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Research Article

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Effect of Changes in Hydrostatic Pressure in Peritubular Capillaries on the Permeability of the Proximal Tubule

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ABSTRACT The effect of increased hydrostatic pressure in the peritubular vessels on net sodium reabsorption from the proximal tubule was examined in the *Necturus*. An increase in the pressure gradient of 2.0 cm H_2O across the wall of the proximal tubule, produced by ligation of the postcaval vein was associated with a marked reduction in net reabsorption and an increased back flux of water and electrolytes. This change was accompanied by a slight, but significant drop in the transepithelial electrical potential but not by an alteration in the steady-state chemical gradient. These studies highlight the importance of changes in the permeability characteristics of the proximal tubule on net sodium transport.

INTRODUCTION

Recent studies have shown that alterations in hydrostatic and oncotic pressure in peritubular capillaries (1, 2), may influence net sodium reabsorption in the proximal tubule. While it is not certain that hydrostatic pressure varies to a great enough extent under physiological conditions to play a significant role in sodium reabsorption (3), studies from our laboratory indicate that changes in oncotic pressure subserve this mechanism as a result of variations in filtration fraction (4). The final pathway by which these factors alter sodium reabsorption remains unclear. It is not known, for instance, whether an increase in the hydrostatic pressure gradient diminishes diffusion from intercellular spaces into capillaries, increases back diffusion into the cell or tubular lumen, or directly influences active sodium transport.

In the present experiments the mechanism by which a rise in the hydrostatic pressure of peritubular capillaries inhibits net proximal reabsorption was studied in the amphibian *Necturus maculosa*. Since transport processes occur at a much slower rate in the amphibian, compared with the mammal, the active and passive components of sodium transport can be more easily characterized. In addition, the dual renal blood supply in the lower vertebrate permitted significant alterations in hydrostatic pressure without affecting oncotic pressure or causing apparent concurrent changes in renal blood flow.

METHODS

Experiments were performed on adult *Necturi* (Lemberger Co. Ashkosh, Wisconsin) weighing 100–200 g which were stored unfed at 15–18°C. Half-time studies were performed during July and August. Studies to determine steady-state sodium values and transepithelial potentials were performed during November to March.

The animals were prepared for micropuncture using techniques similar to those described by Shipp et al. (5). Tricaine methanesulfonate (MS-22, 660 mg/liter) was used for induction of anesthesia. During experiments anesthesia was maintained with MS-22 in a dose of 60 mg/liter. All animals received an infusion of amphibian phosphate buffer solution containing 119 meq Na^+, 2.4 meq K^+, 120 meq Cl^-, 1.0 meq $HPO_4^=$, 0.85 meq $H_2PO_4^-$, and 0.5 meq Ca^{++} per liter at a rate of 0.04 ml/min via a constant infusion pump (Harvard Apparatus Co., Inc., Millis, Mass.; model 901). Amphibian phosphate buffer was used to bathe the kidney surface during all experiments. For measurements of steady-state concentrations of sodium the tip of the collection pipette was sealed with oil before it was withdrawn from the tubular lumen.

In order to increase the hydrostatic pressure within peritubular capillaries the postcaval vein was ligated at the level of its entry into the liver. Approximately 20 min were allowed to elapse after this procedure before beginning micropuncture measurements. Experiments were performed only in animals in which blood flow in peritubular vessels was brisk. It should be noted that the postcaval vein has numerous branches between the renal veins and its entrance into the liver. Presumably alterations in resistance in these branches were responsible for the maintenance of blood flow through the renal venous portal system into the postcaval vein following venous ligation. Ligation of the postcaval vein immediately cephalad to the kidneys resulted in complete secession of blood flow within the portal system. In all cases blood flow in the renal portal system continued in the normal direction, toward the medial border of the kidney, after ligation was applied.

