restoration was observed 24 h after beginning Aldo, with complete restoration achieved by 3 d. (A larger dose of Aldo [50 μg/100 g per d] restored Na-K-ATPase activity fully at 24 h [data not shown].) Serum potassium decreased progressively with Aldo replacement in reciprocal fashion with the increment in Na-K-ATPase activity.

Discussion

The experiments described in this paper demonstrate that the reduction in CCT Na-K-ATPase that follows ADX can be prevented by physiologic doses of Aldo, but not by CS. Furthermore, replacement doses of the mineralocorticoid restored the enzyme activity when it has been allowed to decrease maximally after adrenal ablation, whereas similar treatment with the glucocorticoid hormone was without effect. These observations strongly suggest that modulation of Na-K-ATPase activity in the CCT is a putative mineralocorticoid function.

Analysis of the regulatory role of adrenocortical hormones on renal Na-K-ATPase has been complicated by several factors. Chief among them is that for the most part the enzyme was measured in kidney homogenates that are heterogenous, only a small fraction thereof consisting of target cells of mineralocorticoid hormone. Consequently, a stimulatory effect of mineralocorticoids on their target nephron segment may be offset by a large background of enzyme activity from hormone-insensitive structures. Thus, both ourselves (Mujais, S. K., M. A. Chekal, W. J. Jones, J. P. Hayslett, and A. I. Katz, manuscript in preparation) and others (19, 29) have observed that either high physiologic or pharmacologic doses of mineralocorticoids (Aldo, 5 μg/100 g per d in the rat and deoxycorticosterone acetate, 5 mg/d in the rabbit, respectively) enhanced Na-K-ATPase activity only in certain subdivisions of the collecting tubule. In the present study, the CCT was selected because it is a well characterized target site for Aldo action (30). In addition, this nephron segment contains the highest concentration of

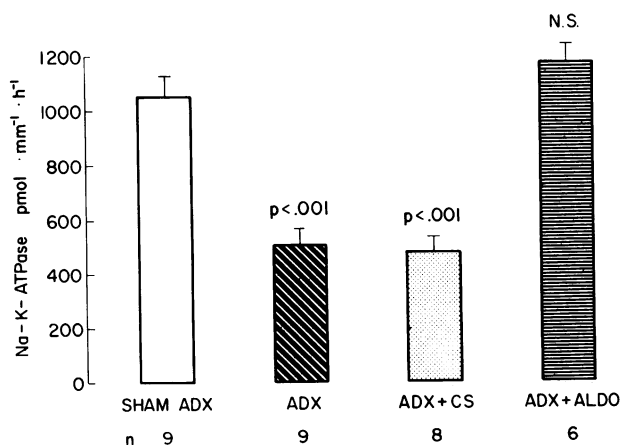


Figure 1. Na-K-ATPase activity in CCT of control, ADX-untreated rats, and ADX animals treated with either CS or Aldo 7 d after ADX. Aldo, but not CS, prevented the decline in enzyme activity.

Table III. Study B: Body Weight, Plasma Electrolytes, and Hormone Levels

Group	n	Body wt			P _{Na}	P _K	P _{ALDO}	P _{CS}
		Day 1	Day 8	Day 15				
		g	g	g	meq · liter ⁻¹	meq · liter ⁻¹	ng · dl ⁻¹	μg · dl ⁻¹
V ADX	6	199±5	202±5	210±8	133±1	9.0±0.2	0.3±0.2	0.8±0.4
VI ADX plus CS	8	200±4	201±3	236±5*	135±2	6.5±0.2*	NT	7.4±0.4*
VII ADX plus ALDO	7	210±2	222±7	266±12*	143±1*‡	4.3±0.2*‡	5.0±0.6*	NT

Results are mean±SE. NT, not tested.

* Significantly ($P < 0.017$) different from ADX.

‡ Significantly different from CS.

binding sites for CS (24) as well as for Aldo (23), and thus probably represents a major locus of action for both hormones.

