The author presents a thorough review of the kidney from both an anatomical and physiological standpoint. Her in-depth study encompasses the kidney's reaction to various diuretic drugs.

The kidneys are two organs, each weighing 125-180 gms (4-6 oz), located retroperitoneally. One is located in each lumbar area, the right slightly lower than the left, the upper pole of the right kidney resting on the 12th rib. The functional unit of the kidney is the nephron. There are approximately 1,200,000 in each kidney. The kidney has an inner layer, the medulla, the substance of which forms the 10-15 pyramids and the outer layer, cortex, in which the base of the pyramids is located.

The blood supply

The kidney receives its blood supply from the abdominal aorta; therefore, the blood flows at a higher pressure when it reaches the capillary area than in other tissue. Blood flow enters through the renal artery (Figure 1) at the kidney hilum; it passes through the interlobar arteries of the medulla to the junction of the medulla and cortex where the flow enters the arciform arteries; the blood then passes through the interlobular arteries which transverse the cortex. Afferent arterioles lead from these interlobular arteries to the nephrons. The afferent arteriole sub-divides into capillaries (the glomerulus), these capillaries converge to form the efferent arteriole. The efferent arteriole further sub-divides into the peritubular capillaries and the vasa recta, if the nephron is a juxtamedullary nephron. The venous blood follows a similar route of return to the renal vein and the inferior vena cava, that is: interlobular, arcuate, interlobar, vein, and vena cava.

The nephron

The nephron (Figure 2) consists of three basic parts.

1. The malpighian corpuscle, which is composed of the glomerulus surrounded by a blind pouch, Bowman’s capsule.

2. The tubule to which the capsule leads, is composed of three segments: (a) the proximal convoluted tubule, about 14 mm in length, which begins in the cortex and has an outstanding brush border on the luminal side which increases surface area; (b) the loop of Henle, which narrows as it dips into the medulla forming descending and ascending limbs which again widen as the tubule passes through the outer medullary zone and back into the cortex (about one out of every eight loops dips deeply

Figure 1—Gross Anatomy of the Kidney.
into the medullary area along with its corresponding capillary, the vasa recta, and is involved in the countercurrent mechanism); and (c) the distal convoluted tubule, one-third the length of the proximal tubule, which is located in the cortex. (Its initiation is associated closely with packed nuclei, called the macula densa; the brush border of the tubule is nearly absent.)

3. The collecting duct, which receives the filtrate from several distal tubules. These ducts empty into short papillary ducts of Bellini which empty into the renal calyces and thus into the renal pelvis.

Processes or functions involved in urine formation

Urine formation is actually a byproduct of the many important functions of the kidney.

The first process is filtration, which occurs over the 1.5 square meters of capillary surface in the glomeruli of both kidneys. In comparison, a 70 kg man has a body surface of 1.73 m² and the lung capillary surface is 70-90 m². Yet, for the kidney size and weight, this is a very large surface. Approximately one-fourth of the cardiac output (21-25 per cent) perfuses the kidney or about 1200 ml/min. Considering the hematocrit and nourishment of the kidney, the total plasma flow through the glomeruli is about 650 ml/min.

Filtration is promoted by filtration pressure differences and permeability, both of which are increased in the glomerular capillaries relative to that of skeletal muscle capillaries, but are decreased in the peritubular capillaries. This filtration per 24 hours in the kidney amounts to 170 liters of water or 1.5 liters/minute which contains a number of important substances (Figure 3).

The kidney’s importance is appreciated when one compares cardiac output of 5.2 liters/min. for a resting 70 kg man to tissue size, function, blood flows and oxygen uptake.
flows to muscle and heart change during exercise, and flow is not constant as it is in the brain.

Oxygen uptake by heart, brain, splanchnic and skeletal muscle is in a greater amount than the kidney, even at rest. To clear the plasma does not require as high oxygen levels as does the nutritive and energy needs of the other organs.

Approximately one-fourth of the cardiac output goes to the kidney, comparable only to that of skeletal muscle or splanchnic areas. This allows for adequate plasma clearance of 1200 ml per minute. Yet, under conditions of exercise, other body priorities will cause sidetracking of this amount.

