Renal Responses to Acute Extracellular Fluid Volume Expansion after Decapsulation of the Kidney (33077)

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The factors leading to the decreased proximal tubule sodium reabsorption (1,2) and increased urine sodium excretion (3,4) during saline infusions in dogs have not been entirely defined. At least two mechanisms have been proposed by which these responses to extracellular fluid (ECF) volume expansion might be mediated. De Wardener *et al.* (3) originally suggested that ECF expansion may stimulate the elaboration of a nonadrenal humoral substance responsible for the natriuretic response. Other investigators (5–7) have suggested that changes in renal hemodynamics may constitute an important factor in the increased sodium excretion during saline infusions. Results of studies attempting to show natriuretic activity in blood of ECF expanded animals have been inconclusive because of the small magnitude of the resultant natriuresis (3,8–10). Martinez-Maldonado *et al.* (11) have, however, shown a depressed fractional reabsorption in the proximal tubule following infusion of plasma from saline-loaded animals. Despite this depression of proximal tubule sodium reabsorption, such plasma infusions did not produce an increase in urine sodium excretion. These studies suggest that while a humoral substance present in plasma may depress proximal tubule sodium reabsorption, other factors may be necessary for the net natriuretic response that follows acute ECF expansion.

A change in hemodynamic factors would seem to be the most likely nonhumoral influence that might affect this response, since renal denervation has been shown not to alter the natriuresis during saline infusions (4). Since it has been suggested that decapsulation of the kidney may significantly alter renal hemodynamics (12–14), the present studies were undertaken to evaluate the role of the renal capsule in mediating the kidneys response to ECF expansion. The response of the decapsulated kidney was compared with that of the contralateral kidney during the infusion of isotonic saline. The results of this study indicate that the renal response to acute ECF expansion is not affected by the presence or absence of the renal capsule.

Methods. Eighteen studies were performed on 14 female mongrel dogs weighing 14–28 kg. The studies were divided into *chronic* and *acute* groups of nine experiments each. In five dogs, designated the *chronic* decapsulation group, the left kidney was decapsulated through a retroperitoneal flank incision and a split bladder was created by the technique of De Sautels (15). The experimental studies were then performed at intervals ranging from the fourth to twenty-third postoperative day.

In nine other dogs, designated the *acute* decapsulation group, the left kidney was also decapsulated through a retroperitoneal incision. The contralateral right kidney was similarly mobilized but not decapsulated through a right flank incision in an attempt to equalize any effect of the surgical manipulation. Experimental studies in these animals were performed approximately 20 hours after the surgical manipulations.

Acute ECF expansion experiments were performed in an identical nanner in both the acute and chronic groups. Eighteen hours prior to study, food was withheld but the animals were allowed free access to water. At this time the dogs received an intramuscular injection of 10 mg of deoxycorticosterone acetate (DOCA). Dogs were anesthetized with pentobarbital (Nembutal) 28 mg/kg intravenously and given additional doses during the study to maintain light anesthesia as evidenced by preservation of eyelid reflexes. One hour prior to study each dog received 5 mg of DOCA and 5 units of vasopressin tan-

nate in oil and an intravenous prime of creatinine (50 mg/kg). A sustaining solution of normal saline containing aqueous pitressin to provide 50 mu/kg per hour and sufficient creatinine to maintain constant blood levels was infused at a rate of 1.5 ml/min throughout the experiments. The animals were maintained on a positive pressure respirator during the studies. In the chronic decapsulation group urine collections were made directly from the split bladder catheters. In the *acute* decapsulation group a suprapubic incision was made and polyethylene catheters inserted in each ureter. In all 18 experiments the left kidney was decapsulated and the right kidney served as the control for same animal.

Each experiment consisted of a 1-hour preinfusion control period and a 2-hour infusion period. During the infusion period acute ECF expansion was accomplished by the infusion of isotonic saline at 38 ml/min for the initial 20 min and 15 ml/min for the remaining 100 min. The initial hour of the saline infusion was utilized as an equilibration period. Three 20-min clearance determinations were obtained during both the preinfusion control period and during the last hour of the infusion period. Blood specimens were drawn at the midpoint of each clearance period. In selected animals sections of the kidneys were obtained after the experiment and histologic studies were performed to examine the kidney surface.

