Short-Term Effects of Uninephrectomy on Electrical Properties of the Cortical Collecting Duct from Rabbit Remnant Kidneys

Shigeaki Muto, Satoru Ebata, and Yasushi Asano
Department of Nephrology, Jichi Medical School, Minamikawachi, Kawachi, Tochigi, 329-04 Japan

Abstract

Microelectrode techniques were used to assess the electrical properties of the collecting duct cell in the isolated perfused cortical collecting duct from remnant kidneys 3, 6, and 24 h after uninephrectomy (UNX); results were compared with those from sham-operated kidneys. Plasma aldosterone levels did not change during the time course after UNX. The lumen-negative transepithelial voltage was elevated significantly 3 h after UNX, and was increased further 24 h after UNX. The basolateral membrane voltage (V_B) was elevated 6 h after UNX, and then was increased further at 24 h. Although the tight junction conductance and the fractional apical membrane resistance (fR_A) were not altered at any time points after UNX, the apical membrane conductance as well as the transepithelial (G_T) and basolateral membrane conductances increased 6 and 24 h after UNX. The changes in apical membrane voltage, G_T, and fR_A upon addition of luminal amiloride increased just 3 h after UNX, and then remained elevated at 6 and 24 h. The changes in apical membrane voltage and G_T upon addition of luminal Ba^{2+}, the changes in V_B upon addition of bath ouabain, and the changes in V_B, G_T, and fR_A upon raising bath K^+ were not influenced 3 h after UNX, but increased at 6 and 24 h. At these latter periods after UNX, the transference number of Cl^- of the basolateral membrane decreased significantly, whereas the transference number of K^+ of the basolateral membrane increased significantly. Simultaneously, addition of Ba^{2+} to the bath caused the V_B to hyperpolarize in parallel with decreases in G_T and fR_A. We conclude: (*a*) the initial effect of UNX (3 h) in the collecting duct cell is an increase in apical membrane Na^+ conductance; (*b*) the delayed effects of UNX (6 and 24 h) are increases in apical membrane K^+ conductance as well as basolateral membrane Na^+-K^+ pump activity and K^+ conductance; (*c*) the hyperpolarization of V_B at 6 and 24 h after UNX may result in the decrease of the ratio of the relative Cl^- conductance to the relative K^+ conductance of the basolateral membrane and also may increase passive K^+ entry into the cell across the basolateral membrane; (*d*) these time-dependent electrical changes occur independently of plasma aldosterone levels. (*J. Clin. Invest.* 1994. 93:286–296.) Key words: electrophysiology • sodium conductance • potassium conductance • sodium pump • uninephrectomy

Introduction

Loss of renal mass results in adaptive increases in the size and the function of the remnant kidney (1, 2). Among the remaining nephrons, the cortical collecting duct (CCD)[1] from remnant kidney during the chronic phase after uninephrectomy (UNX) also exhibits adaptive increase in Na^+ reabsorption (3) and K^+ secretion (4). These functional adaptive changes are accompanied by an increase in Na^+-K^+-ATPase activity (5) and an amplification of the basolateral membrane of the collecting duct (CD) cell (6), which is mainly responsible for Na^+ and K^+ transport in the CCD (7–14). Recently, Ebata et al. (15) have demonstrated that the CCDs from the remnant kidney in rabbits 14 d after UNX had structural hypertrophy, and that conductances of Na^+ and K^+ in the apical membrane as well as active Na^+-K^+-ATPase pump activity and K^+ conductance in the basolateral membrane of the CD cell from the remnant kidney are stimulated. In addition, they found that these electrical changes occurred independently of plasma aldosterone. Thus, the chronic adaptations in both tubular size and Na^+ and K^+ transport properties in the CCD have been well studied. However, no information on the function and the size of the CCD from remnant kidneys during early periods after UNX is available, although enhanced Na^+ reabsorption and K^+ secretion in the distal tubule has been reported 15 h after UNX in rats (16). Therefore, the present study was undertaken to examine the short-term effects of UNX on electrical properties in the apical as well as basolateral membranes of the CD cell in the isolated perfused CCD from UNX rabbits.

This study demonstrates that there is an initial increase in the amiloride-sensitive Na^+ conductance of the apical membrane 3 h after UNX. Secondary effects 6 and 24 h after UNX are expressed subsequently, including increases in apical membrane K^+ conductance as well as basolateral membrane Na^+-K^+-ATPase pump activity and K^+ conductance. These time-dependent electrical changes occur independently of plasma aldosterone.

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Address correspondence to Shigeaki Muto, M.D., Department of Nephrology, Jichi Medical School, Minamikawachi, Tochigi, 329-04 Japan.

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1. *Abbreviations used in this paper:* CCD, cortical collecting duct; CD cell, collecting duct cell; DOCA, deoxycorticosterone acetate; ΔEMF, change in basolateral membrane electromotive force due to ion substitution; fR_A, fractional apical membrane resistance; G_A, apical membrane conductance; G_B, basolateral membrane conductance; G_T, transepithelial conductance; G_{Tj}, tight junction conductance; t_{Cl}, transference number of Cl^- of the basolateral membrane; t_K, transference number of K^+ of the basolateral membrane; UNX, uninephrectomy; V_A, apical membrane voltage; V_B, basolateral membrane voltage; V_T, transepithelial voltage.

Table I. Effects of UNX on Body and Kidney Weights, Plasma Na^+, K^+, and Aldosterone Concentrations

	3 h		6 h		24 h	
	Control	UNX	Control	UNX	Control	UNX
Body weight (*kg*)	1.73±0.07 (*n* = 19)	1.71±0.06 (*n* = 10)	1.79±0.06 (*n* = 9)	1.71±0.05 (*n* = 13)	1.67±0.07 (*n* = 17)	1.66±0.08 (*n* = 14)
Right kidney weight (*g*)	6.1±0.1 (*n* = 19)	6.1±0.2 (*n* = 10)	6.2±0.5 (*n* = 9)	6.1±0.2 (*n* = 11)	6.4±0.4 (*n* = 14)	6.5±0.3 (*n* = 13)
Plasma Na^+ (*meq/liter*)	137.0±0.6 (*n* = 12)	137.8±1.0 (*n* = 6)	138.0±1.5 (*n* = 7)	138.5±0.9 (*n* = 8)	139.0±1.3 (*n* = 14)	136.3±0.7 (*n* = 10)
Plasma K^+ (*meq/liter*)	4.4±0.1 (*n* = 12)	4.2±0.08 (*n* = 6)	4.4±0.1 (*n* = 7)	4.2±0.1 (*n* = 8)	4.1±0.07 (*n* = 14)	4.4±0.2 (*n* = 10)
Plasma aldosterone (*pg/ml*)	74.5±12.3 (*n* = 7)	71.0±6.5 (*n* = 6)	78.0±4.8 (*n* = 5)	69.4±8.2 (*n* = 9)	75.5±8.6 (*n* = 8)	81.6±4.5 (*n* = 8)

Values are mean±SE.

Methods

Animals and surgical procedures. Female Japanese white rabbits weighing 1.5–2.5 kg were used. After a period of acclimation, the rabbits were divided into two groups: sham operation (control) and UNX. The operative procedures were as follows. First, all the animals were anesthetized with sodium pentobarbital (30 mg/kg intravenously). Second, the abdomen of each animal was opened by a left flank incision. After the abdomen was opened, the left kidney in the UNX group was removed via a dorsolateral incision under sterile conditions. The kidney was separated from the adrenal gland and from the associated connective tissue, the renal blood vessels were ligated, and the organ was excised. Then, the abdominal musculature in both groups of animals was sewn. The rabbits from two groups were maintained on standard rabbit chow (Clea Japan, Inc., Meguro, Tokyo, Japan) containing 120 meq/kg of Na^+ diet and 400 meq/kg of K^+ diet and tap water ad lib.