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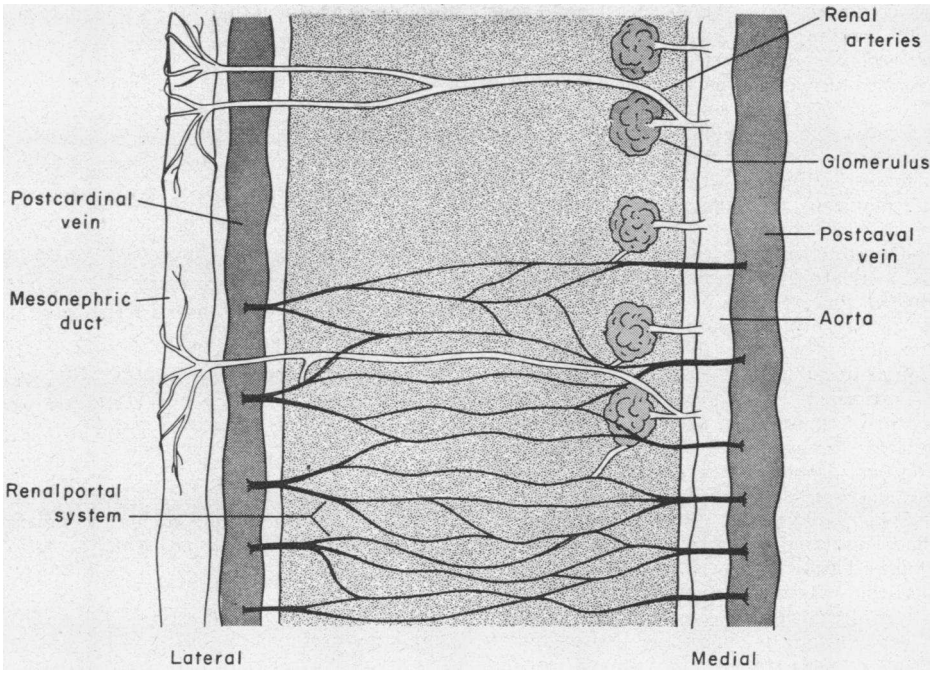

FIGURE 1 This diagram illustrates the relationship of the renal portal system and branches of the renal arteries on the ventral surface of the right kidney of *Necturus maculosa.*

Renal vasculature, measurements of hydrostatic pressure and rate of blood flow in peritubular vessels. The intrarenal branches of the renal venous portal system could be easily distinguished visually via a binocular microscope from branches of the renal arteries by the direction of blood flow. Flow was toward the medial border of the kidney in venous portal vessels and toward the lateral surface in the arterial system. The hydrostatic pressure was measured in vessels using the method of Landis as modified by Flanigan and Oken (6). Since the diameter of all vessels exceeded the outside tip diameter (8–10 μm) of the glass pipette by several fold, occlusion of the vessel did not occur.

Additional studies were performed in another group of animals to verify the origin of vessels selected for pressure measurements. Microfil (Canton Biomedical Co., Boulder, Colo.) was used to perfuse the renal venous system via the caudal vein and the renal arterial system via the abdominal aorta. By using different colors in perfusing each system the entire vascular could be examined after dehydration and clearing with methylsalicylate. The relationship of the two vascular systems is shown in Fig. 1. These studies confirmed the visual observations that tributaries of the renal portal system constituted the largest proportion of the renal vascular and formed the peritubular vessels.