Another difficulty encountered in evaluating earlier studies relates to the frequent use of synthetic glucocorticoids, most commonly dexamethasone. Identification of different receptor types for the naturally occurring CS (type III) and the synthetic dexamethasone (type II) in rat kidney (31, 32), raises the possibility that their mode of action in the kidney may not be identical. In addition, from a renal standpoint physiologic replacement doses of synthetic glucocorticoids can not be deter-

mined with confidence from potency comparisons with the native hormones, and binding affinity of the two types of glucocorticoids to carrier plasma proteins is markedly different (33, 34). The choice of CS in our study was prompted by the fact that this steroid is the natural, and possibly the sole, glucocorticoid in the rat (35).

In many of the previous reports hormones were given in pharmacologic doses, and even when in an attempt to simulate physiologic levels the total dose was lower, administration by bolus injection probably produced transient pharmacologic levels in the circulation, and thus at the receptor sites. High concentrations of mineralocorticoids in ADX animals may lead to receptor cross-occupancy ("illicit occupancy" of glucocorticoid receptors) and thus to expression of a glucocorticoid effect and, conversely, it is possible that pharmacologic concentrations of glucocorticoids generate a mineralocorticoid effect by the same mechanism (30, 36, 37). Furthermore, large doses of glucocorticoids increase renal blood flow and GFR above normal (37, 38). To circumvent these difficulties we took advantage of an

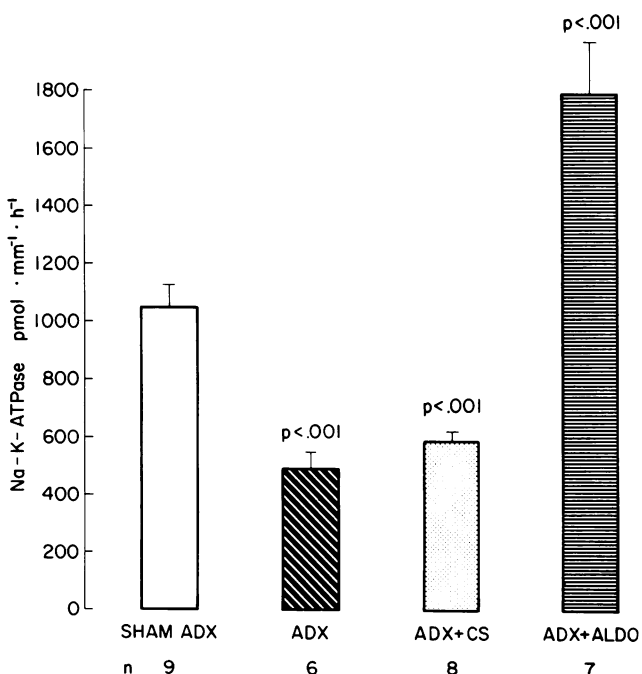


Figure 2. Na-K-ATPase activity in CCT of control, ADX-untreated rats, and ADX animals treated with either CS or Aldo 14 d after ADX and 7 d after beginning of replacement therapy. Aldo, but not CS, restored enzyme activity.

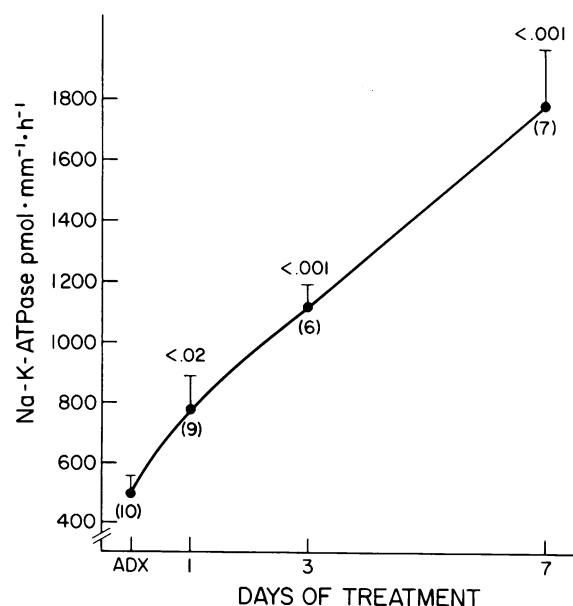


Figure 3. Time course of the restoration of Na-K-ATPase activity in CCT of ADX animals treated with Aldo from the 7th d after ADX.

