Chapter 20 – Renal Filtration and Urine Formation

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To describe the general organization and function of the urinary system, especially the kidney and the nephron.
B. To explain the process of blood filtration by the glomerular capillaries, including glomerular filtration rate.
C. To describe the tubular epithelium and its role in reabsorption.
D. To explain reabsorption in the proximal tubules.
E. To explain reabsorption and formation of an osmotic gradient by the nephron loop.
F. To explain reabsorption in the early distal tubules.
G. To explain reabsorption in the late distal tubules and collecting ducts.
H. To explain how local-factors control renal blood flow and glomerular filtration rate.

The urinary system includes the kidneys, ureters, bladder, and urethra. The primary purpose of the urinary system is to filter the blood plasma, to reabsorb needed fluids and electrolytes, and to excrete unneeded (or excess) substances. The urinary system plays a critical role in maintaining fluid and electrolyte balance and in the long-term regulation of acid-base balance, blood volume and blood pressure.

Organization of the Urinary System

The kidneys are located in the retroperitoneal cavity of the abdomen, as shown in Figure 20.1. The ureters extend from the hilus of each kidney, travel along the psoas muscles and cross over the iliac arteries and veins on their way to the urinary bladder. The urinary bladder rests on the anterior floor of the pelvic cavity.

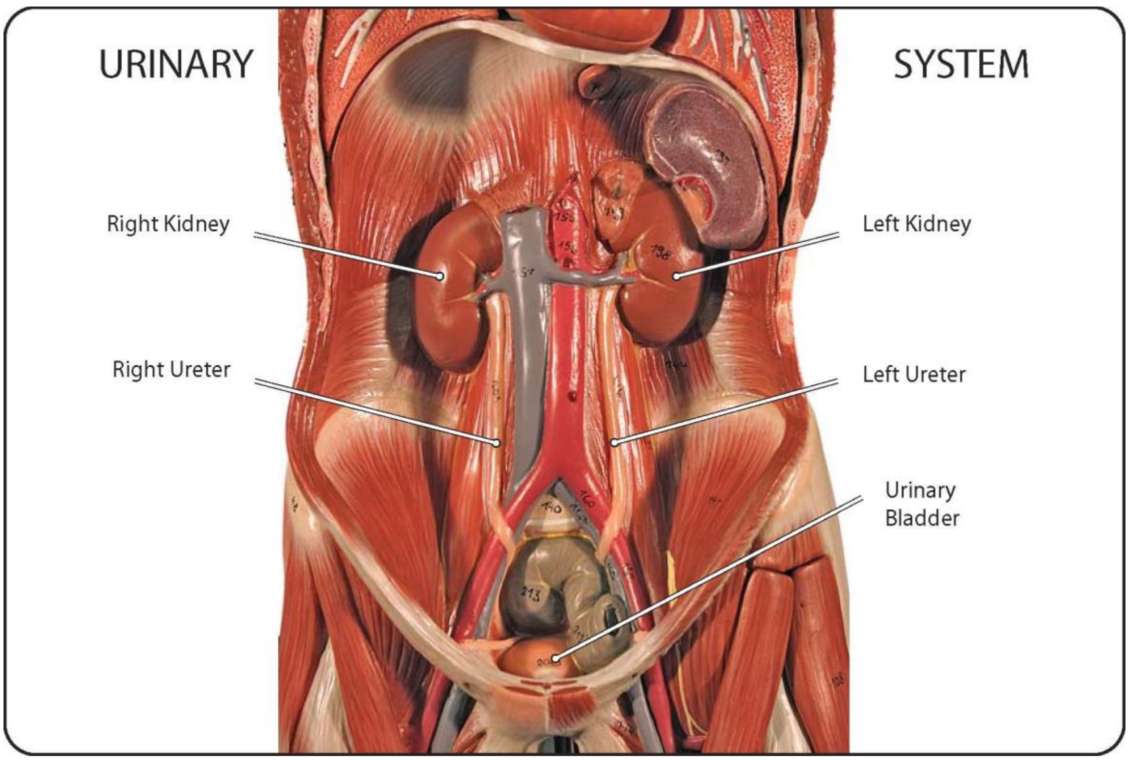


Figure 20.1 © 2007 David G. Ward, Ph.D.

The internal structure of the kidney is shown in Figure 20.2. Each kidney is surrounded by the renal capsule. Internally, the outer region is the cortex and the inner region is the medulla. Blood enters the kidney by way of the renal artery which branches into several segmental arteries (not labeled). The segmental arteries branch into interlobar arteries which pass into the medulla and around the renal pyramids. The interlobar arteries become the arcuate arteries and follow the junction between the medulla and the cortex where interlobular arteries branch off into the cortex. The process of blood filtration occurs in the cortex. Reabsorption begins in the cortex and continues into the pyramids of the medulla. Urine is collected from each pyramid by a minor calyx and transported to the renal pelvis and ureter.

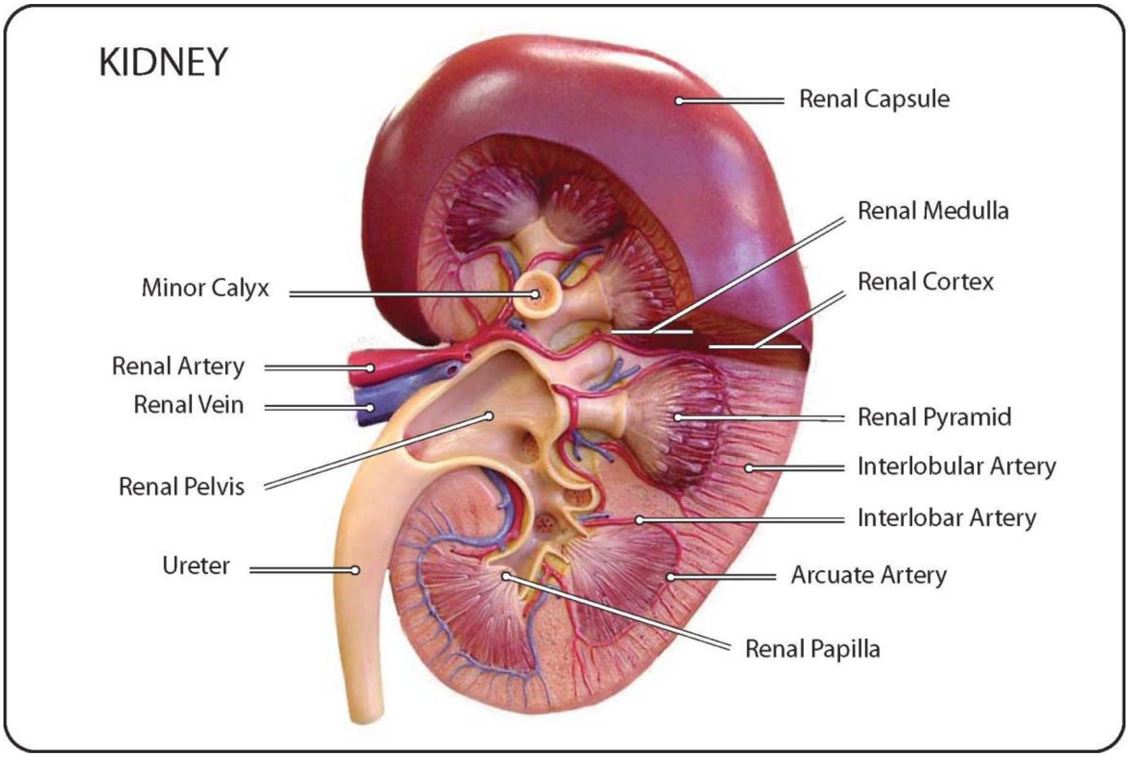


Figure 20.2 © 2007 David G. Ward, Ph.D.