Isolation and perfusion of tubules. To determine plasma concentrations of Na^+, K^+, and aldosterone, blood was taken from control and UNX rabbits 3, 6, and 24 h after surgery. Plasma aldosterone concentrations were radioimmunologically measured by the previously described method (15). The animals of both groups were then reanesthetized with intravenous sodium pentobarbital (35 mg/kg), and the right kidney was removed and weighed. Slices of the coronal section 1–2 mm thick were made and transferred to a dish containing a cold intracellular fluidlike solution of the following composition (mM): 14 KCl, 44 K_2HPO_4, 14 KH_2PO_4, 9 $NaHCO_3$, and 160 sucrose. As described previously (11–15), this dissection medium was selected because it has been reported that intracellular fluid–like solutions are much better at preserving kidney tissue, metabolically as well as functionally. Segments of CCDs were dissected from the cortex and were transferred to a bath mounted on an inverted microscope (Diaphot; Nikon, Tokyo, Japan). Each tubule was perfused in vitro according to the techniques developed by Burg et al. (17) and as modified in this laboratory for the use of intracellular microelectrodes (11–15). Since the details of the technique have been published previously (11–15), they will be presented here only briefly. Tubules were suspended between the two pipettes. The luminal perfusion rate exceeded 20 nl/min in all tubules. The distal end of the tubule was held in the collecting pipette with unpolymerized Sylgard 184 (Dow Corning Corp., Midland, MI). The tubule was perfused in the bathing chamber of ~ 100 μl to permit rapid exchange of the bathing solution within 5 s. The bathing solution flowed at 5–15 ml/min from the reservoirs by gravity through a water jacket to permit the bath temperature to be regulated at 37°C.

Electrical measurements. The transepithelial and cellular electrical properties of the tubule were measured using techniques described previously in this laboratory (11–15). In brief, the transepithelial voltage (V_T) was measured through the perfusion pipette, which was connected to one channel of a dual-channel electrometer (Duo 773; World Precision Instruments, Inc., Sarasota, FL) with a 3 M KCl-3% agar bridge and a calomel half-cell electrode. The basolateral membrane voltage (V_B) was measured with 0.5 M KCl-filled microelectrodes, which were fabricated from borosilicate glass capillaries (GD-1.5; 1.5 mm OD, 1.0 mm I.D.; Narishige Scientific Laboratory, Setagaya, Tokyo, Japan) by using a vertical puller (PE-2; Narishige Scientific Laboratory). Both voltages were referenced to the bath and were recorded on a four-pen chart recorder (R64; Rikadenki Electronics, Meguro, Tokyo, Japan). The electrical potential difference across the apical membrane (V_A) was given by

$$V_A = V_T - V_B$$

Cable analysis was used to calculate the transepithelial conductance (G_T) and the fractional apical membrane resistance (fR_A) as described in detail previously (11–15). Constant-current pulses, 50 nA

Table II. Comparison of Tubular Length and Inner and Outer Diameters between Control and UNX Groups

	3 h		6 h		24 h	
	Control	UNX	Control	UNX	Control	UNX
	(*n* = 12)	(*n* = 15)	(*n* = 14)	(*n* = 11)	(*n* = 20)	(*n* = 16)
Tubular length (*μm*)	1,112.5±59.6	1,080.0±36.0	963.4±51.7	1,072.7±49.7	970.0±45.6	1,039.0±51.6
Inner diameter (*μm*)	28.5±1.0	29.0±1.0	29.1±1.1	28.2±0.7	30.7±0.8	31.5±1.4
Outer diameter (*μm*)	39.3±1.0	39.0±1.1	38.9±1.2	38.8±0.7	40.8±1.0	41.1±1.7

Values are mean±SE.

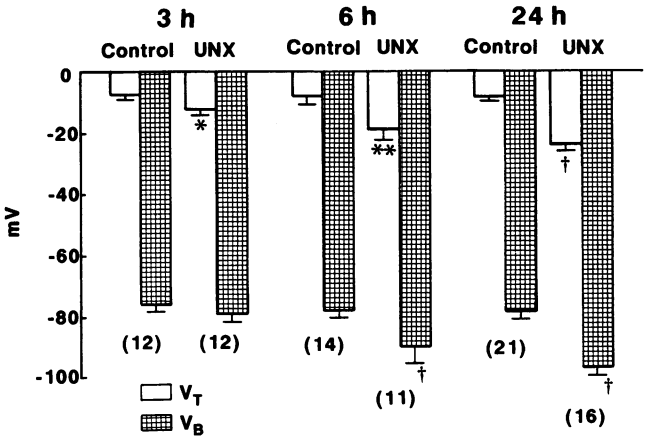

Figure 1. Effects of UNX on V_T and V_B of the CD cell at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. $^*P < 0.05$; $^{**}P < 0.01$; $^{\dagger}P < 0.001$ compared with corresponding control.

(300 ms in duration, 10-s interval), were injected into the tubule lumen via the perfusion pipette. The fR_A was estimated from the ratio of the voltage deflection across the apical membrane to the voltage deflection across the entire epithelium at the point of impalement.

The conductances of the apical and basolateral membranes (G_A and G_B, respectively) and the tight junction conductance (G_{Tj}) were estimated using 2 mM Ba^{2+} in the lumen as a probe to the equation described previously (8–10, 14, 15):

$$G_T = (1 - fR_A)G_B + G_{Tj}.$$

Ion-substitution studies were conducted to determine the relative ion permselectivity of the basolateral membrane. When the ion concentration of the bathing solutions was changed, the initial peak change in V_B was used with fast bath exchange rates (2–5 s) to minimize secondary effects such as changes in cellular ion activities. Voltage changes due to lowering bath Cl^- and raising bath K^+ concentrations were corrected for liquid junction potentials with free-flowing 3 M KCl electrodes. The change in basolateral membrane electromotive force (ΔEMF) due to ion substitution was estimated according to the following equation (14, 15): $\Delta EMF = \Delta V_B - I \cdot R_B$ where ΔV_B is the measured change in the V_B due to ion substitution and $I \cdot R_B$ is the change in membrane potential due to the dissipation of energy from current flowing across the basolateral membrane resistance (R_B). As described previously (14, 15), the circular loop current (I) was estimated from G_{Tj} and the change in V_T on ion substitution (ΔV_T) as $I = G_{Tj} \cdot \Delta V_T$. The transference numbers, which indicate the relative portion of a specific conductance of an ion with respect to the overall conductance, were calculated according to the following equation:

$$t_{ion} = \Delta EMF/[61 \cdot \log (c_1/c_2)],$$

where t_{ion} is the transference number of the respective ion, and where c_1 and c_2 are the two different ion concentrations of the specific ion used in the step-change experiments.

Identification of CD cells. Cell impalements in this study were limited to CD cells. The CD cells were electrophysiologically distinguished from the intercalated cells according to the criteria described previously by Muto et al. (9–14): the CD cells have a lower fR_A, higher V_B, apical Na^+ and K^+ conductances, and basolateral K^+ and Cl^- conductances, whereas the intercalated cells have a higher fR_A, lower V_B, a dominant basolateral Cl^- conductance, and no detectable apical K^+ conductance. Therefore, the CD cells were electrophysiologically identified by the depolarization of V_A and the decrease in fR_A upon raising the luminal perfusate K^+ concentration. In addition, the CD cells showed a depolarization of V_A and an increase in fR_A upon addition of luminal Ba^{2+}, which is a K^+ channel inhibitor. In sharp contrast, the intercalated cells did not show any significant changes in V_A or fR_A upon raising the perfusate K^+ concentration and addition of luminal Ba^{2+}.

Solutions and materials. The composition of the control bathing and perfusing solution contained (mM): 110 NaCl, 5 KCl, 1 $MgCl_2$, 1.8 $CaCl_2$, 25 $NaHCO_3$, 10 Na acetate, 0.8 Na_2HPO_4, 0.2 NaH_2PO_4, 5 L-alanine, and 8.3 D-glucose. This control solution had an osmolality between 285 and 295 mos mol/kg H_2O, and was equilibrated with 95% O_2/5% CO_2 and adjusted to pH 7.4 at 37°C. In some experiments, 45 mM Na^+ was replaced with K^+, or 108.6 mM Cl^- was replaced with cyclamate.

