RENAL MECHANISMS IN MAINTENANCE OF FLUID AND ELECTROLYTE BALANCE

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MAINTENANCE of fluid and electrolyte balance by the kidney implies a conservation at normal levels of the volumes, osmotic concentrations, compositions, and reactions of both extracellular and intracellular fluids. To do this the kidney must have means of adjusting appropriately to all possible stresses of diet and disease. The fluid in contact with the kidney and capable of modifying its functions directly is the blood. Consequently, appropriate renal mechanisms are responsive to changes in blood volume, in osmotic or water concentration, to changes in electrolytes, and also to blood pH.

The nephron, the unit of renal structure which subserves these varied functions, is a composite of vascular and epithelial tissues. The vascular element comprises the afferent and efferent arterioles, and the glomerular and peritubular capillaries. This element is concerned with the rate of renal blood flow, the volume of fluid filtered from the blood through glomerular capillaries and with picking up the fluids reabsorbed by the tubules and restoring them to the circulating systemic blood. The epithelial portion acts on the one hand by selective reabsorption of substances from tubular fluid and on the other by the secretion into it of certain specific materials.

The function of renal maintenance has been summarized by Homer Smith in the axiom that "the composition of blood and body fluids is determined less by what the mouth ingests than by what the kidneys keep." This "keeping" involves both the vascular and the epithelial portions of the nephron. The vascular portion is primarily concerned with adaptation to volume change and the epithelial portion with adaptation to changes in composition and reaction (Table 1).

As concerns volume, a decrease in body fluid usually involves shrinkage of blood volume and, ultimately, a decrease in cardiac output. Whenever cardiac output becomes less than is required for concurrent metabolic needs, there results renal vasoconstriction. This vasoconstriction reduces the rates of renal blood flow and of glomerular filtration. It usually is associated with oliguria and increased sodium reabsorption. Similarly, an abrupt increase in plasma volume and cardiac output, such as can be initiated by injection of hypertonic saline or salt-poor albumin, elicits renal vasodilation, increased glomerular filtration and diuresis. Since, at their outset, these adjustments do not modify the renal epithelium, they are spoken of as "prerenal" or extra-renal," which, of course, they are not. They are "pre-tubular" only.

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Table 1

MECHANISM	AFFECT	DISEASE
1. Vascular	Volume	Shock Heart failure Dehydration
2. Epithelial	Composition water	Diabetes insipidus
	Na, K, Cl	Fluid losses Addison's Nephropathies
	Reaction (pH)	Acidosis Alkalosis

Vasoconstriction in response to a decrease in cardiac output is teleologically useful when, as in early shock, the net result is a deviation of as much as 20 per cent of the cardiac output from the kidney into the more immediately vital channels of the liver, heart, and brain. The oliguria and sodium reabsorption tend to restore the volume of interstitial fluid and thus also to maintain tissue pressure and support an endangered circulation. However, when renal vasoconstriction is excessive and unduly prolonged, the ischemic renal tubules become damaged and the stage is set for one of the many forms of nephron nephrosis, such as crush syndrome. Thus, what at the outset was life-preserving may in the end become lethal. In contrast, in congestive heart failure, where cardiac output is also less than concurrent bodily need, vasoconstriction and retention of fluid in blood and tissue spaces is damaging from the start.

The tubular mechanisms of maintenance proceed in two phases. The first "obligatory" phase consists in reabsorption of water and electrolyte from tubular fluid through the cells of the proximal convoluted tubule. This function accounts for the vast bulk of reabsorbed water, sodium and chloride. It is relatively invariant except as it is altered by changes in filtration rate. Consequently, "obligatory" reabsorption is hardly germane to this discussion. Rather, we are concerned with the residual reabsorptions and excretions which are "facultative" and which vary in response to changes in composition and reaction of body fluids (Table 2). These facultative adjustments are principally made in the distal convoluted tubule.

The first of these mechanisms is concerned with the osmotic concentration of water content of body fluids. The control depends on the responsive-

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ness of the postpituitary and hypothalamus to changes in the water concentration of the blood. A decrease in concentration due to water loss or to solute excess causes liberation of posterior lobe hormone. This acts on specific distal tubular cells to increase reabsorption of water. The result is antidiuresis and excretion of hypertonic urine. Failure of this function at the pituitary level results in diabetes insipidus. Failure at the renal level underlies the fixation of specific gravity and hyposthenuria found in renal disease.

Control of discrete electrolytes, as contrasted with the mass osmotic control, depends in large measure on responses of the adrenal cortex. Its steroids of the desoxycorticosterone series act on the tubular epithelium to increase reabsorption of Na and to increase excretion of K. They are probably liberated in response to a decrease in the ratio of Na/K in the plasma. Loss of secretory function in the adrenal, as in Addison's disease, results in Na depletion and K retention in the blood. Impairment of responsiveness to the hormone in the renal tubules underlies the pseudo-Addisonian syndrome of "salt-losing" nephritis. This phenomenon is seen in advanced chronic glomerulonephritis and also during the onset of diuresis in patients with acute nephron nephroses whose tubular epithelium has just begun to regenerate. It is important to note that the normal mechanism for sodium retention is especially active, so that sodium all but disappears from the urine during sodium depletion. The mechanism for potassium retention is not nearly as adequate. Potassium can continue to be lost in the urine in spite of a potassium deficit and hypopotassemia results.

In contrast to these renal mechanisms with associated extrarenal controls, the renal regulation of the reaction of body fluids is vested wholly in the kidney. It depends on the ability of tubular cells to change the rates of

Table 2

OBJECT	MEANS	CHANGE
Volume	Cardiac output Vasomotor (?)	Blood flow Glomerular filtration
Composition osmotic (water)	Post. pituitary	Water reabsorption
Discrete ions	Adren. cortex	Reabsorption and secretion of ions
Reaction	Renal tubules	NH_4^+, H^+ secretion Na^+ HCO_3^- reabsorption

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secretion of ammonium and hydrogen ions on the one hand and of reabsorption of sodium ion on the other. Acidosis (perhaps most effectively that due to accumulation of beta-hydroxybutyric acid) stimulates formation of ammonia from amino acids and glutamine. Ammonium ion then passes into the tubular fluid where it is exchanged for sodium ion which is reabsorbed together with bicarbonate. Simultaneously, hydrogen ion (H^+), formed in the cell by decomposition of carbonic acid ($H. HCO_3$), is secreted into the tubule and exchanged for sodium ion, so that $Na HCO_3$ is restored to the blood. Consequently, in acidosis the urine is rich in ammonia acid and sodium-poor. Conversely, alkalosis depresses ammonium formation and also the rates of sodium and hydrogen ion exchange, so that the urine becomes ammonia-poor, alkaline, and rich in sodium. Failure of the mechanisms of ion exchange because of renal tubular disease accounts for much of the base depletion and acidosis seen in terminal glomerulonephritis.

When, as is common, the primary defect in any of these mechanisms is renal, the various aspects of ineffective maintenance tend to be concurrent and the changes in body fluids multiple and mixed. Thus, in acidosis with dehydration, the mechanism of renal failure is predominantly hemodynamic. But in hyponatremia and dehydration associated with severe alkalosis, as in gastric vomiting, the distal tubules may necrose. The resultant nephron nephrosis conjoins tubular epithelial and vascular hemodynamic mechanisms.

Failure of these mechanisms cannot be corrected by rule of thumb. Effective treatment demands a consideration of the mechanisms at fault and correction or replacement on physiologic principles.

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