Analyses for serum and urine sodium and creatinine were determined on the Technicon AutoAnalyzer. Creatinine clearances were used as an index of glomerular filtration rates (GFR). Urine (U_{osm}) and plasma osmolalities (P_{osm}) were determined by freezing point depression with the Advanced osmometer.

Based on the above determinations, the following calculations were made: Sodium filtered (F_{Na}) = serum sodium concentration (P_{Na}) × GFR; urine sodium excreted ($U_{Na}V$) = urine flow rate (V) × urine sodium concentration (U_{Na}); percentage filtered sodium excreted (% Na excreted) = $U_{Na}V/F_{Na} \times 100$; osmolar clearance ($C_{osm}$) = $(U_{osm} \times V)/P_{osm}$; and solute free water clearance (C_{H_2O}) = $V - C_{osm}$.

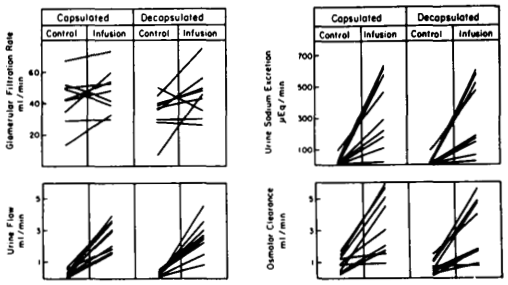

FIG. 1. Effect of chronic decapsulation on the renal responses to acute extracellular fluid volume expansion. Control values are the mean of three 20-min periods prior to the saline infusion and infusion values are the mean of three 20-min periods during the second hour of the saline infusion. The control and infusion glomerular filtration rates, urine flows, urine sodium excretion rates and osmolar clearances were not significantly different in the capsulated and decapsulated kidneys.

Results. Responses to salt loading after chronic decapsulation. The results of the nine experiments are shown in Fig. 1. Recorded volumes for the capsulated and decapsulated kidneys are the mean values for three control clearance periods before saline infusion and the mean values for three clearance periods during the second hour of saline infusion. The mean control GFR in the capsulated kidney was 42.5 ± 5.1[1] ml/min and increased to 48.0 ± 4.6 ml/min with the saline infusions. The mean control GFR of 34.6 ± 4.0 ml/min in the decapsulated kidneys was less but increased to 45.3 ± 4.0 ml/min during ECF expansion, a value very comparable to that of the capsulated kidneys. In Fig. 1 the very similar natriuretic responses of the capsulated and decapsulated kidneys are also demonstrated. In the capsulated kidneys the mean $U_{Na}V$ increased from 15 ± 11 to 340 ± 76 μeq/min while the mean $U_{Na}V$ of the decapsulated kidneys rose from 15 ± 10 to 302 ± 78 μeq/min during the saline infusion. The responses of urine flow (V) and C_{osm} were also quite comparable in the capsulated and decapsulated kidneys (Fig. 1).

Two animals were studied on more than one occasion. The only difference noted in the

[1] All values are means ± standard error of means (SEM).

studies was the apparent increased natriuretic response following the same volume of isotonic saline in the studies performed on the later postoperative days.

Histologic sections of the kidneys revealed evidence of capsule formation as early as the fourth postoperative day. Figure 2 shows the regenerating capsule on the 4th and 23rd days after decapsulation and the normal capsule of a control kidney.