Amiloride (Sigma Chemical Co., St. Louis, MO) was added to the luminal perfusate to achieve a final concentration of 50 μM. Ouabain

Table III. Effects of UNX on Barrier Voltages and Conductances

	3 h		6 h		24 h	
	Control	UNX	Control	UNX	Control	UNX
V_T (*mV*)	−7.4±1.5	−12.2±1.8*	−7.9±2.4	−19.2±2.6‡	−8.3±1.2	−24.1±1.7§
	(*n* = 12)	(*n* = 12)	(*n* = 14)	(*n* = 11)	(*n* = 21)	(*n* = 16)
V_B (*mV*)	−76.1±2.0	−79.1±2.2	−77.9±2.3	−91.0±3.7§	−78.6±1.7	−96.8±2.3§
	(*n* = 12)	(*n* = 12)	(*n* = 14)	(*n* = 11)	(*n* = 21)	(*n* = 16)
V_A (*mV*)	68.7±2.0	66.8±1.5	69.9±2.8	71.8±2.9	70.3±1.7	72.7±1.5
	(*n* = 12)	(*n* = 12)	(*n* = 14)	(*n* = 11)	(*n* = 21)	(*n* = 16)
fR_A	0.44±0.03	0.44±0.04	0.45±0.02	0.43±0.02	0.44±0.02	0.38±0.02
	(*n* = 12)	(*n* = 12)	(*n* = 13)	(*n* = 11)	(*n* = 15)	(*n* = 14)
G_T ($mS \cdot cm^{-2}$)	8.3±0.7	8.1±0.8	7.8±0.5	10.0±1.0	8.0±0.4	11.0±0.6§
	(*n* = 12)	(*n* = 12)	(*n* = 13)	(*n* = 11)	(*n* = 15)	(*n* = 13)
G_A ($mS \cdot cm^{-2}$)	12.1±1.4	12.4±1.9	11.4±1.6	17.7±1.9*	12.4±1.3	23.1±1.6§
	(*n* = 12)	(*n* = 12)	(*n* = 13)	(*n* = 11)	(*n* = 15)	(*n* = 13)
G_B ($mS \cdot cm^{-2}$)	9.2±0.9	9.0±0.6	8.8±0.9	13.3±2.0	9.8±0.9	14.4±1.0‖
	(*n* = 12)	(*n* = 12)	(*n* = 13)	(*n* = 11)	(*n* = 15)	(*n* = 13)
G_{Tj} ($mS \cdot cm^{-2}$)	3.2±0.5	3.2±0.6	3.0±0.3	2.6±0.5	3.0±0.2	2.2±0.4
	(*n* = 12)	(*n* = 12)	(*n* = 13)	(*n* = 11)	(*n* = 15)	(*n* = 13)

Values are mean±SE. * $P < 0.05$; ‡ $P < 0.01$; ‖ $P < 0.005$; § $P < 0.001$ vs corresponding control group.

(Sigma Chemical Co.) was used in the bath at a concentration of 10^{-4} M. $BaCl_2$ was used at a final concentration of 2 mM.

Tubular measurements. Tubular lengths were measured at the end of each experiment, using a calibrated reticle in the eyepiece of the microscope. The tubules were photographed at a proximal, central, and distal site during perfusion at a magnification of 200. Inner and outer diameters were measured at 0.05-mm intervals along the tubule. Reported values are the average of at least five measurements. Since the tubules from the two groups were rapidly perfused at similar rates and pressures, the degree of distension of the lumen is assumed to be similar in all.

Statistics. The data are expressed as mean±SE. Comparisons were performed by the paired or nonpaired Student's *t* test and one-way ANOVA in combination with Scheffe's multiple comparison test, as needed. *P* values less than 0.05 were considered statistically significant.

Results

Effects of UNX on body and kidney weights, plasma Na^+, K^+, and aldosterone concentrations

Body and right kidney weights, plasma Na^+, K^+, and aldosterone concentrations in both groups of animals at different time points after surgery are given in Table I. The body weights of UNX rabbits did not differ significantly from those of the corresponding groups of control rabbits. In addition, the weights of the contralateral right kidneys from UNX animals were not significantly different from those of the control right kidneys at any time points after surgery. Plasma Na^+, K^+, and aldosterone concentrations in UNX animals at different time points after the surgical procedure were all very similar to the corresponding values in control animals.

Electrophysiological data

The tubular length and inner and outer diameters of the CCD segments in both groups of tubules 3, 6, and 24 h after surgery are given in Table II. There were no significant differences of inner and outer diameters between the two groups at any time points after the operation.

Effects of UNX on barrier voltages and conductances of the CD cell from remnant kidneys. The effects of UNX on barrier voltages of the CD cells of tubules from remnant kidneys at different time points after surgery are given in Fig. 1 and Table III. Just 3 h after UNX, the lumen-negative V_T increased from −7.4 to −12.2 mV, indicating that active Na^+ transport had been stimulated. The V_T increased further 6 h after UNX from −7.9 to −19.2 mV and 24 h after UNX from −8.3 to −24.1 mV, indicating that there are additional, possibly secondary, effects of UNX on active Na^+ transport. The V_B was not significantly different from control values at 3 h after UNX, but was hyperpolarized significantly from −77.9 to −91.0 mV 6 h after UNX, and also after 24 h from −78.6 to −96.8 mV. The V_A in the UNX group did not differ significantly from that in the control group at any time points after the operation.

The effects of UNX on barrier conductances at different time points after surgery are also given in Table III. There were no significant differences in fR_A or G_{Tj} between the two groups at any time points after the operation. Although the G_T was not changed significantly 3 and 6 h after UNX, it was elevated significantly 24 h after UNX. The G_A was not altered 3 h after UNX, but was increased significantly 6 and 24 h after UNX. The G_B was unchanged 3 and 6 h after UNX, but was elevated significantly 24 h after UNX.

Effects of UNX on electrical properties of the apical membrane of the CD cell from remnant kidneys. The G_A of the CD cell from normal rabbits is composed of a small Na^+ conductance and a dominant K^+ conductance (7–15). The first set of the studies was therefore designed to examine whether the Na^+ conductance and/or K^+ conductance in the apical membrane of the CD cell is affected at different time points after UNX.

To examine whether a difference in Na^+ conductance of the apical membrane of the CD cell exists between the two groups at different time periods after surgery, we added a Na^+ channel inhibitor, amiloride, to the luminal perfusate and compared the barrier voltages and conductances, as shown in Table IV. Upon addition of 50 μM amiloride to the perfusate,

Table IV. Effects of 50 μM Amiloride in the Lumen on Barrier Voltages and Conductances at the Initial Peak Response

	V_T		V_B		V_A		G_T		fR_A	
Group	C	E	C	E	C	E	C	E	C	E
	mV		*mV*		*mV*		*mS·cm⁻²*			
Control										
3 h	−8.9±2.2	8.7±1.0*	−78.6±3.1	−67.0±4.6*	69.7±4.9	75.7±4.5*	8.9±0.9	7.4±0.6‡	0.42±0.06	0.56±0.07§
	(8)	(8)	(8)	(8)	(8)	(8)	(8)	(8)	(8)	(8)
6 h	−6.8±1.2	6.5±1.3*	−80.0±2.2	−72.1±2.4*	73.2±2.1	78.6±2.4*	8.1±0.6	6.7±0.5*	0.47±0.04	0.60±0.04*
	(12)	(12)	(12)	(12)	(12)	(12)	(10)	(10)	(10)	(10)
24 h	−7.7±0.9	3.0±0.6*	−80.1±2.0	−74.6±2.5*	72.4±2.4	77.7±2.3*	8.1±0.6	6.4±0.5*	0.45±0.05	0.58±0.05*
	(18)	(18)	(18)	(18)	(18)	(18)	(15)	(15)	(15)	(15)
UNX										
3 h	−11.1±1.8	4.9±0.8*	−79.0±2.1	−72.0±2.0‡	67.9±1.6	76.9±1.9*	8.9±0.5	5.8±0.2*	0.41±0.05	0.62±0.06*
	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
6 h	−24.9±1.7	3.9±1.3*	−92.0±2.9	−75.9±2.3*	67.0±2.3	79.8±2.5*	9.2±1.1	5.4±0.6§	0.43±0.03	0.66±0.04*
	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
24 h	−21.8±2.0	4.4±1.4*	−95.0±2.0	−82.1±2.6*	73.2±1.9	86.5±2.3*	10.0±0.7	5.9±0.3§	0.38±0.04	0.66±0.03*
	(13)	(13)	(13)	(13)	(13)	(13)	(9)	(9)	(9)	(9)