The processes of filtration and reabsorption occur in the nephrons which are shown in Figure 20.3. Blood travels from the interlobular arteries to afferent arterioles that enter renal corpuscles where filtration occurs. Filtrate from the blood passes into the proximal convoluted tubules and the blood continues into the efferent arterioles and to the peritubular capillaries. Blood is collected from the peritubular capillaries by the interlobular veins. The filtrate continues through the proximal convoluted tubules, the descending and ascending nephron loops, the distal convoluted tubules, the collecting tubules and ducts where reabsorption occurs. The collecting ducts merge to form papillary ducts which empty into the minor calyx. Cortical nephrons are located predominantly in the cortex. Juxtamedullary nephrons are located closer to the medulla and their nephron loops extend deep into the medulla.

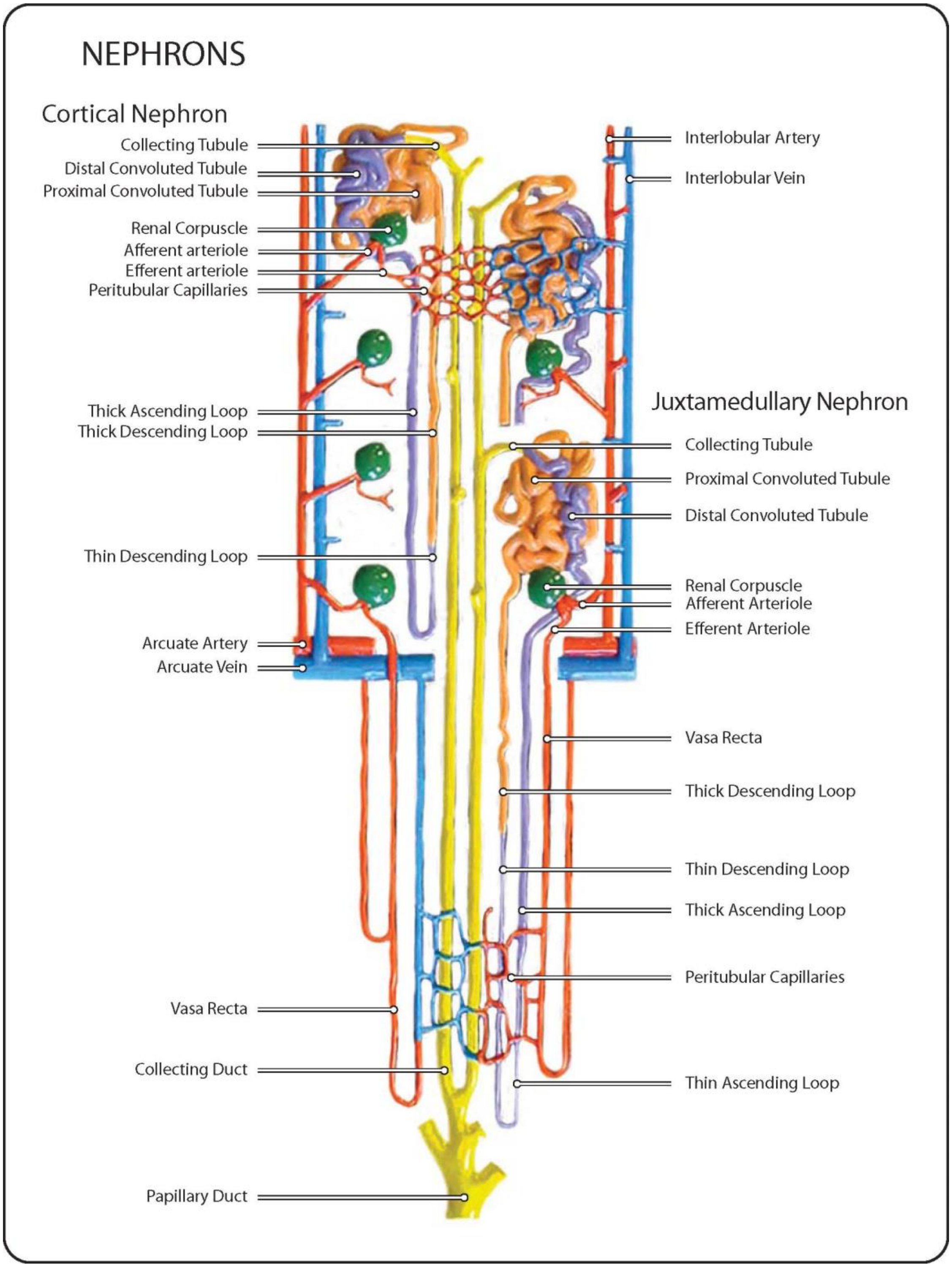


Figure 20.3 © 2007 David G. Ward, Ph.D.

Filtrate Formation

The kidney acts on the blood to filter plasma, to reabsorb needed fluids and electrolytes, and to excrete unneeded substances. Plasma is filtered out of the blood by glomerular filtration. Substances are reabsorbed from the renal tubules back into the blood in the peritubular capillaries.

Glomerular filtration

Filtration of the blood occurs in the renal corpuscles. The internal structure of a renal corpuscle is shown in Figure 20.4. Blood enters the corpuscle by way of an afferent arteriole that connects to a capillary network called the glomerular capillaries (glomerulus). The glomerular capillaries are covered by the visceral epithelium to form two filtration membranes. Water, electrolytes and small molecules pass through the endothelium of the capillaries and through the visceral epithelium and into the capsular space. The renal corpuscle is enclosed in an impermeable epithelium called the parietal epithelium that opens into the proximal convoluted tubule.