animal model in which plasma levels of either CS or Aldo could be maintained in ADX rats at normal endogenous basal levels by replacement of each hormone in doses equal to its basal production rate in the intact animal (25). Physiologic levels of Aldo (~ 5 ng/dl) and of CS (~ 5 μ g/dl) were determined by reference to the values obtained in normal, nonstressed rats, and verified by the transmural potential difference in colon, which was comparable to that of control animals with intact adrenal glands. In this model, chronic, stable hormone levels can be established in the ADX rat by using osmotic minipumps to deliver Aldo and implantable pellets for CS. (The latter does not dissolve well in the small solvent volume the minipump can contain.) In this study, we chose the doses of Aldo and CS that were found to provide physiologic replacement of each hormone, and the results (Table III) confirm that this dosage choice was appropriate.

Adrenal ablation is associated with decreased Na-K-ATPase activity in multiple nephron segments (16, 17). The universal nature of this decrease contrasts with the segment-specific distribution of hormone receptors, and raises the possibility that it is due to the hemodynamic consequences of the ablative procedure. Evaluation of the role of specific hormone replacement on enzyme activity, therefore, must also assess other factors that influence enzyme activity, e.g., GFR and sodium reabsorptive and potassium secretory loads (39). In this study, sodium intake and sodium and potassium excretion were similar in all groups or, if anything, were somewhat lower in the Aldo-replaced animals (Table I). ADX led to a striking decrease in GFR, associated with hyperkalemia and mild hyponatremia. Both CS and Aldo replacement, whether started at ADX or 1 wk later, corrected in full or in part the plasma electrolyte abnormalities without completely restoring either the GFR, net sodium reabsorption, or net potassium excretion.²

The reasons why attainment of normal circulating levels of Aldo, and especially of CS, did not restore fully the GFR are not clear. However, this fact makes it possible to examine the direct effect of each steroid on tubular Na-K-ATPase, independent of changes in renal hemodynamics: whereas CS replacement failed to prevent the decline in enzyme activity or to restore it after ADX, physiologic replacement doses of Aldo accomplished both: When begun at ADX, it fully maintained Na-K-ATPase activity at the levels seen in adrenal-intact controls; when replacement was initiated 1 wk after ADX, enzyme activity was partially restored by 24 h, and complete restoration was achieved by 72 h³ (Fig. 3). Maintenance and restoration of Na-K-ATPase

activity by Aldo in spite of a chronic reduction in GFR suggests a direct hormonal effect on the CCT. Finally, the enhancing effect of Aldo on renal Na-K-ATPase was observed with a protocol that elicits a well-defined mineralocorticoid effect on the colon (25) while providing normal circulating levels of the hormone, which underscores the physiologic relevance of these observations.

In summary, using adrenal ablation combined with selective hormone replacement and a sensitive method for measurement of Na-K-ATPase in a target nephron segment for both classes of corticosteroids, the present study indicates that under physiologic conditions Na-K-ATPase activity in rat kidney CCT is under mineralocorticoid, rather than glucocorticoid control.

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2. These data refer to the kidney as a whole and do not exclude a different effect on electrolyte transport in the CCT.

3. After 7 d Na-K-ATPase activity in this group was higher than in adrenal-intact rats. The explanation for this phenomenon is not apparent, but might reflect up-regulation of Aldo receptors following ADX, since in these rats circulating levels of the hormone were normal. The fact that enzyme activity was only partially restored after 24 h is consistent with our previous observations in another species, which did not document a short-term effect of Aldo on Na-K-ATPase (16).

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