Values are mean±SE. Numerals in parentheses indicate number of experiments. C, control period; E, experimental period. * $P < 0.001$; ‡ $P < 0.01$; § $P < 0.005$ compared with the control period.

the V_T and the V_B in the tubules of the two groups at different time points were depolarized rapidly, resulting in a significant hyperpolarization of V_A. At that time, the G_T was decreased significantly and the fR_A was increased significantly in the two groups. However, the amiloride-sensitive changes in V_A, G_T, and fR_A increased significantly just 3 h after UNX and remained elevated 6 and 24 h after UNX (Fig. 2). Therefore, these results indicate that the amiloride-sensitive Na^+ conductance in the apical membrane of the CD cell is stimulated even 3 h after UNX.

Next, we examined whether the apical membrane K^+ conductance of the CD cell is increased at different time points after UNX. Thus, we added a K^+ channel inhibitor, Ba^{2+}, to the luminal perfusate and observed the electrical properties at the initial peak response (Table V). When 2 mM Ba^{2+} was added to the perfusate in the tubules of the two groups at different time points, the V_T was hyperpolarized rapidly, and the V_B was depolarized rapidly, resulting in a significant depolarization of V_A. At that time, the G_T was decreased significantly, and the fR_A was increased significantly in the tubules of the two groups. However, the Ba^{2+}-sensitive changes in V_A and G_T were different between the two groups at three time points after the operation; they were unchanged 3 h after UNX, but were increased significantly 6 and 24 h after UNX (Fig. 3). Therefore, the Ba^{2+}-sensitive K^+ conductance in the apical membrane is stimulated at these latter periods after UNX. Taken together, it appears that the initial effect of UNX is to increase the Na^+ conductance, with a delayed effect on the K^+ conductance of the apical membrane.

Effects of UNX on electrical properties of the basolateral membrane of the CD cell from remnant kidneys. As shown in Table III and Fig. 1, the $-V_B$ was unchanged 3 h after UNX, but increased by ~ 20 mV 6 and 24 h after UNX, suggesting that the Na^+-K^+-ATPase pump activity in the basolateral membrane of the CD cell from the remaining kidney is stimulated at these latter periods after UNX. To further confirm this notion, we added a Na^+-K^+ pump inhibitor, ouabain, to the bath, and observed the barrier voltages and conductances at the initial peak response. In the two groups of the tubules at different time points after surgery, addition of 10^{-4} M ouabain to the bath caused both V_T and V_B to depolarize significantly without any changes in G_T or fR_A (Table VI). However, the initial peak change was also different between the two groups at three different time points after surgery; it was not influenced 3 h after UNX, but was increased significantly 6 h after UNX and was increased further 24 h after UNX (Fig. 4). These results are consistent with the notion that an increase in the Na^+-K^+ pump activity in the basolateral membrane of the CD cell after UNX is probably secondary to an increase in the Na^+ conductance of the apical membrane.

The conductive pathway of the basolateral membrane from normal rabbit kidneys is composed of a dominant Cl^- conductive pathway and a small K^+ conductive pathway (9–11, 14, 15, 18–20). In the basolateral membrane, the coupled influx of K^+ via the Na^+-K^+-ATPase pump is "recycled" via this basolateral K^+ conductance. Thus, the change in Na^+-K^+ pump activity described above would influence the basolateral K^+ conductance. Also, the G_B was not affected 3 and 6 h after UNX, but increased 24 h after UNX, as shown in Table III. Therefore, K^+ conductance and/or Cl^- conductance would be affected at different time points after UNX. We compared the relative ion conductive properties of the basolateral membrane

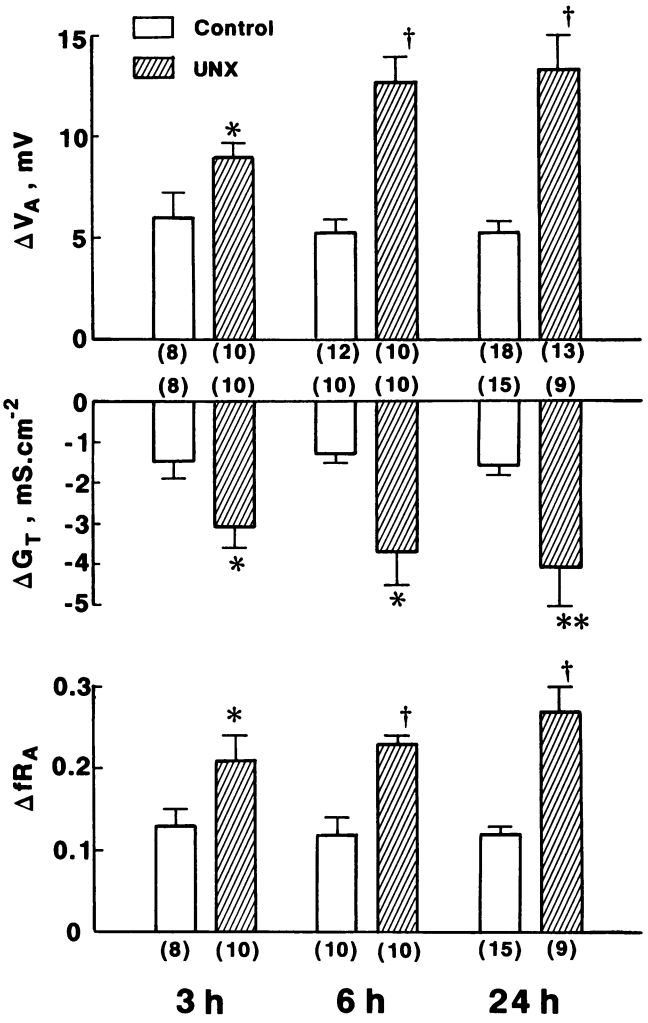

Figure 2. Comparison of the amiloride-sensitive changes in V_A, G_T, and fR_A between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. $^*P < 0.05$; $^{**}P < 0.005$; $^\dagger P < 0.001$ compared with corresponding control.

of the two groups of tubules using rapid exchange rates of bath. When the bath K^+ concentration was increased from 5 to 50 mM, the basolateral membrane in the tubules of the two groups at different time points after surgery was depolarized rapidly. As shown in Fig. 5, however, the initial peak change in V_B was different between the two groups at three time points after surgery; it was unchanged 3 h after UNX (control, 13.0 mV, $n = 16$; UNX, 15.0 mV, $n = 14$), but was elevated significantly 6 h after UNX (control, 12.0 mV, $n = 17$; UNX, 22.7 mV, $n = 25$, $P < 0.001$), and increased further 24 h after UNX (control, 14.0 mV, $n = 17$; UNX, 27.4 mV, $n = 25$, $P < 0.001$). Simultaneously, the transference number for K^+ (t_K) was not affected 3 h after UNX (control, 0.18; UNX, 0.21), but was elevated significantly 6 h after UNX (control, 0.17; UNX, 0.33) and then was increased further 24 h after UNX (control, 0.18; UNX, 0.41) (Fig. 6). When the bath Cl^- concentration was decreased from 120.6 to 12 mM, the basolateral membrane in the tubules of the two groups at different time points after surgery was depolarized rapidly. However, the initial peak change in V_B was also different between the two groups at three

