PHYSIOLOGY

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LECTURE 10, PART (2): RENAL PHYSIOLOGY

Objectives

1. Discuss glomerular filtration rate and regulation of GFR.
2. Describe tubular reabsorption.
3. Explore homeostatic regulation of tubular reabsorption and tubular secretion.
4. Discuss production of dilute and concentrated urine, evaluation of kidney function, and renal plasma clearance.

(Pages 993- 1014 of the reference)

NET FILTRATION PRESSURE

Figure 26.9 The pressures that drive glomerular filtration

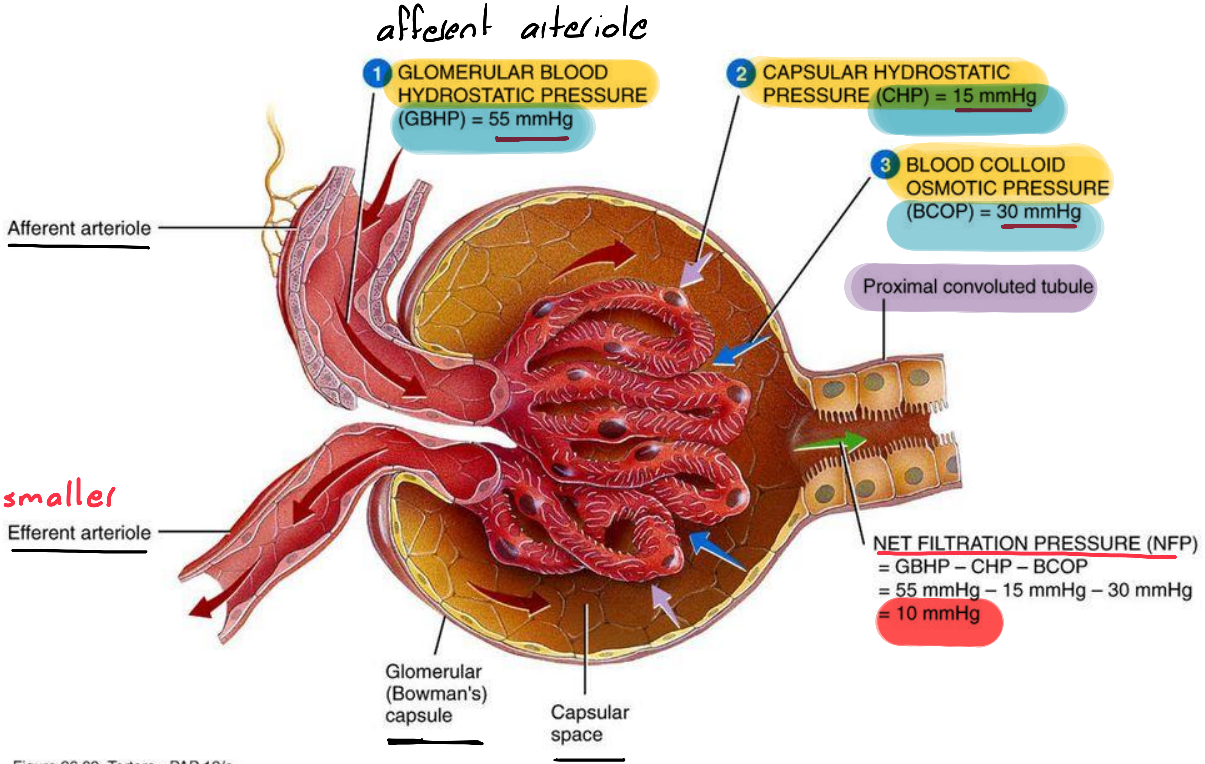
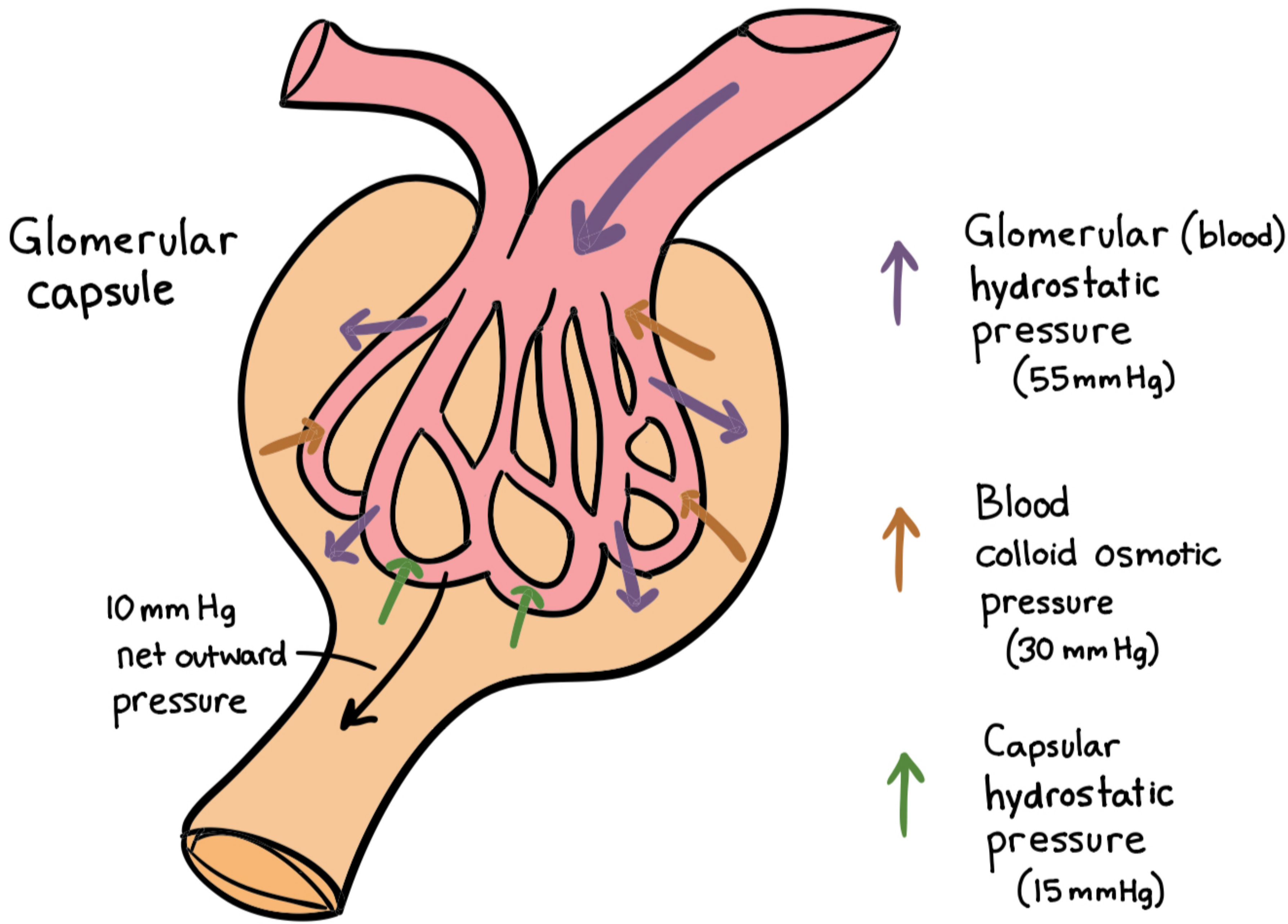