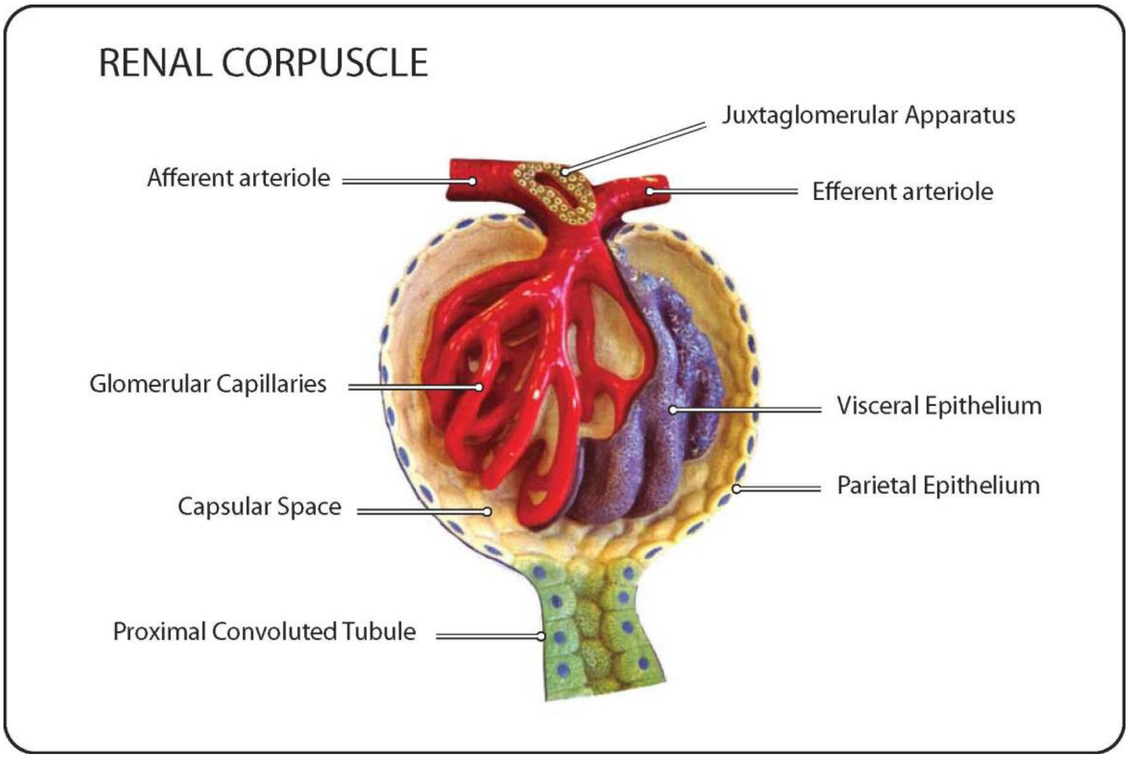


Figure 20.4 © 2007 David G. Ward, Ph.D.

The movement of substances through the capillary endothelium and through the visceral epithelium is largely mediated by diffusion and bulk flow through water filled channels; especially intercellular clefts (refer to chapter 18). In the renal corpuscles, the movement of fluid into the capsular space is largely dependent on glomerular capillary and capsular pressures as shown in Figure 20.5.

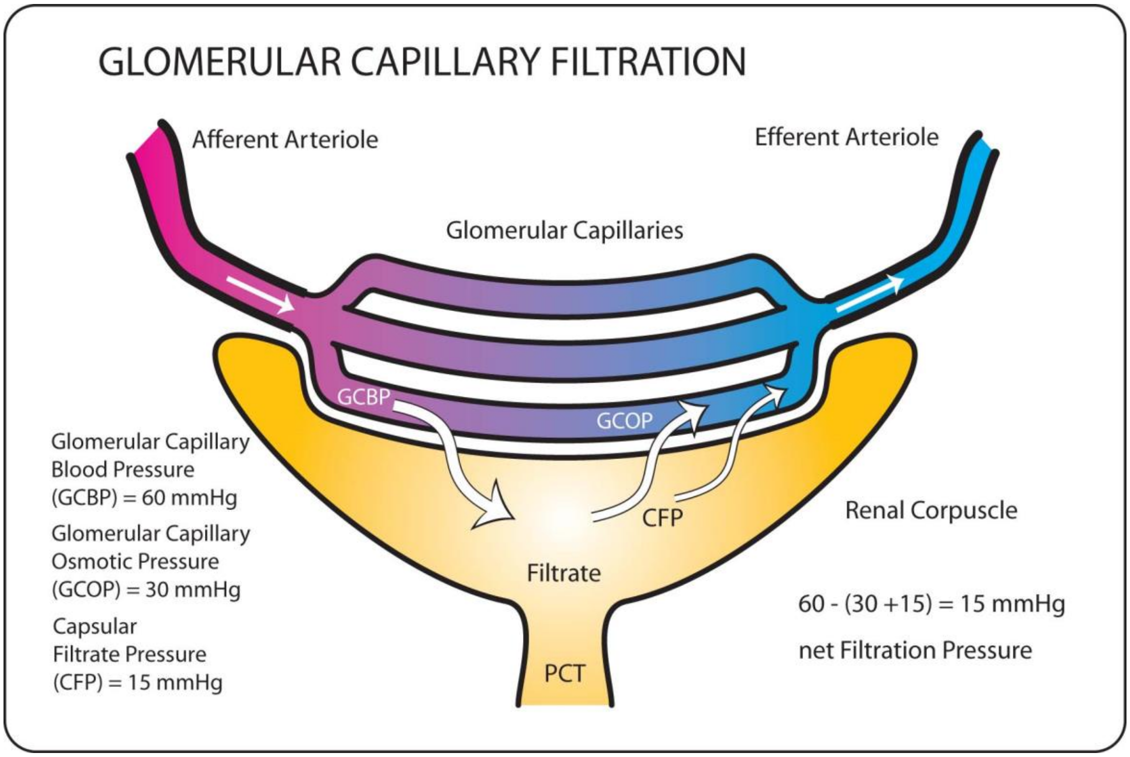


Figure 20.5 © 2010 David G. Ward, Ph.D.

In contrast to most systemic capillaries, the glomerular capillary blood pressure (GCBP) is elevated to about 60 mmHg by constriction of the efferent arteriole. The glomerular capillary osmotic pressure is about 30 mmHg. The capsular filtrate pressure is about 15 mmHg and the capsular osmotic pressure is close to 0 mmHg.

Due to the water filled channels fluid will move from an area of higher pressure to an area of lower pressure. The large glomerular capillary blood pressure (GCBP = 60 mmHg) will push large quantities of fluid out of the capillaries and into the capsular space. As we noted in chapter 15, 6% to 9% of plasma is composed of proteins and these proteins will not be able to pass through the filtration membranes. These proteins together with the loss of fluid generate a large glomerular capillary osmotic force (GCOP = 30 mmHg) that draws fluid back into the glomerular capillaries. The large quantity of fluid that is pushed into the capsular space elevates the capsular filtrate pressure (CFP = 15 mmHg) which pushes some of the fluid back into the glomerular capillaries. Since only a very small number of larger molecules pass through the filtration membranes and into the capsular fluid, the capsular filtrate osmotic force is negligible (0 mmHg). The result is a net filtration pressure of about 15 mmHg [60-(30+15)] causing fluid to move out of the capillaries and into the capsular space.

Glomerular Filtration Rate

The net filtration pressure just described is sufficient to produce a substantial quantity of filtrate. The amount of filtrate formed each minute is called the glomerular filtration rate (GFR).

- Glomerular Filtration Rate (GFR) is about 125 mL/min total for both kidneys.
- GFR is tightly autoregulated when the mean arterial pressure is between about 80 mmHg and 180 mmHg.