Table V. Effects of 2 mM Ba^{2+} in the Lumen on Barrier Voltages and Conductances at the Initial Peak Response

	V_T		V_B		V_A		G_T		fR_A	
Group	C	E	C	E	C	E	C	E	C	E
	mV		*mV*		*mV*		*mS·cm⁻²*			
Control										
3 h	−8.9±1.3	−16.0±1.6*	−78.7±2.3	−55.3±3.4*	69.9±2.6	41.6±2.9*	8.3±0.7	4.8±0.6*	0.44±0.03	0.82±0.02*
	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)
6 h	−8.9±2.0	−16.0±2.0*	−79.3±2.6	−57.7±2.6*	70.4±2.5	41.7±2.5*	7.8±0.5	4.3±0.3*	0.45±0.02	0.85±0.02*
	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)
24 h	−7.4±1.0	−11.6±1.3*	−76.3±1.5	−51.2±2.0*	68.6±1.7	39.5±2.0*	8.0±0.4	4.1±0.2*	0.44±0.02	0.83±0.01*
	(26)	(26)	(20)	(26)	(26)	(26)	(15)	(15)	(15)	(15)
UNX										
3 h	−11.3±2.9	−14.7±3.6‡	−80.4±2.5	−54.1±3.5*	69.1±1.6	39.4±2.6*	8.1±0.8	4.7±0.7*	0.44±0.04	0.84±0.02*
	(13)	(12)	(13)	(13)	(13)	(13)	(12)	(12)	(12)	(12)
6 h	−22.1±1.8	−29.4±2.0*	−92.0±1.8	−62.9±2.1*	69.8±1.6	33.5±1.8*	9.9±0.9	4.4±0.3*	0.43±0.03	0.82±0.01*
	(19)	(19)	(19)	(19)	(19)	(19)	(16)	(16)	(16)	(16)
24 h	−24.2±1.9	−35.7±1.9*	−97.7±2.2	−70.5±3.0*	73.4±1.1	34.8±2.7*	11.0±0.6	4.8±0.5*	0.38±0.02	0.82±0.02*
	(14)	(14)	(14)	(14)	(14)	(14)	(14)	(14)	(14)	(14)

Values are mean±SE. Numerals in parentheses indicate number of experiments. C, control period; E, experimental period. * $P < 0.001$; ‡ $P < 0.01$ compared with the control period.

time points after surgery; it was not influenced 3 h after UNX (control, 24.3 mV, $n = 11$; UNX, 23.6 mV, $n = 19$), but was decreased significantly 6 h after UNX (control, 24.9 mV, $n = 12$; UNX, 21.1 mV, $n = 18$, $P < 0.005$) and was decreased further 24 h after UNX (control, 23.5 mV, $n = 18$; UNX, 17.5 mV, $n = 18$, $P < 0.001$). Simultaneously, the transference number for Cl^- (t_{Cl}) was not affected 3 h after UNX (control, 0.46; UNX, 0.45), but was decreased significantly 6 h after UNX (control, 0.47; UNX, 0.37) and was decreased further 24 h after UNX (control, 0.43; UNX, 0.30) (Fig. 6).

Table VII shows the effects of raising the bath K^+ concentration on barrier voltages and conductances at the initial peak response. Upon raising the bath K^+ concentration in the tubules of the two groups, the G_T and the fR_A were increased significantly. As shown in Fig. 5, the changes in G_T and fR_A were unchanged 3 h after UNX, but were increased significantly 6 and 24 h after UNX. Taken together, these results indicate that both an increase in the relative K^+ conductance and a decrease in the relative Cl^- conductance are delayed effects of UNX in parallel with an increase in Na^+-K^+-ATPase pump activity.

To further characterize the basolateral membrane K^+ conductive property in the UNX group at different time points after surgery, we added 2 mM Ba^{2+} to the bath, and observed the electrical parameters. Table VIII summarizes the effects of Ba^{2+} to the bath on electrical properties at the initial peak response. In the control group at three time points after the operation and in the UNX group at 3 h after surgery, addition of Ba^{2+} to the bath had no significant effects on V_T and V_B although it caused both G_T and fR_A to decrease significantly (Table VIII, Fig. 7). These findings indicate that K^+ is close to equilibrium across the basolateral membrane. In sharp contrast, when 2 mM Ba^{2+} was added to the UNX group at 6 and 24 h after surgery, both V_T and V_B were hyperpolarized rapidly with decreases in G_T and fR_A (Table VIII, Fig. 7). These results are consistent with Ba^{2+} blockade of K^+ current directed into the cell from the bath in the UNX group 6 and 24 h after the operation. These findings are also reported in the CCDs from rabbits with a long-term treatment of deoxycorticosterone acetate (DOCA) (19) and in the CCDs from the remnant kidney 14 d after UNX (15).

Discussion

This study was designed to determine the electrical properties of the apical and the basolateral membranes of the CD cell from contralateral kidneys during early periods after UNX. Although the chronic effects of UNX in the CCD are increases in both Na^+ and K^+ conductances of the apical membrane as well as the Na^+-K^+ pump and K^+ conductance of the basolateral membrane (15), the acute effects appear to be temporally separated. We observed that the initial effect of UNX was an increase in the apical membrane Na^+ conductance with delayed effects of increases in the apical membrane K^+ conductance as well as basolateral membrane Na^+-K^+ pump activity and K^+ conductance. These time-dependent electrical changes occurred independently of plasma aldosterone. In addition, the CCDs from remnant kidneys did not exhibit structural hypertrophy during early stages after UNX. This study was the first to demonstrate the short-term effects of UNX on electrical properties in the CD cell from remnant kidneys.

Electrical properties of the apical as well as basolateral membranes of the CD cell from remnant kidneys at different time points after UNX. As described in Table III, at 3 h after UNX only $-V_T$ was increased significantly, but the other electrical parameters, including the G_A, fR_A, G_T, and V_B, were not altered significantly. A significant change would be hard to detect unless many experiments were performed in the two groups of animals. On the other hand, both $-V_B$ and G_A were elevated significantly 6 and 24 h after UNX. To detect the significant changes in the apical membrane conductance at different time points, especially at 3 h after UNX, we observed the

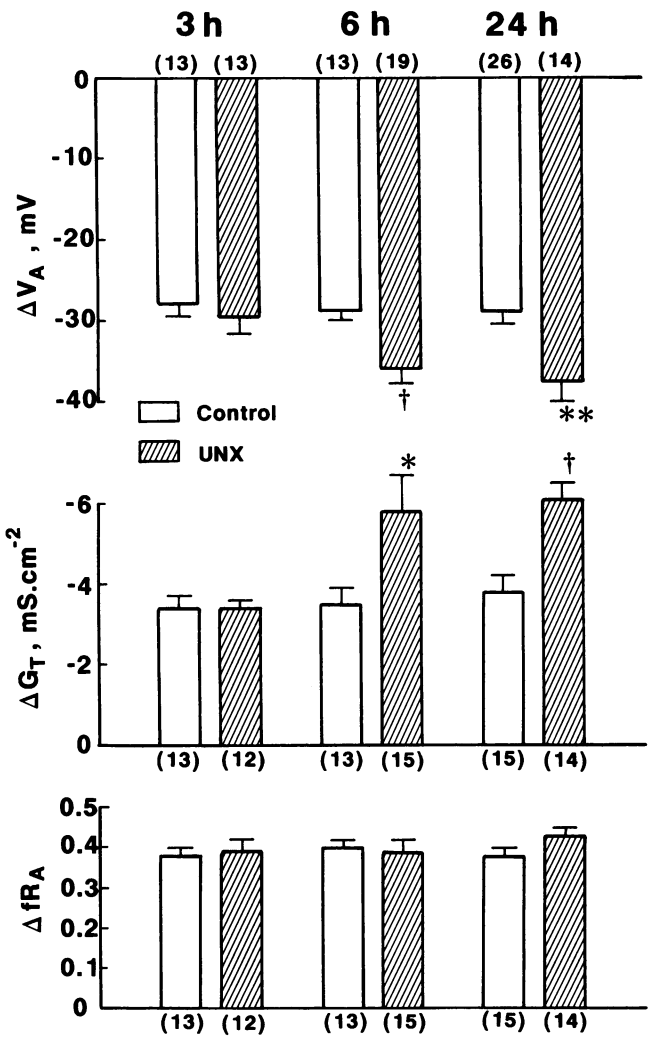

Figure 3. Comparison of the changes in V_A, G_T, and fR_A upon addition of luminal Ba^{2+} between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. $^*P < 0.05$; $^{**}P < 0.005$; $^{\dagger}P < 0.001$ compared with corresponding control.