Studies were performed in five animals to determine the effect of ligation of the postcaval vein on the rate of blood flow through peritubular vessels before and after ligation. The same criteria was used in selecting these animals for study as was used in the other physiological experiments. Since the urine flow rate was insufficient to permit measurements of para-aminohippuric acid clearance in the non-diuretic state, the velocity of blood flow was estimated visually. After introduction of a micropipette into a straight segment of a peritubular vessel a bolus of 5% lissamine green was injected and the velocity of the day front over a distance of approximately 1.0 mm was measured with the aid of a filar eye piece micrometer. The edge of the dye front was easily distinguishable in these experiments. The average value of three to five measurements from the control and experimental period was determined for each animal. In order to determine whether the diameter of the peritubular vessels changed as a result of venous ligation and increase in hydrostatic pressure photomicrographs, using Ethachrome E daylight film, were taken of the same surface areas before and after ligation under the same magnification. Measurement of vessel diameters were made from projections of the transparencies onto a glass screen. The values for the diameter before and after ligation at the same loci are expressed as a ratio. Estimates of volume were not made because of the apparent change in vessel diameter that is normally observed in surface vessels.

Reabsorptive half-time. The rate of net proximal reabsorption was measured using the split droplet technique of Gertz (7). All studies were performed on the early portion of the proximal tubule and only straight segments were used. Phosphate buffer amphibian Ringer's solution was used as perfusate. The length of the oil column on both sides of the aqueous droplet averaged about 10 times the diameter of the tubule. Measurements of tubular diameter and droplet length were made using a filar eye piece micrometer calibrated with a stage micrometer. The diameter of the droplet was measured as the diameter of the oil column and droplet length as the distance between menisci of the oil droplets. Approximately 60 s elapsed after completion of perfusion before the initial length of the droplet was measured. The change in droplet length was expressed as a ratio of the initial length and the slope of each droplet series was calculated as a regression curve. The results are expressed as the reabsorptive half-time ($t_{\frac{1}{2}}$)—the time required for the droplet shrink to 50% of its original length.

Observations were continued until the droplet length have reached at least 50% of the initial length.

Studies of permeability characteristics. Split droplet studies were performed using isosomotic raffinose solution (200 mosm/liter) as the perfusion solution. The change in droplet length in relationship to the initial length was estimated in a way similar to the reabsorptive half-time study. When isotonic raffinose is injected between oil droplets the initial increase in volume of the raffinose solution will reflect the passive isotonic entry of electrolytes and water and isotonic exit of raffinose down their concentration gradient. Since raffinose is a relatively impermeant non-electrolyte and the initial luminal concentration of electrolytes is zero, the early expansion of the droplet is primarily an expression of the permeability of the tubular wall for water. In these studies only the initial linear portion of the ascending phase of expansion was estimated. From this slope the doubling time (t_2ho), the time required for the initial volume to double, was calculated. In these experiments and in studies of isotonic reabsorption, droplet length was used as an estimation of volume since droplet diameter was constant.

Steady-state sodium concentration. A solution containing an isosmotic raffinose solution was perfused into the proximal tubule previously blocked with oil, and 20-μl samples of fluid were collected. All samples were collected when the raffinose droplet was decreasing in size. Under these conditions a state of zero net flux is approached and electrolyte concentration reaches a steady-state equilibrium (8). Tubular fluid samples were analyzed for sodium using an ultramicro flame photometer. Serum from the abdominal aorta was analyzed for sodium using an IL integrating flame photometer (Instrumentation Laboratory, Inc., Lexington, Mass.).

Transepithelial potentials. Transepithelial electrical potentials were measured using Ling-Gerard electrodes coupled to a high impedance millivoltmeter (Medistor Instrument Co., Seattle, Wash.) through calomel half cells. The glass microelectrodes had resistances of 10–20 megohms and tip potentials of less than 5 mV in solutions containing raffinose and salts in equilibrium concentration. Only potentials which were stable for at least 1 min and fell to no greater than 1 mV upon withdrawal were accepted as adequate.

Isosmotic raffinose solution was used as the perfusate and all measurements were made during the descending exponential phase of the raffinose curve as determined visually.

Studies of peritubular capillary protein concentration. During control and experimental periods samples of approximately 30 nl of peritubular blood were taken by direct micropuncture in four animals for measurement of plasma protein concentration. The method used in these determinations in this laboratory has been described (4). Preliminary studies showed that measurement of plasma protein values in *Necturi* by the Lowry method, utilized in these experiments, gave approximately the same value as determined by the biuret technique. The ratio of Lowry to biuret values determined on the same samples from six animals was 0.92.