A normal GFR of 125 mL/min is equal to 7.5 L/hr and 180 L/day. Therefore, the total plasma volume is filtered 2.5 times each hour and 60 times each day. A normal 24-hour urine volume is about 1.8 L which is only 1% of the 24-hour glomerular filtration. Therefore about 99% of the glomerular filtration is reabsorbed.

- About 1% of filtrate is excreted as urine; about 99% of filtrate is reabsorbed.

Reabsorption and Secretion – General Mechanisms

The organization of the tubular epithelium is illustrated in Figure 20. 6. The tubular epithelial cells are connected laterally by tight junctions. Therefore, substances must pass through the plasma membranes of the epithelial cells. The plasma membrane facing the tubular lumen is called the apical (or luminal) membrane, and the membrane facing the interstitial fluid is the basolateral membrane.

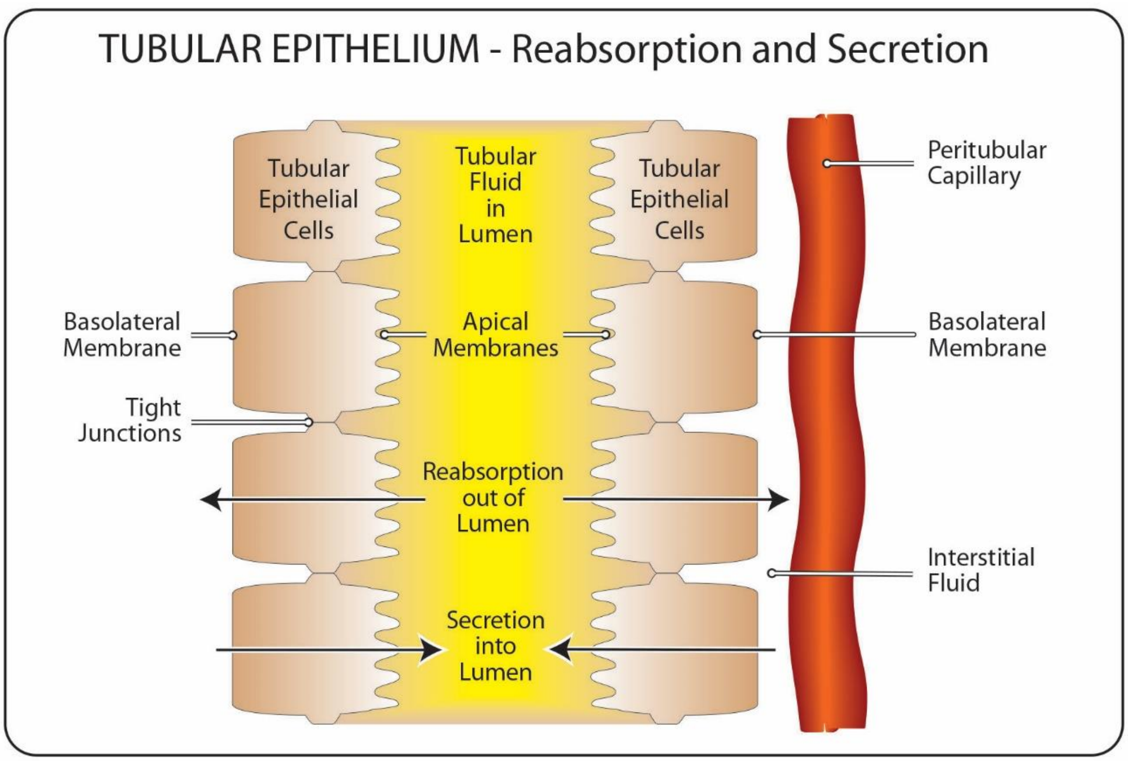


Figure 20.6 © 2016 David G. Ward, Ph.D.

Reabsorption involves movement of water, electrolytes, and small molecules <u>from the tubular fluid</u> (in the lumen), through the apical membrane, into the intracellular fluid (in the tubular cells), then through the basolateral membrane, <u>into the interstitial fluid</u>, and finally into the peritubular capillaries that surround the tubules.

Secretion involves movement of water, electrolytes, and small molecules from the interstitial fluid, through the basolateral membrane into the intracellular fluid (in the tubular cells), then through the apical membrane, and finally into the tubular fluid (in lumen).

The mechanisms for transport through the tubular epithelium follow the general principles outlined in chapter 5, Figure 5.9. Most of the reabsorption of water and solutes is driven by the Na^+ / K^+ pumps located in the basolateral membrane. Reabsorption from the renal tubules depends on a combination of diffusion, active transport, and co-and counter-transport, as illustrated by a few examples in Figure 20.7.

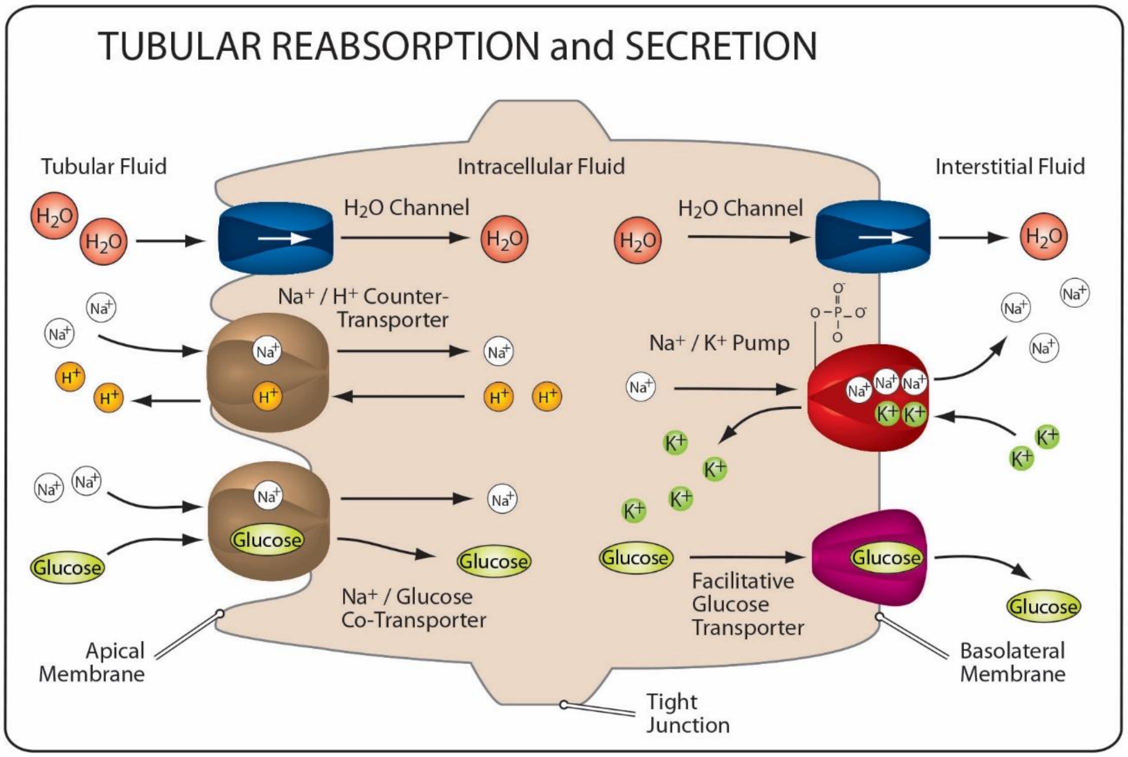


Figure 20.7 © 2016 David G. Ward, Ph.D.