Glomerular filtration pressure equals the hydrostatic pressure minus the sum of colloid osmotic and capsular pressures. Glomerular hydrostatic pressure is 70 mm Hg, glomerular colloid osmotic pressure is 32 mm Hg (due to retention of protein), and capsular tissue pressure is 14 mm Hg, giving a net filtration pressure of 24 mm Hg to favor the filtration of 125 ml/min.

The skeletal muscle, in comparison, has a hydrostatic pressure of 25 mm Hg. The colloid osmotic pressure is 28 mm Hg. Negative interstitial fluid pressure and colloid osmotic pressure together exert a pressure of 11.5 mm Hg, which assist the hydrostatic pressure to yield a net filtration of 8.5 mm Hg into the interstitial space in favor of cellular nutrition. On the venous side, because of a drop in capillary hydrostatic pressure, there is a net flow back into the capillary with removal of cellular wastes.

The second important process is reabsorption which occurs in the proximal and distal tubules. In the peritubular capillaries, the hydrostatic pressure (Figure 7) is less than that in other tissues. This lowered pressure facilitates net filtration of substances from the tubule lumen into the capillaries, thus aiding in the reabsorption process. It is primarily in the proximal tubule that the active and passive reabsorption occurs.
phosphate  
sulfate  
uric acid  
potassium  
ascorbic acid  
ketones as aceto-acetic acid  
Beta-hydroxy-butyrate

**Passive absorption** includes chloride and other electrolytes that are filtered, as well as the osmotically absorbed water and urea. In the proximal tubule, some of the substances such as glucose are absorbed completely if levels are physiological; sodium and water are absorbed to 80 per cent of the filtered amount, and other substances to lesser amounts. Therefore, the osmolarity of tubular fluid in the proximal tubule is still 285 mOSM, isotonic with that of plasma.

The third process is secretion, (Figure 8) sometimes called tubular excretion. Secretion occurs primarily in the proximal tubule and involves such compounds as:

- PAH
- penicillin
- sulfonphthaleins
- iodinated compounds such as Diodrast®, conjugated foreign substances

In the distal tubule, sodium, under the control of aldosterone, is exchanged for potassium and hydrogen ions. This area is involved in acid-base balance and electrolyte control as well as fluid balance control.

**Regulation of kidney function**

The three processes—filtration, reabsorption, and secretion—are regulated by three mechanisms.

The first, autoregulation (Figure 9) affects the glomerular filtration rate (GFR) because of the control on the hydrostatic pressure of the capillaries by the afferents and the resistance of the arterioles due to vasoconstriction or dilation. Sympathetic innervation to the afferent arterioles has been demonstrated but there seems to exist an intrinsic control by which the kidney itself regulates the arteriole pressure so that the GFR is kept constant.

The second, countercurrent exchange, (Figure 9) is a mechanism whereby the isotonic filtrate of the proximal tubule becomes hypertonic in the longer juxtamedullary loops as the filtrate flows down the descending loop of Henle through an increasingly hypertonic interstitium. Osmo-
increasingly hypertonic interstitium to the ducts of Bellini. Approximately 14 per cent of the water in the filtrate is reabsorbed in this area, and the final concentration of urine occurs here. One per cent of the GFR or 1 ml/min of urine is formed.

Physiological regulation in the body by the kidney

A review of the many filtrate statistics and functions of the kidney reveals its great importance in body homeostasis. Besides the adjustment of electrolyte or ion concentrations, osmolarity, fluid volumes of extracellular fluid and blood, and removal of waste products and toxic substances, acid-base balance is one of interest and intrigue. The long term regulation of the pH to maintain a bicarbonate to carbonic acid ratio of 20:1 in the blood occurs primarily in the distal tubule. Here is what happens as the filtrate passes through the distal tubule.

The sodium of the filtrate (Figure 10) is exchanged for the hydrogen ion generated by the tubular cell metabolism. In this metabolism CO₂ and H₂O are produced; these form carbonic acid facilitated by the enzyme carbonic anhydrase. The carbonic acid then splits into hydrogen and bicarbonate. The hydrogen exchanges with the tubular sodium. The sodium is actively pumped into the blood stream and the cellular bicarbonate is passively reabsorbed with the sodium into the peritubular capillaries. A common exchange of hydrogen is made with the dissociated sodium from the filtrate's sodium bicarbonate.