Figure 26.09 Tortora - PAP 12/e

Glomerular filtration depends on three main pressures. One pressure promotes filtration, and two pressures oppose filtration.

Glomerular blood hydrostatic pressure promotes filtration, whereas capsular hydrostatic pressure and blood colloid osmotic pressure oppose filtration.


Glomerular capsule
10 mm Hg net outward pressure
Glomerular (blood) hydrostatic pressure (55 mmHg)
Blood colloid osmotic pressure (30 mm Hg)
Capsular hydrostatic pressure (15 mmHg)

NET FILTRATION PRESSURE

- **Glomerular blood hydrostatic pressure (GBHP)** is the blood pressure in glomerular capillaries. Generally, GBHP is about 55 mmHg (millimetre of mercury). It promotes filtration by forcing water and solutes in blood plasma through the filtration membrane.

يبذل

- **Capsular hydrostatic pressure (CHP)** is the hydrostatic pressure exerted against the filtration membrane by fluid already in the capsular space and renal tubule. CHP opposes filtration and represents a "back pressure" of about 15 mmHg.

- **Blood colloid osmotic pressure (BCOP)**, which is due to the presence of proteins such as albumin, globulins, and fibrinogen in blood plasma, also opposes filtration. The average BCOP in glomerular capillaries is 30 mmHg.

NET FILTRATION PRESSURE

Net filtration pressure (NFP), the total pressure that promotes filtration, is determined as follows:

Net filtration pressure (NFP) = GBHP − CHP − BCOP

By substituting the values just given, normal NFP may be calculated:

$$\begin{aligned} \text{NFP} &= 55 \text{ mmHg} - 15 \text{ mmHg} - 30 \text{ mmHg} \\ &= 10 \text{ mmHg} \end{aligned}$$

Thus, a pressure of only 10 mmHg causes a normal amount of blood plasma (minus plasma proteins) to filter from the glomerulus into the capsular space.

GLOMERULAR FILTRATION RATE

- The amount of filtrate formed in all renal corpuscles of both kidneys each minute is the **glomerular filtration rate (GFR).**

- In adults, the **GFR averages** 125 mL/min in males and 105 mL/min in females.

- **Homeostasis of body fluids** requires that the kidneys maintain a relatively constant GFR.

GLOMERULAR FILTRATION RATE

- **If the GFR is too high**, needed substances may pass so quickly through the renal tubules that some are not reabsorbed and are lost in the urine. GFR ↑ reabsorption ↓ secretion ↑
- **If the GFR is too low**, nearly all the filtrate may be reabsorbed and certain waste products may not be adequately excreted.

GFR ↓ reabsorption ↑ secretion ↓

- **GFR is directly related to the pressures that determine net filtration pressure**; any change in net filtration pressure will affect GFR.

GLOMERULAR FILTRATION RATE

- **The mechanisms that regulate glomerular filtration rate operate in two main ways**:

BF ↑ GFR ↑

- (1) **by adjusting blood flow into and out of the glomerulus**. GFR increases when blood flow into the glomerular capillaries increases.
- (2) **by altering the glomerular capillary surface area available for filtration**. Coordinated control of the diameter of both afferent and efferent arterioles regulates glomerular blood flow. Constriction of the afferent arteriole decreases blood flow into the glomerulus; dilation of the afferent arteriole increases it.

afferent vasoconstriction BF ↓ afferent dilation BF ↑

- **Three mechanisms control GFR: renal autoregulation, neural regulation, and hormonal regulation.**

1- myogenic
2- tubuloglomerular feed back

RENAL AUTOREGULATION OF GFR

- The kidneys themselves help **maintain a constant renal blood flow and GFR despite normal, everyday changes in blood pressure**, like those that occur during exercise. This capability is called **renal autoregulation**.

- It consists of two mechanisms—the **myogenic mechanism** and **tubuloglomerular feedback**. **Working together, they can maintain nearly constant GFR over a wide range of systemic blood pressures.**

