Chapter 1
Urine: The Golden Elixir of Life

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Objectives

- Understand the basic anatomy of the urinary system
- Discuss glomerular filtration as the process of urine formation
- Describe how urine composition and amount are determined by a series of specialized tubules

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Overview

Many scientists as well as philosophers have recognized the importance of urination and how this basic physiologic function is vital to sustain life. The urinary system and tract are responsible for the production, refinement and elimination of urine from the body. A thorough examination of urine provides valuable information that assists in patient care. This book is dedicated to the clinical application of urine tests; however before test application, one should understand some basic principles of urine production, refinement and elimination.

The kidney presents in the highest degree the phenomenon of sensibility, the power of reacting to various stimuli in a direction which is appropriate for the survival of the organism; a power of adaptation which almost gives one the idea that its component parts must be endowed with intelligence. (Frank Starling, 1909)

Urine Production

The kidney is the organ responsible for urine production. Humans normally have two separate "bean shaped" kidney organs located to the left and right of the spine in the retroperitoneal space. The kidneys are highly vascular organs receiving an average 20–25% of the cardiac output, which is remarkable since the kidneys only comprise 0.5% of total body weight [1, 2].

The basic filtering unit of the kidney is the nephron. The nephron is composed of a glomerulus, a series of tubules and a collecting duct. Exact nephron number across individuals is variable but total number is determined/finalized at birth. After birth, new nephrons cannot be developed and lost nephrons cannot be replaced. Each kidney on average contains approximately one million nephrons [1, 2].

Blood is supplied to the nephron through a series of arteries finally reaching the glomerular capillaries via the afferent arteriole and leaving the capillary bed via the efferent arteriole (Fig. 1.1). The hydrostatic pressure in the capillary bed forces

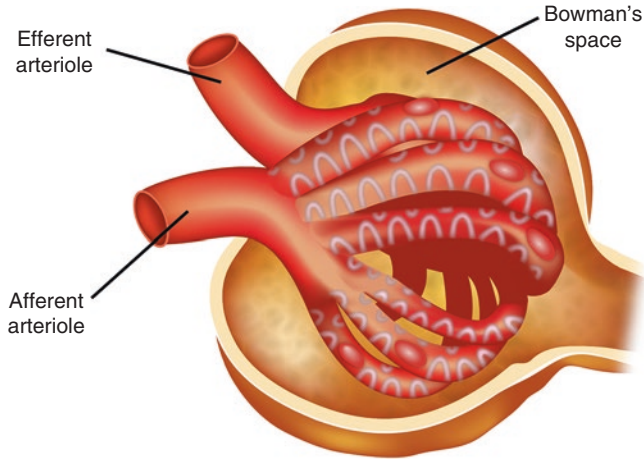

FIGURE 1.1 Capillary bed of the glomerulus. (Courtesy of Teresa Ruggle, University of Iowa.)

fluid to move from the blood compartment across the semi-permeable glomerular membrane into the urinary space (Bowman's space). This ultrafiltrate is essentially the same osmolality as plasma and includes water, small molecules, and ions that easily pass through the filtration membrane [1, 2].

Larger molecules such as proteins and red blood cells are normally prevented from passing through the filtration membrane. This filtration membrane or barrier is comprised of three components: (a) the endothelial cells of the renal capillaries, (b) the basement membrane and (c) the epithelial cells lining the urinary space. Evidence of protein (see Chap. 5) or red blood cells (see Chap. 9) in the urine could therefore be a sign that this barrier is compromised [3–5].

Urine Refinement

The ultrafiltrate in Bowman's space will then pass through a series of tubules and a collecting duct. This refinement process allows for the secretion of additional waste products in

addition to reabsorption of water and solutes from the ultrafiltrate. This refinement process is also required to sustain life. In a typical 70 kilogram individual, the kidney filters approximately 180 liters of fluid daily. Life would cease to exist without the ability to reabsorb solutes and water from the filtrate. The kidneys are very efficient at this process as only 1–2 liters of urine on average are excreted daily while maintaining electrolyte, mineral and pH balance in the blood.