Responses to salt loading after acute decapsulation. In the chronic studies, the relative tensile strength of the regenerating capsule was no doubt not comparable to the normal capsule, particularly in the early postoperative days. However, the acute decapsulation experiments were done to study the renal responses to ECF expansion in kidneys without either a natural or regenerating capsule. The results of these acute experiments were similar to the chronic studies. A typical experiment is illustrated in Table I. In Fig. 3 are illustrated the comparable renal responses to the acute ECF expansion in the capsulated and decapsulated kidneys. The mean control GFR in the capsulated kidneys was 40.3 ± 3.5 ml/min and increased to 51.2 ± 6.3 ml/min during the saline infusion. In the contralateral decapsulated kidney the mean control GFR was 40.2 ± 6.0 ml/min and rose to 49.8 ± 6 ml/min during ECF expansion. These comparable changes in GFR were also associated with very similar natriuretic responses. The mean $U_{Na}V$ increased from 37 ± 12 to 454 ± 68 μeq/min in the capsulated kidneys from 48 ± 22 to 465 ± 75 μeq/min in the decapsulated kidneys during the saline infusions. The control and infusion urine flows and C_{osm} were also quite comparable in the capsulated and decapsulated kidneys as is illustrated in Fig. 3. Figure 4 shows the complete absence of the renal capsule 20 hours after decapsulation as compared to the normal capsule in the contralateral control kidney.

Discussion. The possible role of the renal capsule in the natriuretic response to saline infusions in dogs has not heretofore been examined. Since there is some evidence that renal pressure and hemodynamics (5–7) may be factors in this natriuresis and in turn

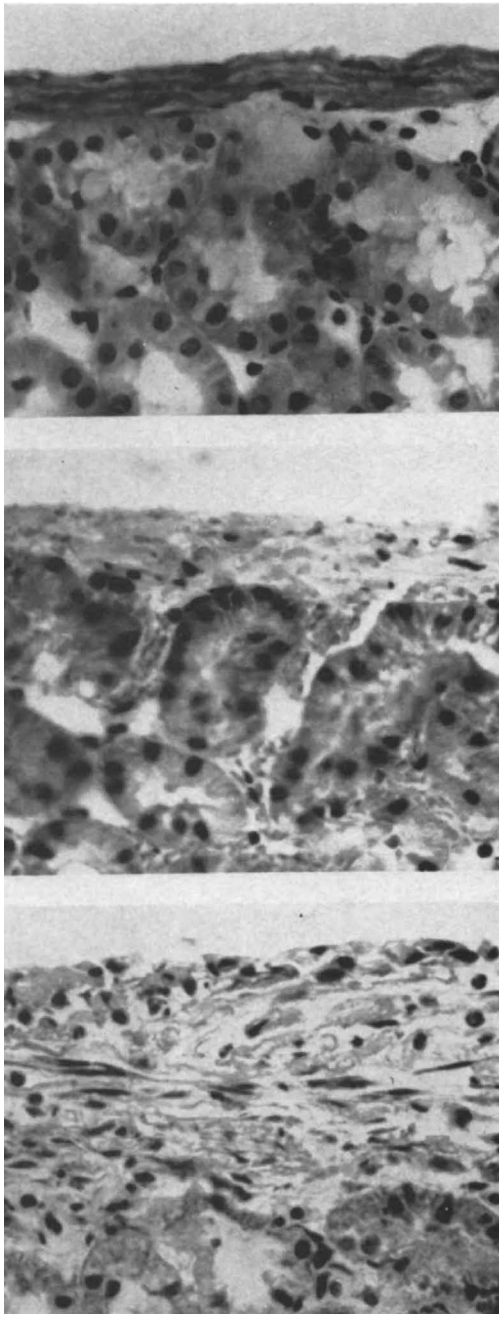

FIG. 2. Photomicrographs from chronic group showing surface of: A normal control kidney with intact capsule (above); kidney 4 days after decapsulation (middle) and kidney 23 days after decapsulation (lower). Capsule regeneration is demonstrated both at 4 and 23 days after decapsulation.