changes in V_A, G_T, and fR_A before and after addition of luminal amiloride and Ba^{2+} because the apical membrane conductive pathways of the CD cell in the CCDs from normal rabbits are an amiloride-sensitive Na^+ conductive pathway and a Ba^{2+}-sensitive K^+ conductive pathway (7–15). As shown in Fig. 2, the amiloride-sensitive changes in V_A, G_T, and fR_A were increased just 3 h after UNX, and remained elevated 6 and 24 h after UNX. Furthermore, as shown in Fig. 3, the changes in V_A and G_T upon addition of luminal Ba^{2+} were not influenced 3 h after UNX, but increased 6 and 24 h after UNX. These results indicate that the initial effect of UNX is on the apical membrane Na^+ conductance, with a delayed effect of an increase in the apical membrane K^+ conductance. Although increases in RNA (21), DNA (22), and protein synthesis (23) are evident within hours after UNX, it is not known at the present time whether this initial effect of UNX on the apical membrane Na^+ conductance is due to insertion of new Na^+ channels in the apical membrane or to an increase in the open state of preexisting channels.

As shown in Table III and Fig. 1, the V_B was not significantly changed 3 h after UNX, but 6 and 24 h after UNX hyperpolarized by ~ 20 mV above the corresponding values in the control. Simultaneously, the initial peak changes in V_B upon addition of ouabain to the bath were not altered 3 h after UNX, but were increased significantly 6 and 24 h after UNX. Based on these two observations, it is indicated that the effect of UNX on the Na^+-K^+ pump activity in the basolateral membrane is probably a delayed or secondary effect to the increase in Na^+ entry into the cell.

In the CD cell from the normal rabbit, K^+ goes across the basolateral membrane via active uptake by the Na^+-K^+-ATPase pump and passive movement through a K^+ conductive pathway. The parallel coupling between the magnitude of the K^+ conductance and the Na^+-K^+ pump activity across the basolateral membrane exists in nearly all salt-transporting epithelia, including the CD cell. Thus, the relative K^+ conductance in the basolateral membrane would be expected to be stimulated at 6 and 24 h after UNX because the Na^+-K^+ pump activity in the basolateral membrane is stimulated significantly, as described above. Using the transference numbers for Cl^- and K^+, we can estimate the relative Cl^- and K^+ conductances across the basolateral membrane. In this study we found that the relative K^+ conductance is not influenced 3 h after UNX, but was increased significantly 6 and 24 h after UNX, as was expected. In sharp contrast, the relative Cl^- conductance decreased significantly at these latter periods after UNX. These changes in the relative conductances of K^+ and Cl^- at 6 and 24 h after UNX strikingly resemble those seen in the basolateral membrane of the CD cell in the CCD from chronic mineralocorticoid-treated rabbits (19, 20) and from remaining kidneys in rabbits 14 d after UNX (15). It should be noted that the basolateral membrane of the CD cell is more selective to K^+ 24 h after UNX, whereas it is more selective to Cl^- 3 h after UNX. A stimulation of the Na^+-K^+ pump activity in parallel with an increase in the basolateral membrane K^+ conductance at 6 and 24 h after UNX is associated with hyperpolarization of V_B. Alternatively, this hyperpolarization of V_B would induce a decrease in relative Cl^- conductance because the Cl^- channel in the basolateral membrane of the CD cell from rabbit kidneys is reported to be voltage-dependent at physiological potentials (24). Muto et al. (14) also have shown that the relative Cl^- conductance in the basolateral membrane of the CD cell from sham-operated and obstructed rabbit kidneys 24 h after unilateral ureteral obstruction was related directly to V_B. This direct correlation between V_B and the relative Cl^- conductance is also observed in the CD cell from normal and chronic DOCA-treated rabbits (20).

In the CD cell from normal rabbits, V_B is known to be near the Nerst equilibrium potential for K^+ across the basolateral membrane (14, 15, 19). In this study, we also observed the same electrical property in the basolateral membrane of the CD cell from the control kidney at three different periods after surgery and the UNX group at 3 h after surgery because addition of Ba^{2+}, an effective inhibitor of K^+ channel, to the bath had no effect on V_B. On the other hand, $-V_B$ in the UNX group at 6 and 24 h after surgery was elevated by ~ 20 mV so a driving force for K^+ entry into the cell could exist because addition of Ba^{2+} to the bath caused the basolateral membrane to hyperpolarize significantly (Table VIII). Therefore, increases in both K^+ conductance and the driving force for K^+ across the basolateral membrane could result in an increased

Table VI. Effects of 10^{-4} M Ouabain in the Bath on Barrier Voltages and Conductances at the Initial Peak Response

Group	V_T		V_B		G_T		fR_A	
	C	E	C	E	C	E	C	E
	mV		*mV*		*mS·cm⁻²*			
Control								
3 h	−7.2±1.1	1.2±1.0*	−75.0±2.4	−65.4±2.3‡	7.9±0.3	7.7±0.3	0.46±0.03	0.47±0.02
	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
6 h	−8.1±0.8	−1.5±1.1*	−76.8±2.2	−67.8±2.6*	8.1±0.2	7.9±0.3	0.42±0.03	0.42±0.02
	(5)	(5)	(5)	(5)	(5)	(5)	(5)	(5)
24 h	−8.9±1.5	0.3±1.0‡	−80.2±4.5	−69.5±4.5‡	8.8±0.4	8.6±0.4	0.45±0.05	0.45±0.05
	(8)	(8)	(8)	(8)	(8)	(8)	(8)	(8)
UNX								
3 h	−11.3±1.0	−1.8±1.4*	−81.6±5.4	−72.0±5.3*	8.1±0.4	7.8±0.5	0.41±0.03	0.42±0.03
	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)
6 h	−17.8±1.7	−2.6±2.7‡	−92.6±3.5	−76.5±2.8‡	9.8±0.3	9.6±0.4	0.39±0.03	0.40±0.03
	(6)	(6)	(6)	(6)	(6)	(6)	(6)	(6)
24 h	−19.1±2.5	−2.0±1.8‡	−93.6±2.2	−70.7±2.2‡	10.0±1.0	9.7±0.9	0.36±0.04	0.38±0.04
	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)

Values are mean±SE. Numerals in parentheses indicate number of experiments. C, control period; E, experimental period. * $P < 0.005$; ‡ $P < 0.001$ compared with the control period.