All data is expressed as mean ±SE and comparison between groups was made using Fishers or Student's *t* test.

RESULTS

Ligation of the postcaval vein at its entry into the liver resulted in a prompt and sustained increase in the hydrostatic pressure in the peritubular branches of the renal portal system. Since blood flow either continued to be brisk or was reconstituted within minutes after constriction it was assumed that sufficient collateral circulation was present cephalad to the kidneys. As shown in Table I the hydrostatic pressure was 2.64±0.12 cm H_2O in control animals and rose to 5.22±0.26 in experimental animals ($P < 0.001$). In a group of five animals the hydrostatic pressure was simultaneously measured in the peritubular vessel and intratubular lumen within a droplet of isotonic Ringer's solution before and after venous ligation to determine whether the experimental procedure caused a measurable gradient across the wall of the proximal tubule. Three to five observations were made during the control and experimental period in each animal. During the control period the hydrostatic pressure in peritubular vessels was 3.18±0.73 cm H_2O and 3.38±0.73 in the lumen (P = NS). After ligation of the abdominal cava the pressure in the vessel rose to 6.18±0.91 cm H_2O but remained unchanged in the intratubular lumen, 3.82±0.91 H_2O. Under the experimental condition, therefore, a pressure gradient of 2.36±0.34 cm H_2O was produced, which was highly significant ($P < 0.005$).

Measurement of the velocity of blood flow in peritubular vessels was unchanged following venous obstruction. The linear flow rate was 2.21±0.36 mm/s during the control period and 2.01±0.24 mm/s (P = NS) in the experimental condition. The ratio of vessel diameter from 15 observations in five animals was 1.04±0.06 (P = NS). Since blood flow was unchanged by ligation of the postcaval vein at its entrance into the liver, it seems likely that dilation of collateral vessels cephalad to the kidney accounted for the maintenance of blood flow through the renal portal system. Venous obstruction did not apparently cause an alteration in the hydrostatic pressure of the intrarenal arterioles.

There was a marked reduction in net fluid reabsorption, associated with increased hydrostatic pressure of peritubular vessels. Reabsorption half-time ($t_{\frac{1}{2}}$) increased from 20.7±2.2 min to 123.6±34.2 min ($P < 0.005$). Water outflux calculated from the individual $t_{\frac{1}{2}}$ values and tubular radii (r), as $Jv = (0.347/t_{\frac{1}{2}})\ r$ mm^3/mm^2 min, was also significantly reduced in the experimental animals compared with control animals. These observations were not influenced by variations in the size of the aqueous droplet between groups, since both initial droplet length and droplet diameter were similar.

Studies were performed with an isosmotic raffinose solution in order to determine whether an increase in peritubular hydrostatic pressure altered passive permeability of the tubule to electrolytes and water. Analysis of the initial ascending phase of expansion of the droplet demonstrated a significant increase in passive permeability to electrolytes and water in experimental animals. The t_2ho fell from 6.4±0.6 min in control animals to 4.1±0.5 in the experimental group. During volume expansion in the Necturus an increase in permeability to

TABLE I

*Effect of Hydrostatic Pressure in Peritubular Vessels on Net Fluid Reabsorption and Permeability in the Proximal Tubule**