RENAL AUTOREGULATION OF GFR

BP ↑ GFR ↑ RBF ↑

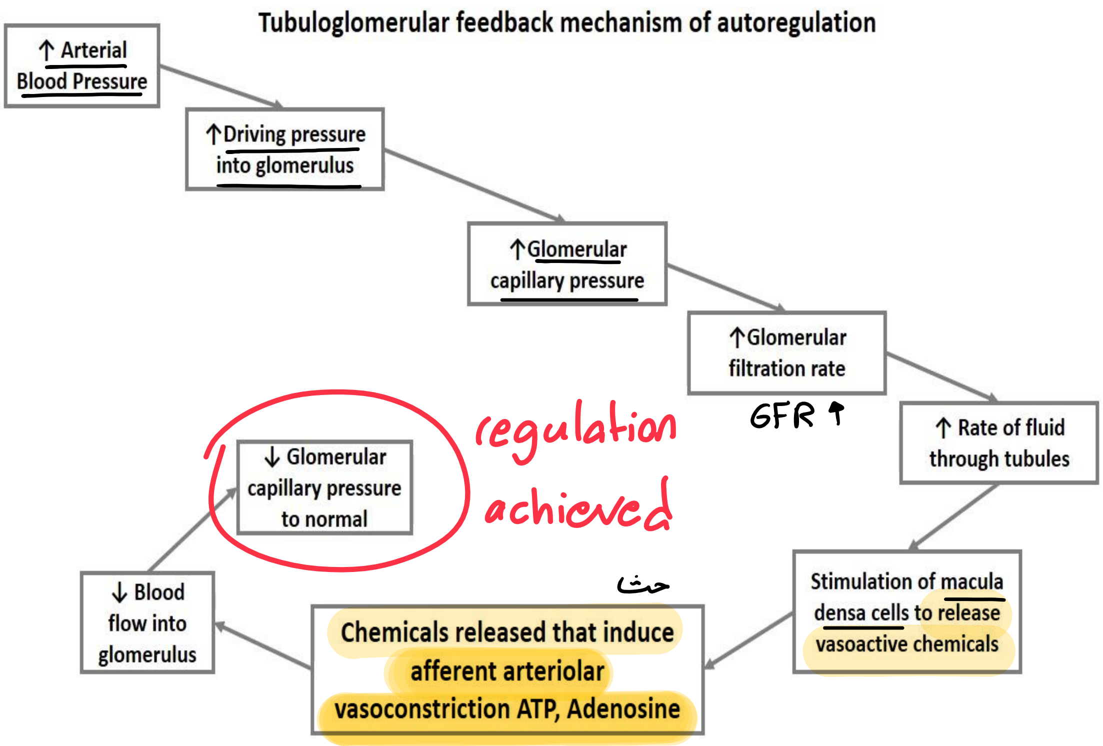
- The **myogenic mechanism** occurs when stretching triggers contraction of smooth muscle cells in the walls of afferent arterioles. As blood pressure rises, GFR also rises because renal blood flow increases. However, the elevated blood pressure stretches the walls of the afferent arterioles, which narrows the arteriole's lumen. As a result, renal blood flow decreases, thus reducing GFR to its previous level.