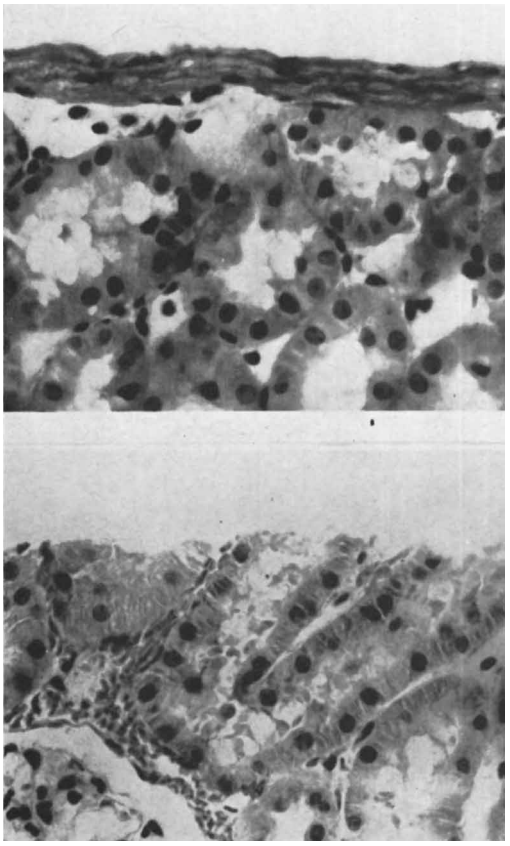

FIG. 4. Photomicrographs from acute group showing surface of: A normal control kidney with intact natural capsule (above); decapsulated kidney 20 hours after decapsulation demonstrating absence of any capsule regeneration (lower).

that the renal capsule may influence these parameters (12–14), it seemed logical to investigate the renal response to ECF expansion after decapsulation of the kidney. Furthermore, the enlargement of the kidney and tenseness of the capsule which accompanies salt loading and the bulging of parenchyma which follows renal capsulotomy in these circumstances also suggested a possible importance of the renal capsule during ECF expansion. However, results of both the acute and chronic decapsulation studies demonstrate that the renal capsule does not play a significant role in the kidney's ability to excrete an acute salt load. The chronic studies demonstrated that kidneys from 4–23 days after decapsulation have varying degrees of regeneration of the capsule. These kidneys with reforming capsules did not respond differently to ECF volume expansion than the contralateral control kidneys with normal capsules (Fig. 1). The acute decapsulation studies further demonstrated that kidneys with complete absence of renal capsules have rises in glomerular filtration rates, urine sodium excretion, urine flows and osmolar clearances which were not different from the contralateral kidneys with intact capsules (Fig. 3).

The prime purpose and design of the present investigation was to examine the effect of decapsulation on the natriuretic response to ECF expansion. Whether such decapsulation alters intrarenal pressure gradients during saline infusions awaits adequate methods to measure interstitial pressure of the kidney. The conflicting results in the literature (13–14,16) of the effect of renal decapsulation on intrarenal pressure may be explained, at least in part, by the difficulties in the methodology used to measure intrarenal pressure. Miles and De Wardener (16) have emphasized that the acute manipulation of the kidney may affect intrarenal pressure independent of decapsulation. In the present studies sufficient time (20 hours–23 days) was allowed between decapsulation and the saline infusion experiments to circumvent any effect of surgical manipulation. If in-

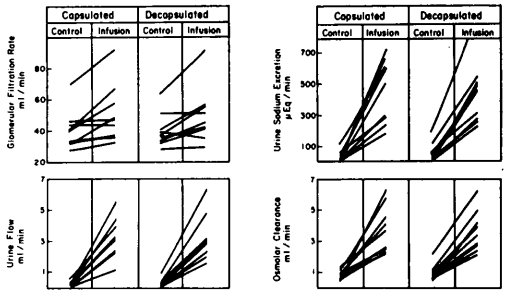

FIG. 3. Effect of acute decapsulation on the renal responses to acute extracellular fluid volume expansion. Control values are the mean of three 20-minute periods prior to the saline infusion and infusion values are the mean of three 20-min periods during the second hour of the saline infusion. The control and infusion glomerular filtration rates, urine flows, urine sodium excretion rates and osmolar clearances were not significantly different in the capsulated and decapsulated kidneys.