	Control	Experimental	P
Hydrostatic pressure, cm H_2O			
Peritibular vessels	2.64±0.12	5.22±0.26	<0.001
	n = 28	n = 32	
	a = 15	a = 13	
Intrarenal arterioles	11.6±0.54	10.5±0.55	NS
	n = 8	n = 13	
	a = 8	a = 9	
Reabsorptive half-time ($t_{\frac{1}{2}}$), min	20.7±2.2	123.6±34.2	<0.005
	n = 21	n = 17	
	a = 8	a = 6	
Net fluid outflow	2.17×10^{-5}±0.28	0.58×10^{-5}±0.10	<0.001
	n = 21	n = 17	
$Jv = (0.347/t_{\frac{1}{2}})r$ mm³/mm² min	a = 8	a = 6	
Droplet diameter, μm	118.5±6.2	119.1±6.1	NS
	n = 21	n = 17	
	a = 8	a = 6	
Initial droplet length, μm	207.5±34.7	223.8±30.5	NS
	n = 21	n = 17	
	a = 8	a = 6	
Inflow doubling time ($t_2$ho), min	6.4±0.6	4.1±0.5	<0.01
	n = 22	n = 25	
	a = 5	a = 5	
Initial fluid inflow	5.85×10^{-5}±0.67	8.63×10^{-5}±0.84	<0.02
	n = 27	n = 25	
$Jv = (0.347/t_2\text{ho})r$ mm³/mm² min	a = 5	a = 5	
Droplet diameter, μm	106.8±4.7	100.8±2.8	NS
	n = 22	n = 25	
	a = 5	a = 5	
Initial droplet length, μm	100.5±7.6	107.3±12.6	NS
	n = 22	n = 25	
	a = 5	a = 5	

n represents number of observations, and a represents number of animals studied.

* Values are mean ±SE.

raffinose, as well as to electrolytes and water has been demonstrated (9). If a similar increase in permeability occurred in the present study, the observed changes would have underestimated the relatively increased backflux of electrolytes and water during experimental conditions. As in the studies on net isotonic reabsorption, there was no difference in droplet diameter or initial droplet length between the experimental and control groups.

In stationary perfusions with isosmotic solutions of raffinose the relatively slow negative volume change, which follows initial expansion, is due to the raffinose leak, since the reflection coefficient (δ) does not equal 1. During this phase the ionic concentration of sodium in the intraluminal fluid approximates the steady-state limiting conditions. As shown in Table II the steady-state luminal concentration of sodium was approximately 69 meq/liter in both control and experimental animals and the chemical gradient for sodium across the tubular epithelium was unchanged by the increase in hydrostatic pressure. Under the same conditions there was a small but significant drop in the transepithelial electrical potential from

TABLE II

*Steady-state Equilibrium Concentrations and Transepithelial Potential Measurements**

	Control	Experimental	*P*
Plasma sodium concentration, meq/liter	90.1±3.3 *n* = 7 *a* = 7	95.8±3.5 *n* = 6 *a* = 6	NS
Intraluminal sodium concentration, meq/liter	67.5±2.6 *n* = 28 *a* = 7	68.5±1.9 *n* = 24 *a* = 5	NS
Concentration gradient, TF/P_{Na}	0.75±0.14 *n* = 28 *a* = 7	0.74±0.13 *n* = 26 *a* = 6	NS
Transepithelial electrical potential, mV	14.6±0.6 *n* = 45 *a* = 10	12.9±0.5 *n* = 54 *a* = 8	<0.05

n represents number of observations, and *a* represents number of animals studied.

* Values are means ±SE.

14.6±0.6 mV in control animals to 12.9±0.5 in animals with increased hydrostatic pressure.

Although no change in the protein concentration of the venous blood in the portal system was expected to have occurred as a result of ligation the protein concentration in peritubular vessels was determined. Ligation of the postcaval vein did not change this value which was 4.93±0.13 g/100 ml under control and 4.88±0.23 during experimental conditions (P = NS). There is no apparent explanation for the high absolute values obtained which were greater than the usually reported levels of 2–3 g/100 ml in *Necturus* plasma.