vaso constriction

RBF ↓ GFR back to normal

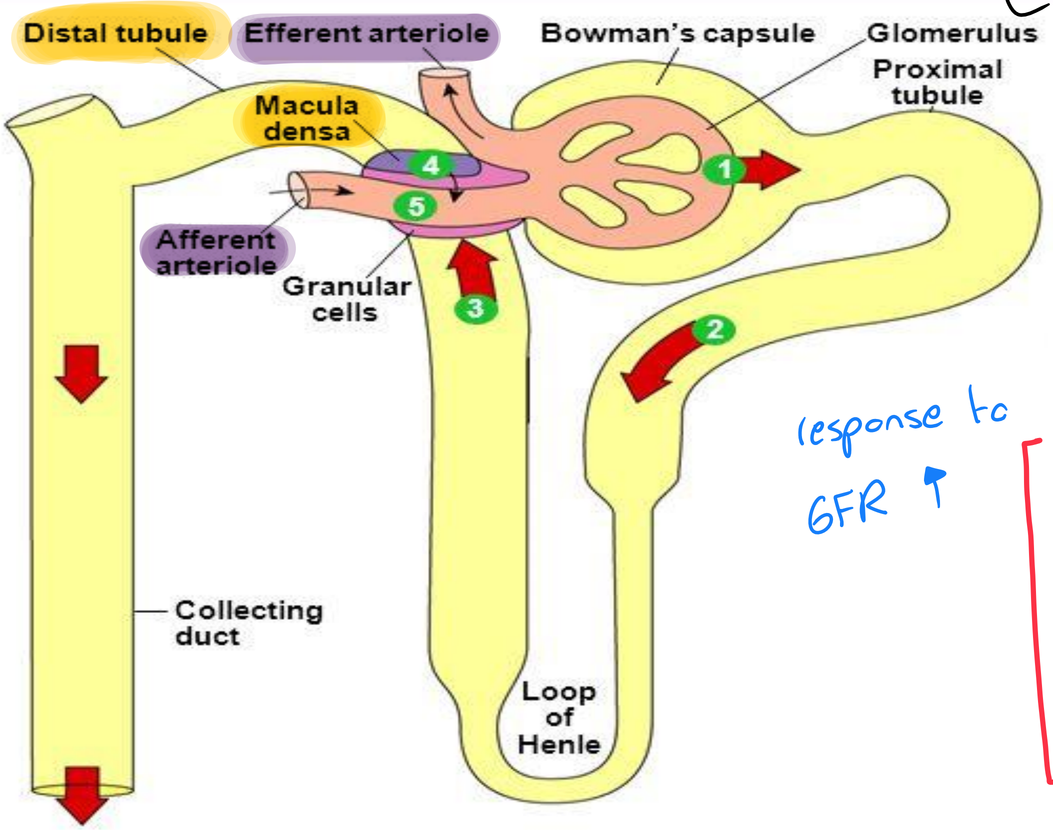
RENAL AUTOREGULATION OF GFR

- The **second contributor to renal autoregulation**, **tubuloglomerular feedback**, is so named because part of the renal tubules—the macula densa (is an area of closely packed specialized cells lining the wall of the distal tubule, at the point where the thick ascending limb of the Loop of Henle meets the distal convoluted tubule.)—provides feedback to the glomerulus.



Tubuloglomerular Feedback

BP↑ → GHP↑ → GFR↑
↳ afferent arteriole stretch ↑ Na↑ Ca^{+2}↑ → contraction ↑ ↓ vasoconstriction ↓ GBF↓ ↓ oliguria ↓GFR



response to GFR ↑

1. GFR increases. GFR ↑
2. Flow through tubule increases.
3. Flow past macula densa increases.
4. Paracrine diffuses from macula densa to afferent arteriole.
5. Afferent arteriole constricts. vasoconstriction

Resistance in afferent arteriole increases. → arteriole diameter↓ resistence ↑

Hydrostatic pressure in glomerulus decreases. GHR ↓

GFR decreases. GFR ↓

NEURAL REGULATION OF GFR

- Like most blood vessels of the body, those of the kidneys are supplied by sympathetic ANS fibers that release norepinephrine.

- **At rest**, sympathetic stimulation is moderately low, the afferent and efferent arterioles are dilated, and renal autoregulation of GFR prevails.

dominate

- **With moderate sympathetic stimulation**, both afferent and efferent arterioles constrict to the same degree. Blood flow into and out of the glomerulus is restricted to the same extent, which decreases GFR only slightly.

NEURAL REGULATION OF GFR

- **With greater sympathetic stimulation**, however, as occurs during exercise or hemorrhage, vasoconstriction of the afferent arterioles predominates. As a result, blood flow into glomerular capillaries is greatly decreased, and GFR drops.

RBF ↓

- **This lowering of renal blood flow has two consequences:** (1) It reduces urine output, which helps conserve blood volume. (2) It permits greater blood flow to other body tissues.

BF to systemic circulation ↑
urine output ↓

HORMONAL REGULATION OF GFR

Two hormones contribute to regulation of GFR:

1. Angiotensin II (very potent vasoconstrictor) reduces GFR.

2. Atrial natriuretic peptide (ANP) increases GFR because ANP increases the capillary surface area available for filtration.

جدول مهم جداً

TABLE 26.2

Regulation of Glomerular Filtration Rate (GFR)