Four major tubular segments of the nephron (Fig. 1.2) determine the final composition and volume of the urine: (a) proximal convoluted tubule, (b) loop of Henle, (c) distal convoluted tubule and (d) collecting duct. Each individual segment of the tubule possesses a unique set of channels and transporters that allow reabsorption and excretion to occur. The main ion that is reabsorbed through these segments is sodium. Filtering 180 liters a day would lead to the theoretical excretion of approximately 25,500 mmol per day of sodium, a

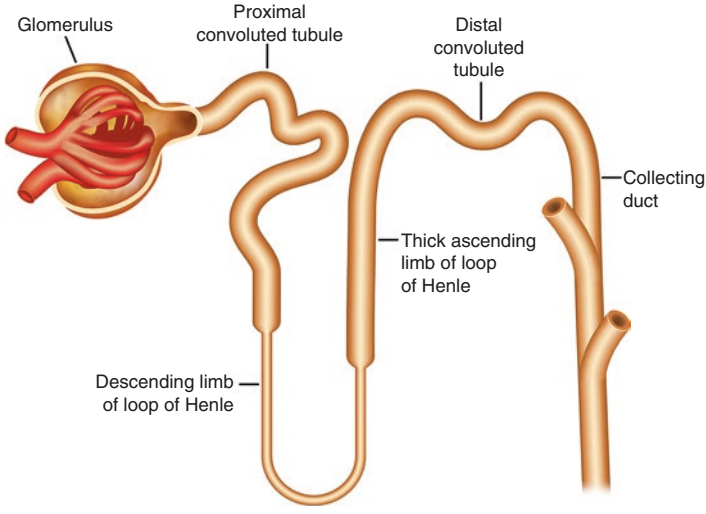

FIGURE 1.2 The nephron of the kidney. (Courtesy of Teresa Ruggle, University of Iowa.)

loss that would be incompatible with life. The efficient reabsorption mechanism of the renal tubules allows for over 99% of this sodium to be reabsorbed, leading to only about 100 mmol per day sodium excretion [1, 2]. Additional examples of the reabsorption efficiency of the kidney are listed in Table 1.1.

The proximal convoluted tubule is the workhorse of the kidney and reabsorbs more solute and water than any other segment of the nephron. Approximately 55–65% of the total ultrafiltrate is reabsorbed in this segment. Almost all of the filtered glucose and amino acids are reabsorbed in this segment along with 90% of the bicarbonate, 65% of the sodium and 55% of the chloride. Since both solutes/ions and water are reabsorbed in the proximal convoluted tubule, the ultrafiltrate leaving the proximal tubule is essentially the same osmolality as the ultrafiltrate that entered. Stated another way, urine is neither concentrated nor diluted in this segment [1, 2].

The loop of Henle is composed of a descending limb and an ascending limb. The descending limb is relatively impermeable to solutes but freely permeable to water. The ascending limb is water impermeable; thus here begins the diluting

Table 1.1 Filtration, excretion, and reabsorption of water, electrolytes, and solutes by the kidney in a normal adult

Substance	Amount	Filtered	Excreted	Reabsorbed	% Filtered amount reabsorbed
H_2O	L/day	180	1.5	178.5	99.2
Na^+	mEq/day	25,200	150	25,050	99.4
K^+	mEq/day	720	100	620	86.1
Ca^{++}	mEq/day	540	10	530	98.2
HCO_3^-	mEq/day	4320	2	4,318	99.9+
Cl^-	mEq/day	18,000	150	17,850	99.2
Glucose	mmol/day	800	0	800	100.0
Urea	g/day	56	28	25	50.0

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segment of the nephron because removal of solutes and not water dilutes the ultrafiltrate concentration. The $Na^+K^+2Cl^-$ symporter on the apical membrane of the thick ascending limb allows for 25% of the filtered sodium and chloride to be reabsorbed in this segment of the nephron [1, 2]. This transporter is the site of action for the class of diuretics known as loop diuretics. Hereditary or acquired dysfunction of this transporter results in Bartter syndrome. This disorder has clinical features (hypokalemia, metabolic alkalosis, hypercalciuria) similar to those seen in patients given a loop diuretic [6–8].

The distal tubule is relatively impermeable to water, continuing the diluting segment of the nephron. The Na^+Cl^- symporter on the apical membrane of the distal convoluted tubule allows for an additional 5–10% of filtered sodium and chloride to be reabsorbed in this segment of the nephron [1, 2]. This transporter is the site of action for the class of diuretics known as thiazide diuretics. Hereditary or acquired dysfunction of this transporter results in Gitelman syndrome. This disorder has clinical features (hypokalemia, metabolic alkalosis, hypocalciuria) similar to those seen in patients given a thiazide diuretic [6–8].