DISCUSSION

It seems clear from recent studies that sodium reabsorption in the proximal tubule varies in a proportional way to the oncotic pressure in peritubular capillaries (2, 4) and inversely to the hydrostatic pressure (3, 10). Since both hydrostatic pressure and oncotic pressure contribute in a similar way to the pressure gradients between the capillary and intercellular spaces, it is likely that the mechanism by which changes in these factors exert their effect on net sodium reabsorption is also similar. In the present experiments it was possible to study the effect of increased hydrostatic pressure on proximal tubular function in vivo without changes in oncotic pressure or renal blood flow. In addition, the use of stopped flow methods provided a means for evaluating sodium transport independently of changes in the filtered load of sodium, tubular geometry, and tubule fluid velocity.

When the gradient for hydrostatic pressure across the tubular wall was increased by at least 2.0 cm H_2O there was a marked reduction in net sodium reabsorption. Studies of tubular wall permeability demonstrated that under these same conditions there was an enhanced backflux of water and electrolytes into the tubular lumen. Since previous observations have demonstrated (11) that net sodium efflux is associated with a large sodium backflux into the tubule, these data support the concept that an increased pressure gradient exerts its action primarily through augmentation of this process. Using ^{14}C-labeled sucrose as a marker for small molecules, Bank, Yarger, and Aynedjian (12) have recently reported that during renal vein constriction in the rat an increase in the permeability of the proximal tubule occurs. In this study, however, alterations in the physical characteristics of the proximal tubule could not be dissociated from marked changes in cortical blood flow. Moreover, a change in the pressure gradient across the tubular wall was not demonstrated. Grandchamp, Baechtold-Fowler, and Boulpaep have reported data in abstract form (13) from experiments designed to study the effect of hydrostatic and oncotic pressure on sodium reabsorption in the doubly perfused *Necturus* kidney. Although a decrease of the oncotic pressure of the perfusate (from 20 g/liter polyvinylpyrrolidone to 0 g/liter) reduced net reabsorption, no change in reabsorption was found after a twofold increase of capillary venous pressure. It is difficult to compare that study with the present experiments because of the differences in technique. In the doubly perfused kidney preparation, the organ is perfused with a blood-free artificial plasma at an undetermined capillary flow rate, in contrast to these in vivo studies where the organ was blood perfused. An alteration in the reflection coefficient of the proximal tubules when perfused with artificial plasma might explain the lack of change in sodium reabsorption after a twofold increase in hydrostatic pressure while a marked reduction was found in vivo after a onefold increase.

Although it seems likely that the mechanism by which hydrostatic pressure and oncotic pressure exert their effect on the rate of net reabsorption is similar for different epithelial membranes, this study and previous reports indicate that quantitative differences exist. For example, relatively large changes in oncotic pressure are necessary to influence the net reabsorption of fluid and electrolytes in the proximal tubule of the rat (4), while gradients as small as 0.5 cm H_2O, opposite to the direction of flow, have been reported to inhibit transport across frog skin (14) and gallbladder (15).

Electrical measurement, summarized recently by Giebisch, Baulpaep, and Wittembury (16) have shown that the total transepithelial conductance greatly exceeds that expected on the basis of resistive contributions of the bordering cell membranes. This observation suggests that the presence of a low resistance shunt path parallel with cell membrane resistances and the inter-

cellular space has appeared to provide the logical anatomical counterpart. In an elegant series of experiments Boulpaep (9) has demonstrated that reduced net sodium reabsorption in the volume expanded *Necturus* results primarily from increased backflux along the intercellular path, reducing the efficiency of the active transport mechanism. He showed a significant rise in transepithelial conductance, without an alteration in cell membrane resistance, and an increase in proximal tubular permeability for electrolytes and water and non-electrolytes such as raffinose.

The fall in transepithelial potential difference during venous ligation is compatible with an increased shunt conduction. Under these same conditions, however, the tubular epithelial cells were capable of producing a normal steady-state concentration gradient during a phase when zero net flux was approached. Since this measurement in part reflects the active component of sodium transport, this observation suggests that alteration in the pressure gradient does not alter the characteristics of the transport mechanism.