- Water diffuses according to concentration gradient through water channels in the apical and basolateral membranes.
- Sodium ions (Na^+) are actively transported out of tubular cells and into interstitial fluid, and potassium ions (K^+) are transported out of interstitial fluid and into tubular cells by Na^+ / K^+ pumps in the basolateral membrane.
- The removal of Na^+ from the cells establishes a concentration gradient that favors movement of Na^+ into the cell from the tubular fluid. By using Na^+ linked trans-porters, as Na^+ moves into the cells, other substances are moved either out or in.
    - Na^+ / H^+ counter-transporters move hydrogen ions (H^+) out of the tubular cells and into the tubular fluid as Na^+ moves into the tubular cells.
    - Na^+ / glucose co-transporters move glucose out of the tubular fluid and into tubular cells as Na^+ moves into the tubular cells.

Reabsorption and Secretion – Renal Tubules and Ducts

Emphasis is placed on the reabsorption and secretion of Na^+, Cl^-, and K^+.

Proximal convoluted tubule

The proximal convoluted tubule acts as a mass absorber. About two-thirds (67%) of filtered water and solutes are reabsorbed in this region, as shown in Figure 20.8.

- Water is a major substance reabsorbed
- Major solutes reabsorbed include sodium, chloride, potassium, calcium, bicarbonate, glucose, amino acids, fatty acids, and urea.
- In addition, some solutes are secreted into the tubular fluid and include hydrogen ions and various anions such as sulfate and oxalate.

Transport mechanisms *(follow the transport using Figure 20. 6)*

Throughout all the proximal tubules,

- Water and urea transported into and out of tubular cells by water and urea channels in the apical and basolateral membrane.
- Sodium ions (Na^+) are transported *out of* tubular cells and potassium ions (K^+) are transported *into* tubular cells by Na^+ / K^+ pumps in the basolateral membrane.
- The removal of sodium ions (Na^+) from the tubular cells establishes a concentration gradient that favors movement of sodium ions (Na^+) from the tubular fluid *into* the tubular cells.

In the first half of the proximal tubule,

- Sodium ions (Na^+) are transported into tubular cells and hydrogen ion (H^+) are transported *out of* tubular cells by Na^+/ H^+ counter-transporters in the apical membrane.
- Sodium ions (Na^+) and bicarbonate ions (HCO_3^-) are transported *out of* tubular cells by Na^+/HCO_3^- co-transporters in the basolateral membrane.
- Sodium ions (Na^+) and glucose (or other organic solute) are transported *into* tubular cells by Na^+/ glucose co-transporters in the apical membrane.
- Glucose (and other organic solutes) are transported *out of* tubular cells by facilitated transporters in the basolateral membrane.
- Potassium ions (K^+) are transported *out of* tubular cells by K^+ channels in the basolateral membrane.

In the second half of the proximal tubule,

- Sodium ions (Na^+) and chlorine ion ($Cl^–$) are transported *into* tubular cells by Na^+/ $Cl^–$ co-transporters in the apical membrane.
- Potassium ions (K^+) and chloride ions ($Cl^–$) ions are transported *out of* tubular cells by K^+/ $Cl^–$ co-transporters in the basolateral membrane.

Hormonal Control

- The reabsorption of sodium and chloride is stimulated, in part, by angiotensin II (independent of aldosterone).

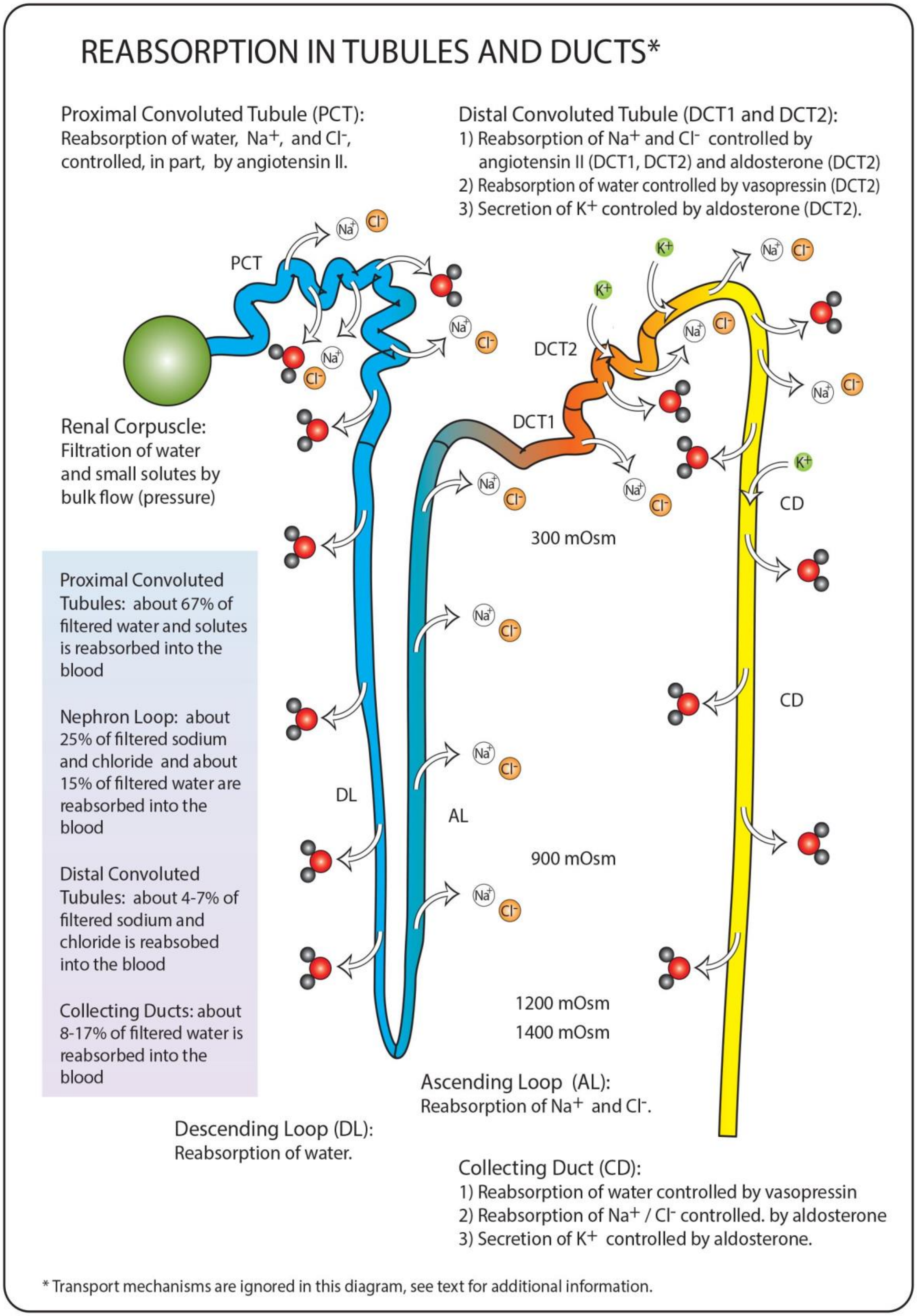


Figure 20.8 © 2019 David G. Ward, Ph.D.