TABLE I. Typical Infusion Study—Acute Decapsulation.[a]

Time	C_{Cr} (ml/min)		F_{Na} (μeq/min)		$U_{Na}V$ (μeq/min)		Na (%) excreted		V (ml/min)		C_{osm} (ml/min)		C_{H_2O} (ml/min)		Plasma		
	Cap	Decap	Cap	Decap	Cap	Decap	Cap	Decap	Cap	Decap	Cap	Decap	Cap	Decap	Cr (mg /100 ml)	Osmolality (millios-mols/liter)	Na (meq /liter)
(hours)																	
—20	Decapsulate left kidney; expose and manipulate right kidney; infuse 500 ml of Ringer's lactate solution																
—18	Inject 10 mg of deoxycorticosterone acetate (DOCA)																
(min)																	
—60	Give 5 mg of DOCA and 5 units of pitressin tannate in oil; give creatinine prime and start creatinine sustaining infusion at 1.5 ml/min																
0–20	37.8	40.5	5719	6128	25	25	0.43	0.40	0.2	0.2	1.1	1.0	—0.9	—0.8	15.0	306	151.3
20–40	28.0	35.6	4208	5351	65	64	1.53	1.20	0.5	0.5	0.9	1.0	—0.4	—0.5	16.1	306	150.3
40–60	32.8	41.2	4966	6238	21	20	0.41	0.32	0.2	0.2	0.6	0.6	—0.4	—0.4	16.2	306	151.4
	Infuse 0.9% NaCl at 38 ml/min for 20 min; then slow to 15 ml/min																
120–140[b]	36.4	35.0	5617	5401	518	384	9.21	7.11	4.6	3.7	4.0	3.3	+0.6	+0.4	16.3	305	154.3
140–160	33.8	35.0	5334	5523	591	528	11.07	9.55	5.6	5.0	4.6	4.0	+1.0	+1.0	16.3	305	157.8
160–180	36.7	35.0	5747	5622	681	584	11.85	10.39	6.5	5.8	5.2	4.5	+1.3	+1.3	17.7	306	156.6

[a] Abbrev.: Cap = Capsulated control (right) kidney; Decap = Decapsulated (left) kidney; C_{Cr} = rate of clearance of creatinine; F_{Na} = rate of filtration of sodium; $U_{Na}V$ = rate of excretion of sodium; Na (%) excreted = Percentage of filtered sodium excreted; V = rate of urine flow; C_{osm} = rate of osmolar clearance; C_{H_2O} = rate of solute-free water clearance.

[b] Periods during the first hour of saline loading have been omitted from the table.

trarenal pressure is important in the natriuretic response to ECF volume expansion, these decapsulation studies provide indirect evidence that the presence or absence of the kidney capsule does not influence intrarenal pressure during salt loading. Miles and De Wardener (16) also concluded that the status of the renal vascular bed and renal parenchyma, rather than the renal capsule, were the major determinants of intrarenal pressure.

It has also been suggested that decapsulation abolishes renal autoregulation (12). In the present studies there were, however, no significant differences in the glomerular filtration rates of the capsulated and decapsulated kidneys during the acute ECF volume expansion studies.

Summary. In the present study the importance of the kidney capsule in the renal responses to acute extracellular fluid (ECF) volume expansion was examined. Studies were performed 20 hours to 23 days after decapsulation of the left kidney. The increased rates of glomerular filtration (GFR), urine flow, sodium excretion and osmolar clearance during the ECF expansion were not significantly different in the kidneys with no capsules or reforming capsules as compared to the contralateral control kidneys with intact capsules. The present studies therefore demonstrated that decapsulation of the kidney does not affect the renal response to ECF expansion during the first 3 weeks after removal of the capsule. If intrarenal pressure is an important factor in the natriuretic response to ECF expansion, these decapsulation studies provide indirect evidence that the renal capsule is not an important determinant of intrarenal pressure during salt loading. While it has been suggested that renal decapsulation abolishes renal autoregulation, there was no such influence of decapsulation on the responses of the glomerular filtration rate during ECF expansion.

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