Taken together, therefore, these observations and the study of Boulpaep in volume expanded animals highlight the importance of intercellular pathways in the regulation of net sodium transport by the proximal tubule.

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REFERENCES

1. Lewy, J. E., and E. E. Windhager. 1968. Peritubular control of proximal tubular fluid reabsorption in the rat kidney. *Am. J. Physiol.* **214**: 943.
2. Brenner, B. M., K. H. Falchuk, R. I. Keimowitz, and R. W. Berliner. 1969. The relationship between peritubular capillary protein concentration and fluid reabsorption by the renal proximal tubule. *J. Clin. Invest.* **48**: 1519.
3. Falchuk, K. H., B. M. Brenner, M. Tadakoro, and R. W. Berliner. 1971. Oncotic and hydrostatic pressures in peritubular capillaries and fluid reabsorption by proximal tubule. *Am. J. Physiol.* **220**: 1427.
4. Weinman, E. J., M. Kashgarian, and J. P. Hayslett. 1971. Role of peritubular protein concentration in sodium reabsorption. *Am. J. Physiol.* **221**: 1521.
5. Shipp, J. C., I. B. Hanenson, E. E. Windhager, H. J. Schatzmann, G. Whittembury, H. Yoshimura, and A. K. Solomon. 1958. Single proximal tubules of the Necturus kidney. Methods of micropuncture and microperfusion. *Am. J. Physiol.* **195**: 563.
6. Flanigan, W. J., and D. E. Oken. 1965. Renal micropuncture study of the development of anuria in the rat with mercury-induced acute renal failure. *J. Clin. Invest.* **44**: 449.
7. Gertz, K. H. 1963. Transtubulare natriumchloridflosse und permeabilitat fur nichtelekrolyte im proximalen und distalen konvolut det rattennierre. *Pfluegers Arch. Gesamte. Physiol.* **276**: 336.
8. Kashgarian, M., H. Stockle, C. W. Gottschalk, and K. J. Ullrich. 1963. Transtubular electrochemical potentials of sodium and chloride in proximal and distal renal tubules of rats during antidiuresis and water diuresis (diabetes insipidus). *Pfluegers Arch. Gesamte Physiol.* **277**: 89.
9. Boulpaep, E. L. 1972. Permeability changes of the proximal tubule of Necturus during saline loading. *Am. J. Physiol.* **222**: 517.
10. Koch, K. M., H. S. Aynedjian, and N. Bank. 1968. Effect of acute hypertension on sodium reabsorption by the proximal tubule. *J. Clin. Invest.* **47**: 1696.
11. Oken, D. E., G. Whittembury, E. E. Windhager, and A. K. Solomon. 1963. Single proximal tubules of Necturus kidney. V. Unidirectional sodium movement. *Am. J. Physiol.* **204**: 372.
12. Bank, N., W. E. Yarger, and H. S. Aynedjian. 1971. A microperfusion study of sucrose movement across the rat proximal tubules during renal vein constriction. *J. Clin. Invest.* **50**: 294.
13. Grandchamp, A., H. Baechtold-Fowler, and E. L. Boulpaep. 1971. Influence of peritubular physical factors on proximal sodium reabsorption in perfused Necturus kidneys. *Fifth Annual Meeting, American Society of Nephrology.* **5**: 28.
14. Nutbourne, D. M. 1968. The effect of small hydrostatic pressure gradients on the rate of active sodium transport across isolated living frog-skin membranes. *J. Physiol.* **195**: 1.
15. Keimowitz, R. I., and T. L Stanton. Large decrements in gallbladder transport as a result of small serosal hydrostatic pressure gradients. *Clin. Res.* **20**: 598.
16. Giebisch, G., E. L. Boulpaep, and G. Wittembury. 1971. Electrolyte transport in kidney tubule cells. *Philos. Trans. R. Soc. Lond. Ser. B. Biol. Sci.* **262**: 175.