Nephron loop

The nephron loop acts in part as a mass absorber and in part to create an osmotic gradient for reabsorption of water. About 15% of filtered water and 25% of filtered Na^+, Cl^-, and K^+ are reabsorbed in this region, as shown in Figure 20.8.

- Water is the major substance reabsorbed
- The major solutes reabsorbed include sodium, chloride, potassium, calcium, and bicarbonate. In addition, hydrogen ions are secreted into the tubular fluid.

Transport mechanisms *(follow the transport using Figure 20. 6)*

In the thin descending limb,

- Water is transported *into* and *out of* tubular cells by water channels in the apical and basolateral membrane.

In the thick ascending limb,

- Sodium ions (Na^+) are transported *out of* tubular cells and potassium ions (K^+) are transported *into* tubular cells by Na^+ / K^+ pumps in the basolateral membrane.
- Sodium ions (Na^+), potassium ions (K^+), and chloride ions (Cl^-) are transported *into* tubular cells by $Na^+/K^+/2Cl^-$ co-transporters in the apical membrane and *out of* tubular cells by ion channels in the basolateral membrane (the apical transport is inhibited by Furosemide).
- Sodium ions (Na^+) are transported *into* tubular cells and hydrogen ions (H^+) are transported *out of* tubular cells by Na^+/ H^+ counter-transporters in the apical membrane.

The reabsorption of Na^+, Cl^-, and K^+ from the ascending limb increases the osmolarity of the interstitial fluid and is responsible for water reabsorption from the descending limb and the collecting ducts. The interstitial osmolarity is about 1400 mOsm at the bend of the nephron loop and is about 300 mOsm near the distal tubule. As filtrate moves through the collecting duct, water is reabsorbed and the urine becomes more concentrated.

Distal convoluted tubule (early segment) (DCT1)

The early distal tubule (DCT1) acts mainly to fine tune the reabsorption of sodium and chloride ions. In the early segment of the distal convoluted tubule about 4% of filtered +Na^+ and Cl^- is reabsorbed, as shown in Figure 20.8.

- The major solutes reabsorbed include sodium and chloride. In addition, some potassium ions (K^+) may be secreted back into the tubular fluid.

Transport mechanisms *(follow the transport using Figure 20. 6)*

Throughout all of DCT1,

- Sodium ions (Na^+) and chloride ions (Cl^-) are transported *into* tubular cells by Na^+ / Cl^- co-transporters in the apical membrane (the apical transport is inhibited by Thiazides [Hydrochlorothiazide]).
- Sodium ions (Na^+) are transported *out of* tubular cells and potassium ions (K^+) are transported *into* tubular cells by Na^+ / K^+ pumps in the basolateral membrane.

Hormonal Control

- The reabsorption of sodium and chloride is stimulated by angiotensin II (independent of aldosterone).

Distal convoluted tubule (late segment) (DCT2), collecting tubules, and ducts

The late distal tubules (DCT2) and collecting tubules and ducts act mainly to fine tune the reabsorption of sodium, chloride, potassium and calcium ions and the reabsorption of water. This region also fine tunes secretion of potassium and plays a role in acid-base balance by fine tuning the reabsorption of bicarbonate ions and the secretion of hydrogen ions. In the late segment of the distal convoluted tubule and the collecting tubule and duct about 8-17% of filtered water and 3% of filtered Na^+ are reabsorbed, as shown in Figure 20.8. The reabsorption of water, sodium and potassium, and the secretion of potassium is shown in more detail in Figure 20.9.

- Water is the major substance reabsorbed
- The major solutes reabsorbed include sodium, chloride, potassium.
- In addition, potassium ions are secreted into the tubular fluid.
- (Although not shown, calcium and bicarbonate ions are also reabsorbed, and hydrogen ions are secreted into tubular fluid)

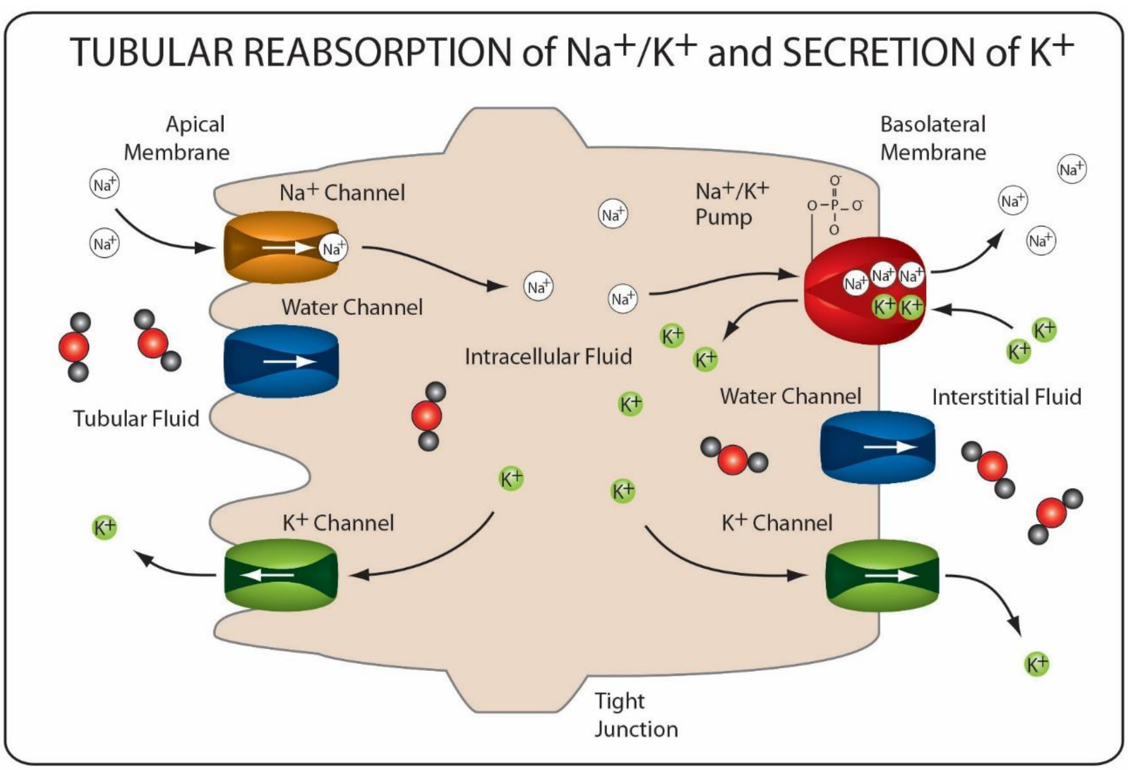


Figure 20.9 © 2016 David G. Ward, Ph.D.