In the tubule, (Figure 11) the exchanged hydrogen and filtrate bicarbonate form carbonic acid which dissociates into water. The water, in turn, is excreted as urine and carbon dioxide which is reabsorbed into the blood stream and excreted by the lungs.

In the event of acidosis, (Figure 12) more sodium is needed for exchange with hydrogen. The titratable acid Na₂HPO₄ is utilized. This acid is present in the filtrate and dissociates into two sodiums and HPO₄⁻. The cellular hydrogen exchanges for one of the two sodiums. The sodium is reabsorbed with the cellular bicarbonate, and the hydrogen forms NaH₂PO₄ which is excreted.

With increasing acidosis, (Figure 13) ammonium is formed from glutamine. Sodium chloride, which is in the filtrate, dissociates into sodium and chloride. The sodium is exchanged for the cellular hydrogen ion and is reabsorbed with the cellular bicarbonate. The hydrogen ion along with the amine NH₃ forms the compound ammonium (NH₄⁺). Ammonium along with the chloride forms ammonium chloride which is excreted in the urine.

In the state of alkalosis, the hydrogen ion may be sparse. Cellular potassium may
<table>
<thead>
<tr>
<th>Drug</th>
<th>Site of action</th>
<th>Indications</th>
<th>Side effects</th>
<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannitol</td>
<td>Osmotic</td>
<td>Potentiate excretion of salicylates and phenobarbitone, reduce brain volume, prevent acute renal failure, protect against nephrotoxins</td>
<td>Ensure against extravascular linkage</td>
<td>Ineffective in azotemia</td>
</tr>
<tr>
<td>Urea</td>
<td>Osmotic</td>
<td>Similar to mannitol</td>
<td>Arrhythmias and increase blood pressure, hemolysis</td>
<td>Less effective than mannitol</td>
</tr>
<tr>
<td>Mercurials</td>
<td></td>
<td>Acts on several sites and by inhibiting intracellular enzyme systems, therefore transport processes, note decreased Na⁺ and Cl⁻ reabsorption</td>
<td>Increase causes renal tubular damage metabolic alkalosis with less of Cl⁻</td>
<td>Variable: if acidotic, more effective</td>
</tr>
<tr>
<td>Mersalyl acid</td>
<td></td>
<td>Rarely used, other agents safer and more reliable</td>
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<td>Merphyllin®</td>
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<td>Salyrgan®</td>
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<td>Thiomerin®</td>
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<tr>
<td>Acoxalamide</td>
<td></td>
<td>Inhibit carbonic anhydrase, decreases H⁺ and HCO₃⁻ production, therefore decreases Na⁺ and HCO₃⁻ reabsorption, Affects whole nephron</td>
<td>Used with organic mercurials in treatment of edema association with CHF and glaucoma</td>
<td>Metabolic acidosis with retention of Cl⁻, K⁺ excreted with HCO₃⁻ in exchange for some Na⁺ rather than H⁺</td>
</tr>
<tr>
<td>Diamox®, (a sulphonamide derivative)</td>
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<td>Metroapore</td>
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<td>Metopirone®</td>
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<td>Spironolactone</td>
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<td>Aldactone®</td>
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Table 1
Diuretic agents effects on kidney function
<table>
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<tr>
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<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium chloride (NH₄Cl)</td>
<td>Acidifies, decreases urine pH. Liver forms urea, NH₄⁺ picks up H⁺ in exchange for Na⁺. Urea and Cl⁻ act as osmotic diuretic.</td>
<td>Used in pethidine, lead, and bromide intoxication, enhances المساليح and resupplies lost Cl⁻.</td>
<td>Enhances metabolic acidosis. Dangerous in liver and renal failure.</td>
<td>Mild diuresis</td>
</tr>
<tr>
<td>Ethacrynic acid (Edecrin®)</td>
<td>Proximal convoluted tubule ascending limb loop of Henle first part distal tubule increases excretion of Na⁺, K⁺, H⁺ and Cl⁻.</td>
<td>Acute pulmonary edema and other emergencies, in edema resistant to other diuretics</td>
<td>Hypokalemia, hypochloremic akalosis and sudden fluid loss</td>
<td>Effective in azotemia and decreases GFR, 5X as powerful as thiazides</td>
</tr>
<tr>
<td>Furosemide (Lasix®)</td>
<td>Proximal tubule, ascending limb loop of Henle and first part of distal tubule</td>
<td>For cases resistant to milder diuretics, enhances effect with spironolactone</td>
<td>Ototoxicity and hypochloremic akalosis</td>
<td>Effective in poor renal function and in pulmonary edema. Similar to Edecrin®</td>
</tr>
<tr>
<td>Thiazides</td>
<td>Preveny Na⁺ reabsorption in distal loop of Henle and early part of distal tubule, weak inhibitor of carbonic anhydrase, increases HCO₃⁻ and K⁺ excretion, decreases blood pressure, direct action on total peripheral resistance</td>
<td>Edema of chronic CHF, hepatic or renal disease, and in hypertensive disease</td>
<td>Excreted slowly if impaired renal or cardiac function. Tendency to hyperkalemia in uremia.</td>
<td>Similar to mercurials</td>
</tr>
<tr>
<td>Triamterene (Dyrenium®)</td>
<td>Effect on distal tubule, increases pH urine, increases HCO₃⁻ excretion, does not inhibit carbonic anhydrase</td>
<td>Edema with CHF, cirrhosis, nephrotic syndrome, idiopathic and drug-induced edema; used with thiazides</td>
<td>Minor of itself, some azotemia slight increase of Na⁺, Cl⁻, and H⁺ excretion but K⁺ excretion due to other diuretics is blunted if given in conjunction with these drugs</td>
<td>Weaker natriuretic effect than thiazides, similar to aldactone</td>
</tr>
<tr>
<td>Amiloridine</td>
<td>Similar to triamterene, blocks Na⁺—K⁺ exchange directly</td>
<td>Similar to triamterene</td>
<td>Similar to triamterene</td>
<td>Similar to triamterene</td>
</tr>
</tbody>
</table>
exchange with sodium instead of the cellular hydrogen so as to conserve the hydrogen and allow bicarbonate excretion.