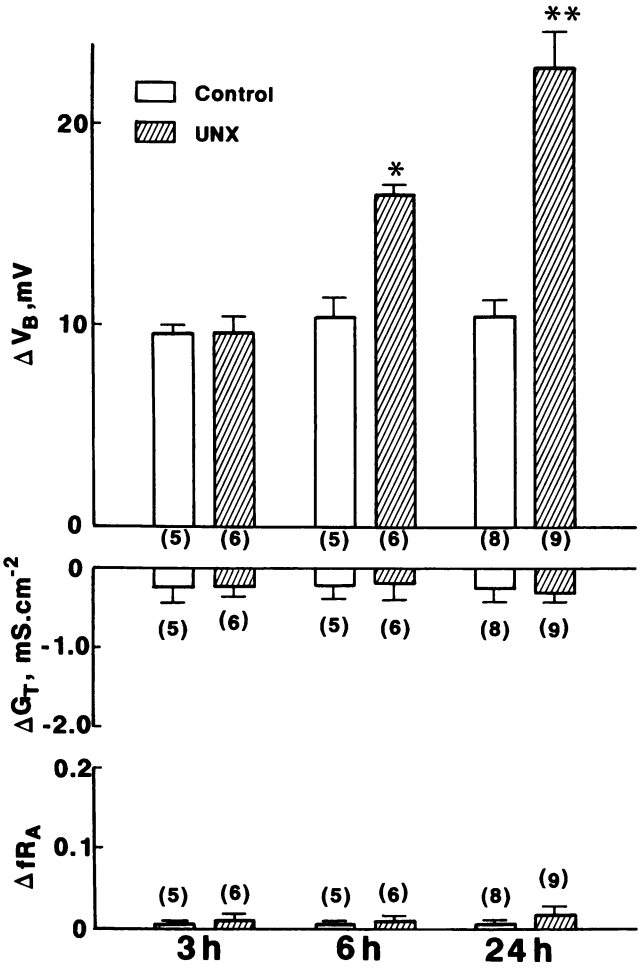

Figure 4. Comparison of the changes in V_B, G_T, and fR_A upon addition of ouabain to the bath between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. * $P < 0.005$; ** $P < 0.001$ compared with corresponding control.

K^+ uptake across the basolateral membrane in the CCDs from the contralateral kidney 6 and 24 h after UNX.

Mechanisms responsible for the acute adaptation in the CD cell from remnant kidneys after UNX. Long-term treatment with mineralocorticoids such as aldosterone and DOCA is known to increase the apical membrane Na^+ and K^+ conductances as well as the basolateral membrane Na^+-K^+ pump and K^+ conductance (7, 18, 19, 25). On the other hand, short-term effects of mineralocorticoid treatment in the rabbit CCD are a primary effect of an increase in the apical Na^+ conductance, with delayed effects of increases in apical K^+ conductance as well as basolateral Na^+-K^+ pump and K^+ conductance. Sansom and O'Neil (25), using electrophysiological techniques, reported that an effect of DOCA treatment of rabbits with intact adrenal glands was an increase in the apical membrane Na^+ conductance of the CD cell within 24 h. A secondary, delayed effect, occurring after 24 h, was an increase in the apical membrane K^+ conductance and hyperpolarization of V_B. O'Neil and Hayhurst (26) have also shown that Na^+-K^+-ATPase activity in the CCD from adrenal intact rabbits was also increased by DOCA treatment, but again with a delay of at least 24 h. This time-dependent electrophysiological behavior seems to be similar to that seen after UNX in the present study. However, the time course of the electrical properties at early periods after UNX was quite different from that seen after the short-term treatment with DOCA. Compared with DOCA effects in the adrenal intact rabbits, effects of UNX act much faster to induce an increase in Na^+ and K^+ transport in the present study. Furthermore, the present study demonstrates that UNX had no significant effect on plasma aldosterone concentration at any time points after surgery. Therefore, it is concluded that the acute functional adaptations of the CD cell after UNX occur independently of plasma aldosterone levels.

The aldosterone-independent mechanism(s) by which UNX initially stimulates apical membrane Na^+ conductance with delayed effects of increases in apical membrane K^+ conductance as well as basolateral membrane Na^+-K^+ pump activity and K^+ conductance are not known presently. According to

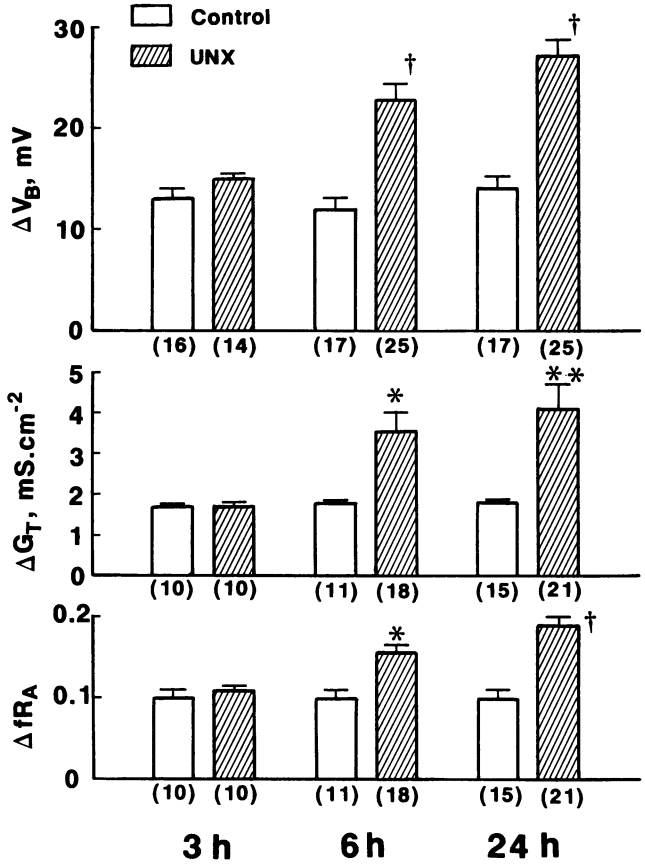

Figure 5. Comparison of the changes in V_B, G_T, and fR_A upon raising bath K^+ concentration between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. $^*P < 0.05$; $^{**}P < 0.005$; $^{\dagger}P < 0.001$ compared with corresponding control.

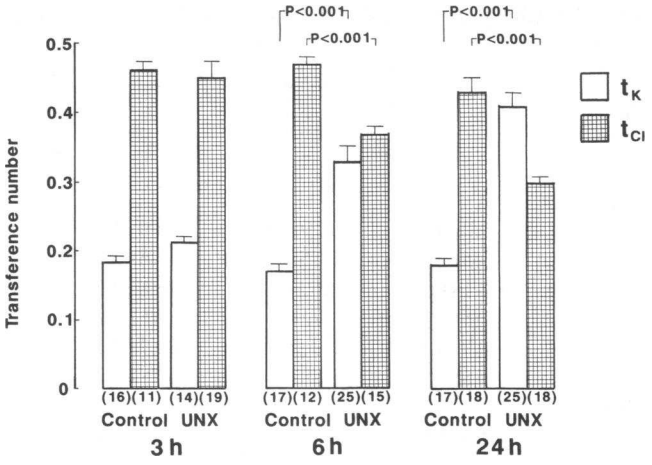

Figure 6. Comparison of the transference numbers of the basolateral membrane (t_K and t_{Cl}) between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. The t_K and t_{Cl} reflect the relative K^+ and Cl^- conductances of the basolateral membrane, respectively. The ratio of the relative Cl^- conductance to the relative K^+ conductance of the basolateral membrane gradually decreased between 6 and 24 h after UNX.