Transport mechanisms

Throughout all of DCT2, collecting tubules, and ducts

- Water is transported *into* and *out of* tubular cells by water channels in the apical and basolateral membrane.
- Sodium ions are transported from tubular fluid *into* tubular cells by epithelial Na^+ channels (ENaC) in the apical membrane (the apical transport is inhibited by Amiloride).
- Sodium ions (Na^+) are transported *out of* tubular cells and potassium ions (K^+) are transported *into* tubular cells by Na^+ / K^+ pumps in the basolateral membrane.
- Sodium ions (Na^+) are transported *into* tubular cells and hydrogen ions (H^+) are transported *out of* tubular cells (and *into* tubular fluid) by Na^+/ H^+ counter-transporters in the apical membrane (of some cells).
- Sodium ions (Na^+) and bicarbonate ions (HCO_3^-) are transported *out of* tubular cells (and *into* interstitial fluid) by Na^+/ HCO_3^- co-transporters in the basolateral membrane (of some cells).
- Potassium ions (K^+) are transported *out of* tubular cells (and *into interstitial fluid*) by K^+ channels in the basolateral membrane.
- Potassium ions (K^+) are transported *out of* tubular cells (and *into tubular fluid*) by K^+ channels in the apical membrane.

Hormonal Control

- The reabsorption of water is directly stimulated by vasopressin.
- The reabsorption of sodium and chloride is stimulated by aldosterone (and to a lesser extent by angiotensin II.)
- The secretion of potassium is stimulated by aldosterone.

Reabsorption of sodium and chloride ions increases the osmolarity of the peritubular interstitial fluid and may increase reabsorption of water. However, the reabsorption of water depends on open water channels. Vasopressin causes the insertion of aquaporin-2 water channels into the luminal membrane of the tubular cells and thus allows reabsorption of water. In the absence of vasopressin very little water is reabsorbed from the late distal tubules, and from the collecting tubules and ducts, and urine flow can increase to 400 mL/hour (10 L/24 hr).

Local, Neural and Hormonal Control of the Kidney

Control of glomerular filtration rate and the fine tuning of reabsorption and secretion are critical for maintaining fluid, electrolyte, and acid-base balance.

Local control of renal blood flow and GFR

As we noted earlier glomerular filtration rate (GFR) is tightly autoregulated when mean arterial pressure is between about 80 mmHg and 180 mmHg. Glomerular filtration rate is proportional to renal blood flow, which in turn is dependent on the pressure driving the blood through the kidney and the resistance of the renal blood vessels. Formally, renal blood flow (BF_{renal}) equals the blood pressure gradient (mean arterial pressure (MAP) - renal venous pressure (VP_{renal})) divided by the renal vascular resistance (R_{renal}).

$$BF_{renal} = \frac{MAP - VP_{renal}}{R_{renal}}$$

In order to maintain renal blood flow constant, renal vascular resistance must be increased if mean arterial pressure increases, and decreased if arterial pressure decreases. Renal blood flow best parallels glomerular filtration rate with changes in the resistance of the afferent arterioles. Changes in resistance are mediated by two mechanisms.

The first is a myogenic mechanism where stretch of a vessel causes vasoconstriction (see chapter 17, Figure 17.7). Accordingly, when the arterial pressure rises and the renal afferent arteriole stretches, the smooth muscle contracts, the resistance of the arteriole increases, and blood flow decreases.

The second mechanism is a flow dependent mechanism known as tuberoglomerular feedback. The macula densa of the distal tubule measures tubular flow and elicits changes in resistance of the afferent arteriole. The macula densa cells are in the wall of the distal tubule at the point where it passes by the juxtaglomerular apparatus of the afferent arteriole (see Figure 20.4). Increases in tubular flow lead to vasoconstriction; decreases in tubular flow lead to vasodilation.

Increases in many paracrines such as adenosine, nitric oxide, prostaglandins, bradykinin, histamine, and dopamine lead locally to renal arteriolar vasodilation.

Neural and hormonal factors

Postganglionic neurons of the sympathetic nervous system secrete norepinephrine and the adrenal medulla secretes epinephrine which acts on renal blood vessels to cause vasoconstriction, on renal tubules to cause increased sodium reabsorption, and on the juxtaglomerular cells to stimulate secretion of renin.

- Stimulation of alpha-1 receptors on the afferent arterioles leads to vasoconstriction, and decreases renal blood flow and glomerular filtration rate.
- Stimulation of adrenergic receptors in the proximal tubule, thick ascending limb of the nephron loop, and distal tubule / collecting duct leads to increased sodium reabsorption.
- Stimulation of beta-1 receptors on the juxtaglomerular cells increases the secretion of renin.

The renin-angiotensin system produces angiotensin II which acts directly on the kidney to increase sodium reabsorption and on the adrenal cortex to stimulate the synthesis and release of aldosterone, as shown in Figure 20.10.

The liver produces angiotensinogen which circulates in the blood. The kidney secretes renin into the blood in response to local decreases in blood pressure in the afferent arteriole, and to stimulation of beta-1 receptors of the juxtaglomerular cells by norepinephrine or epinephrine. Renin cleaves angiotensinogen into angiotensin I. The endothelium of blood vessels produces angiotensin converting enzyme (ACE) which converts angiotensin I to angiotensin II.