**Figure 13.**

**Alteration of functions**

Pathology of the kidney could alter any of these mechanisms, whether it be glomerular or tubular disease. Blood pressure extremes could affect the GFR by overriding autoregulation.

Drugs affecting GFR, hormones, osmolality or electrolytes also could alter the response of these functions.

An example of this alteration is found in diuretics. They can affect kidney function in five ways (Figure 14) by:

1. Increasing the blood supply to the kidney such that (a) aminophyllin causes vasodilation, (b) digitalis increases cardiac output, and (c) water intake increases plasma volume.

2. Preventing tubular reabsorption of water by use of osmotic urea, glucose, sucrose, or mannitol.

3. Preventing tubular reabsorption of sodium or inhibiting carbonic anhydrase which interfere with chloride, bicarbonate, potassium, and water absorption and excretion.

4. Decreasing hormonal control, that is, ADH and aldosterone.

5. Decreasing production of aldosterone and cortisone by the adrenal cortex by use of drugs as metyrapone.

**Figure 14—Effect of Diuretics on Renal Function.**

Thus, various diuretics may have effects on fluid and electrolyte balance as well as on acid base balance. (See Table I.)

Osmolarity will have some relationship to specific gravity, but the two are not directly interchangeable. Specific gravity depends on concentration and the nature of the solutes. (See Table II.)

**REFERENCES**


| Table II |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Correlation of specific gravity with mOsm of solute in urine** | | | | | | | | |
| **SG.** | 1.005 | 1.010 | 1.015 | 1.020 | 1.025 | 1.030 | 1.035 | 1.040 |
| **mOsm** | 200 | 400 | 600 | 800 | 1000 | 1200 | 1400 | 1600 |
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