The collecting duct fine tunes sodium reabsorption as well as potassium and acid excretion. The epithelial sodium channel (ENaC) on the apical membrane of the principal cell in the collecting duct allows for an additional 1–3% of the filtered sodium load to be reabsorbed. This channel is upregulated by the mineralocorticoid aldosterone [1, 2]. Mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, cause a downregulation of ENaC resulting in sodium diuresis. A hereditary or acquired activating mutation of ENaC results in Liddle syndrome, which is a disorder with clinical characteristics similar to those of a high aldosterone state (excessive sodium reabsorption, hypervolemia, hypertension, hypokalemia) [8–10]. An inactivating mutation has also been described that results in clinical char-

acteristics similar to those of a low aldosterone state (sodium wasting, hypovolemia, hyperkalemia) [11].

The collecting duct is impermeable to water in the absence of antidiuretic hormone (ADH). When ADH is present, the collecting duct becomes permeable to water through the use of aquaporin channels. It is here in the collecting duct that the urine can be further diluted or concentrated depending on the needs of an individual. The major stimuli for ADH secretion are hyperosmolality and effective circulatory volume depletion [1, 2].

Urine Elimination

Urine flows from the collecting duct of the nephron to join a converging system of tubules with other collecting ducts. These ducts then join together to form the minor calyces followed by the major calyces that ultimately converge in the renal pelvis (Fig. 1.3). Urine continues to flow from the renal pelvis into the ureter, transporting urine into the urinary bladder. Urine from both kidneys is stored in the bladder until the process of micturition (urination) occurs.

The first urge to void is felt at a bladder volume of approximately 150 milliliters (mL). A marked sense of fullness is felt at about 400 mL and bladder capacity is approximately 500 mL [12]. Urine is normally excreted voluntarily from the body by flowing through the urethra away from the bladder.

Average daily urine production for adults is usually between 1–2 liters (L) depending on the state of hydration, activity level, and health of the individual. Producing too much or too little urine requires medical attention. Polyuria (see Chap. 15) is a condition of excessive urine production (more than 3 L/day). Oliguria is the production of less than 400–500 mL/day and anuria is the production of less than 50–100 mL/day.

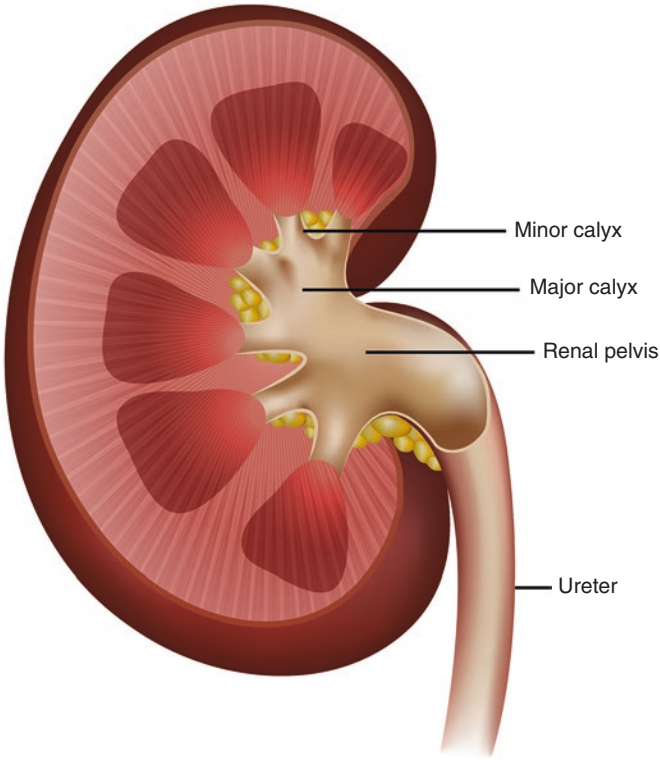

FIGURE 1.3 Anatomy for urine flow through the kidney. (Courtesy of Teresa Ruggle, University of Iowa.)

Summary

Normal urinary system anatomy consists of two kidneys, two ureters, one urinary bladder and one urethra. The urinary system is responsible for urine production, refinement and elimination. The final composition and amount of urine is determined by the specialized actions of glomerular filtration followed by tubular reabsorption and secretion. Urine can be collected from a patient and its contents provide additional clinical information to the provider. This information may be obtained by a urinalysis using a dipstick to determine chemical composition; microscopic analysis to look for cells, casts or

crystals; cultures to assist with infection diagnosis; or specialized tests to assess for cancer, electrolyte abnormalities or substance abuse. Whatever the test, analyzing this golden elixir of life provides a valuable, noninvasive means to assist with patient care.

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