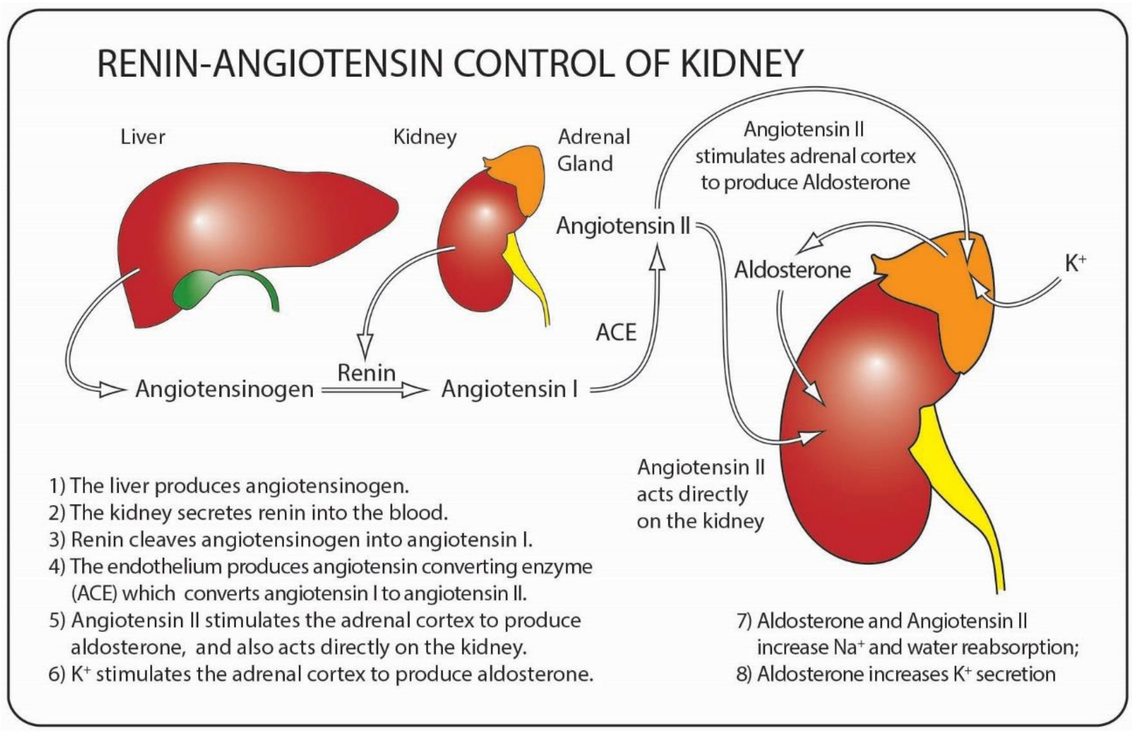
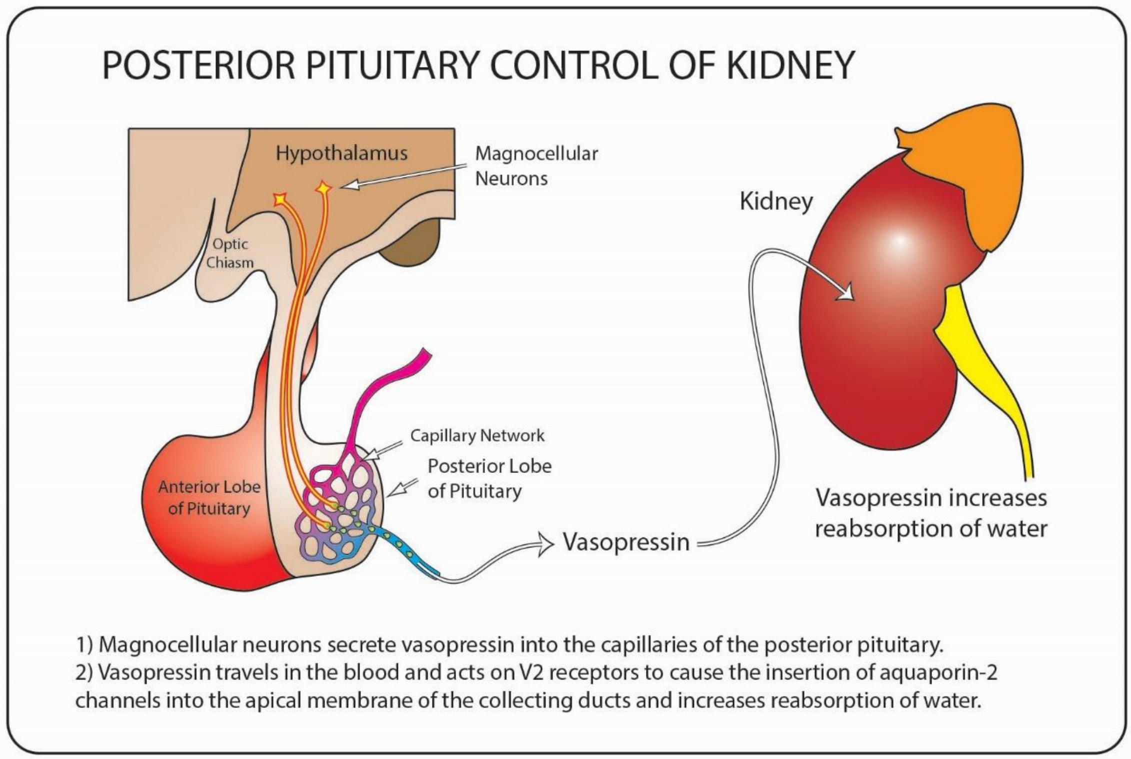


Figure 20.10 © 2020 David G. Ward, Ph.D.

- Angiotensin II acts on AT-1 receptors
  - In the kidney to cause vasoconstriction of renal afferent arterioles.
  - In the proximal and distal tubules of the kidney to increase sodium (Na^+) and chloride (Cl^-) reabsorption.
  - In the zona glomerulosa of the adrenal cortex to stimulate the synthesis and release of aldosterone.
  - In the posterior pituitary to stimulate the secretion of vasopressin.
- Aldosterone, in turn, acts on the late distal tubule / collecting duct to increase reabsorption of sodium (Na^+) and chloride (Cl^-) and secretion of potassium (K^+).

The posterior pituitary produces vasopressin, which acts on the kidney to increase water reabsorption and to cause vasoconstriction, as shown in Figure 20.11.



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- Vasopressin acts on V1a receptors to cause vasoconstriction of renal arterioles.
- Vasopressin acts on V2 receptors in the collecting tubules and ducts to cause the insertion of aquaporin-2 channels into the apical membrane and thus increases reabsorption of water.

Quiz Yourself

1-5. Matching

A)	125 mL/min	normal reabsorption of tubular fluids by the kidney	1) _____
B)	123.5 to 124 mL/min	urine formation by the kidney without vasopressin	2) _____
C)	5 to 10 mL/min	normal filtrate formation by the kidney	3) _____
D)	1 to 1.5 mL/min	normal urine formation by the kidney	4) _____
E)	none of the above	normal cardiac output	5) _____

6-10. Matching (major hormonal control)

A)	Controlled by angiotensin II	PCT	6) _____
B)	Controlled by vasopressin	DCT1	7) _____
C)	Controlled by aldosterone	DCT2 and Collecting duct	8) _____
D)	None of the above	Thick ascending nephron loop	9) _____
E)	B and C	Thin descending nephron loop	10) _____

11-15. True or False (True = A; False = B) (reabsorption into the blood from tubules)

A)	The PCT acts as a mass absorber	11) _____
B)	The nephron loop (of Henle) creates an osmotic gradient	12) _____
C)	The DCT and collecting system are regulated by hormones	13) _____
D)	Water reabsorption occurs by osmosis (diffusion) in the renal tubules	14) _____
E)	Na^+ is actively transported by Na^+ / K^+ pumps in the basolateral membrane	15) _____

16-20. Matching

A)	atrial natriuretic hormone	stimulates aldosterone	16) _____
B)	converting enzyme	causes renal excretion of sodium	17) _____
C)	angiotensin II	causes renal conservation of water	18) _____
D)	vasopressin	causes renal conservation of sodium	19) _____
E)	aldosterone	converts angiotensin I to angiotensin II	20) _____

Fill in

21. About 67% of water and sodium reabsorption occurs from the _____________ ___________.

22. H^+ is secreted usually via counter-transport with _______________.

23. __________________ (hormone) is inhibited by excess water consumption.

24. Sodium reabsorption is dependent on __________________ __________________.

25. Sodium reabsorption from the renal tubules is stimulated largely by _______________ (hormone).

Study Questions

1. Explain the process of glomerular filtration in the kidney. Include a description of the mechanisms involved.
2. Compare and contrast reabsorption and secretion in the proximal tubules, nephron loop, distal tubules, and collecting ducts. Include a description of the mechanisms involved.
3. Explain the significance of the reabsorption and secretion processes.