Shirley and Walter (27), the GFR and single nephron GFR increased in the remnant kidney in rats 2–5 h after UNX. Diezi et al. (16), using the in vivo micropuncture technique, reported that a significant increase in single nephron GFR and increased delivery of fluid into the distal tubule existed in the rats 15 h after UNX. Therefore, we propose that an increased rate of Na^+ delivery to the CCD may result in an increase in the Na^+ uptake into the cell across the apical membrane, leading to stimulation of the basolateral membrane Na^+-K^+ pump activity. This may induce a hyperpolarization of V_B, which could increase K^+ entry into the cell across the basolateral membrane, as discussed above. This in turn would increase the cell K^+ concentration, which could activate the apical membrane K^+ conductance. A tight coupling between the basolateral membrane Na^+-K^+ pump activity and the apical membrane K^+ conductance has been reported in the CD cell from rabbit kidneys (9, 28, 29). Kaissling et al. (30–32) increased Na^+

Table VII. Effects of Bath K^+ Elevation from 5 to 50 mM on Barrier Voltages and Conductances at the Initial Peak Response

	V_T		V_B		G_T		fR_A	
Group	C	E	C	E	C	E	C	E
	mV		*mV*		*mS·cm⁻²*			
Control								
3 h	−9.3±1.4	−0.4±0.9*	−76.0±0.4	−64.2±2.1*	7.7±0.5	9.4±0.7*	0.46±0.03	0.56±0.03*
	(16)	(16)	(16)	(16)	(10)	(10)	(10)	(10)
6 h	−7.1±1.8	0.3±1.3*	−78.8±2.0	−67.9±2.2*	8.2±0.5	9.9±0.8*	0.41±0.05	0.51±0.06*
	(17)	(17)	(17)	(17)	(11)	(11)	(11)	(11)
24 h	−8.4±1.7	3.9±1.5*	−78.7±2.5	−65.9±2.4*	8.2±0.5	10.1±0.6*	0.41±0.05	0.52±0.05*
	(17)	(17)	(17)	(17)	(15)	(15)	(15)	(15)
UNX								
3 h	−11.0±1.5	−0.4±1.7*	−82.3±2.1	−68.4±2.3*	7.9±0.6	9.6±0.6‡	0.44±0.08	0.56±0.07‡
	(14)	(14)	(14)	(14)	(10)	(10)	(10)	(10)
6 h	−21.3±1.6	−3.0±1.3*	−92.8±2.0	−71.2±1.5*	9.7±0.8	13.2±1.1*	0.38±0.03	0.54±0.06*
	(25)	(25)	(25)	(25)	(18)	(18)	(18)	(18)
24 h	−21.3±1.6	1.0±2.4*	−98.5±1.6	−72.5±2.3*	10.4±0.4	14.4±0.7*	0.35±0.03	0.54±0.03*
	(25)	(25)	(25)	(25)	(21)	(21)	(21)	(21)

Values are mean±SE. Numerals in parentheses indicate number of experiments. C, control period; E, experimental period. * $P < 0.001$; ‡ $P < 0.005$ compared with the control period.

Table VIII. Effects of 2 mM Ba^{2+} in the Bath on Barrier Voltages and Conductances at the Initial Peak Response

Group	V_T		V_B		G_T		fR_A	
	C	E	C	E	C	E	C	E
	mV		*mV*		*mS·cm⁻²*			
Control								
3 h	−8.7±2.2	−8.4±2.3	−82.4±2.5	−82.6±2.8	7.8±0.4	7.2±0.4*	0.45±0.03	0.42±0.04*
	(10)	(10)	(10)	(10)	(9)	(9)	(9)	(9)
6 h	−7.3±2.4	−7.2±2.8	−83.2±2.0	−80.7±2.9	7.8±0.5	7.1±0.4‡	0.53±0.03	0.51±0.03§
	(14)	(14)	(14)	(14)	(13)	(13)	(13)	(13)
24 h	−9.1±1.6	−9.4±2.1	−78.0±1.9	−77.6±2.8	8.2±0.4	7.5±0.3§	0.46±0.05	0.43±0.05§
	(20)	(20)	(20)	(20)	(14)	(14)	(14)	(14)
UNX								
3 h	−11.3±2.0	−10.4±2.1	−81.2±3.0	−78.8±2.9	7.9±0.7	7.3±0.7§	0.45±0.07	0.42±0.07§
	(14)	(14)	(14)	(14)	(13)	(13)	(13)	(13)
6 h	−22.3±1.3	−25.1±1.6§	−90.0±1.7	−94.9±2.1§	9.2±0.8	7.3±0.5‖	0.43±0.03	0.36±0.04§
	(13)	(13)	(13)	(13)	(13)	(13)	(13)	(13)
24 h	−21.3±2.1	−25.0±2.5§	−98.0±2.1	−102.8±2.4§	9.9±0.9	7.3±0.6*	0.40±0.03	0.33±0.04§
	(16)	(16)	(16)	(16)	(11)	(11)	(11)	(11)

Values are mean±SE. Numerals in parentheses indicate number of experiments. C control period; E experimental period. ‡ $P < 0.05$; ‖ $P < 0.01$; * $P < 0.005$; § $P < 0.001$ compared with the control period.

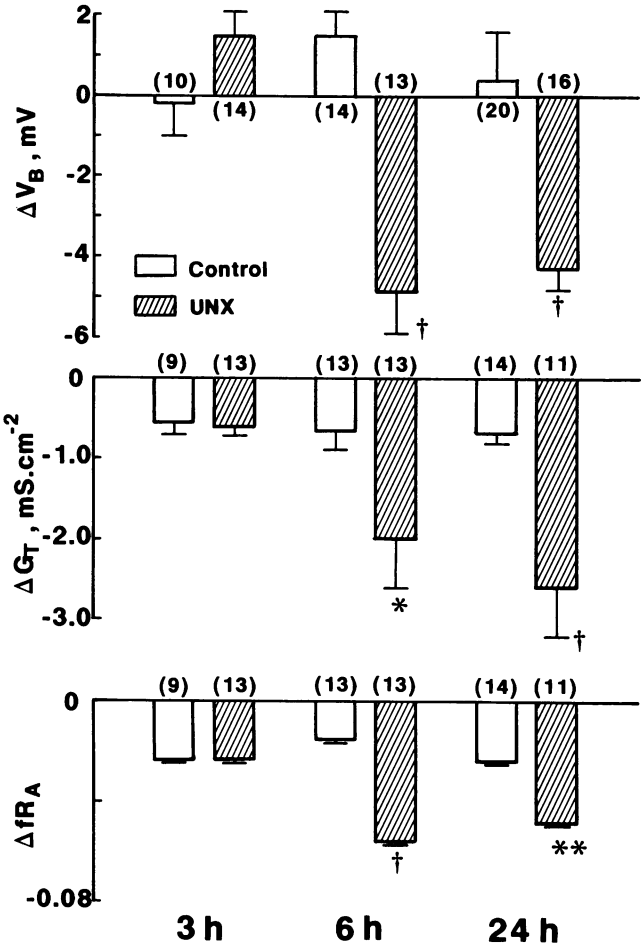

Figure 7. Comparison of the changes in V_B, G_T, and fR_A upon addition of bath Ba^{2+} between the two groups at different time points after surgery. Values are mean±SE. Numerals in parentheses indicate number of experiments. * $P < 0.05$; ** $P < 0.01$; † $P < 0.005$ compared with corresponding control.

delivery into the distal nephron by giving rats a high Na^+ diet and infusing furosemide, a diuretic that inhibits Na^+ and Cl^- absorption by the thick ascending limb. These experimental maneuvers increased the Na^+ concentration in the tubular fluid, enhanced the electrochemical gradient promoting Na^+ influx across the apical membrane, and stimulated Na^+ absorption by the distal tubule (33) and CCD (34). These functional changes were paralleled with an increase in cell area, basolateral membrane area, and mitochondrial volume of the Na^+-absorbing cells in the distal nephrons including distal convoluted tubule cells, connecting tubule cells, and CD cells. This hypertrophy was also accompanied by a parallel increase in the Na^+-K^+-ATPase activity (35) and by a sharp rise in the transport capacity of the superficial distal tubule (36–38).

It has long been known that changes in the rate of Na^+ entry into cells can bring about changes in various cellular parameters such as cellular size and the activity of plasma membrane transporters (e.g., the Na^+-K^+ pump) (39). Because the delayed effects of UNX in the CCD occur after the initial stimulation of Na^+ entry, the question arises as to whether the delayed effects occur as a result of increased Na^+ entry. The answer to this question remains elusive. Further studies will be required to determine a role in intracellular Na^+ in regulating these events.

In summary, we have clearly characterized the electrical properties of the CD cell from remnant kidneys at early periods after UNX.

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