TYPE OF REGULATION	MAJOR STIMULUS	MECHANISM AND SITE OF ACTION	EFFECT ON GFR
Renal autoregulation	BP ↑ → stretch ↑	stretch ↑ → Ca^{+2} ↑ → contraction	GFR ↓
- **Myogenic mechanism**	Increased stretching of smooth muscle fibers in afferent arteriole walls due to increased blood pressure.	Stretched smooth muscle fibers contract, thereby narrowing lumen of afferent arterioles. afferent vasoconstriction	Decrease.
- **Tubuloglomerular feedback**	Rapid delivery of Na^+ and Cl^- to the macula densa due to high systemic blood pressure.	Decreased release of nitric oxide (NO) by juxtaglomerular apparatus causes constriction of afferent arterioles. NO↓ afferent vasoconstriction	Decrease. GFR ↓
Neural regulation	Increase in activity level of renal sympathetic nerves releases norepinephrine. SNS ↑ renin release	Constriction of afferent arterioles through activation of α_1 receptors and increased release of renin. α_1 receptor activation	Decrease. GFR↓
Hormone regulation			
- **Angiotensin II**	Decreased blood volume or blood pressure stimulates production of angiotensin II.	Constriction of afferent and efferent arterioles.	Decrease.
- **Atrial natriuretic peptide (ANP)**	Stretching of atria of heart stimulates secretion of ANP.	Relaxation of mesangial cells in glomerulus increases capillary surface area available for filtration. ANP ↑ mesangial cells relaxed capillary surface area for filtration ↑	Increase. GFR↑

TUBULAR REABSORPTION AND TUBULAR SECRETION

- **Reabsorption:** Na^+
  - The return of most of the filtered water and many of the filtered solutes (as sodium, potassium, chloride, bicarbonate and phosphate ions) to the bloodstream.

    K^+ Cl^- HCO_3^- PO_4^{-3}

- **Tubular secretion:**
  - the transfer of materials (as hydrogen (H^+), potassium ions (K^+) and ammonium ions, creatinine, and certain drugs such as penicillin) from the blood and tubule cells into glomerular filtrate. Tubular secretion has two important outcomes: 100%
  - (1) The secretion of hydrogen ions helps control blood pH. H^+ secretion pH regulation
  - (2) The secretion of other substances helps eliminate them from the body in urine

Substances Filtered, Reabsorbed, and Excreted in Urine per Day

TABLE 21.1

Substances Filtered, Reabsorbed, and Excreted in Urine per Day

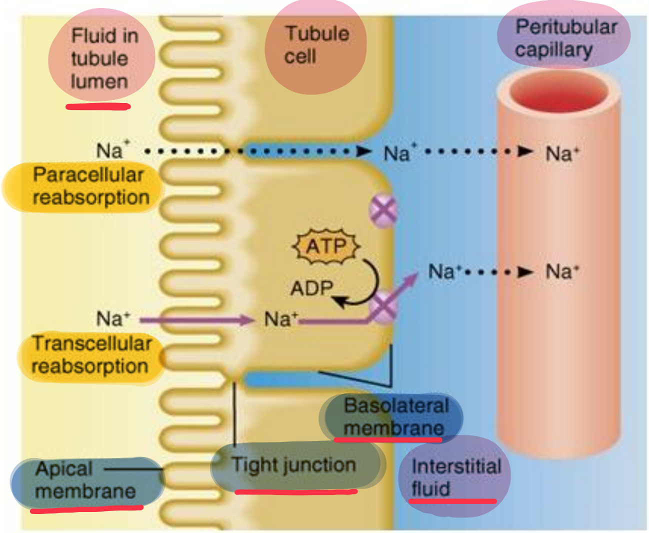
SUBSTANCE	FILTERED* (ENTERS RENAL TUBULE)	REABSORBED (RETURNED TO BLOOD)	SECRETED IN URINE
Water	180 liters	178–179 liters	1–2 liters
Chloride ions (Cl^-)	640 g	633.7 g	6.3 g
Sodium ions (Na^+)	579 g	575 g	4 g
Bicarbonate ions (HCO_3^-)	275 g	274.97 g	0.03 g
Glucose (100% reabsorbed)	162 g	162 g	0
Urea	54 g	24 g	30 g†
Potassium ions (K^+)	29.6 g	29.6 g	2.0 g‡
Uric acid	8.5 g	7.7 g	0.8 g
Creatinine (100% secreted)	1.6 g	0	1.6 g

*Assuming glomerular filtration is 180 liters per day.
†In addition to being filtered and reabsorbed, urea is secreted.
‡After virtually all filtered K^+ is reabsorbed in the convoluted tubules and loop of Henle, a variable amount of K^+ is secreted in the collecting duct.

REABSORPTION ROUTES

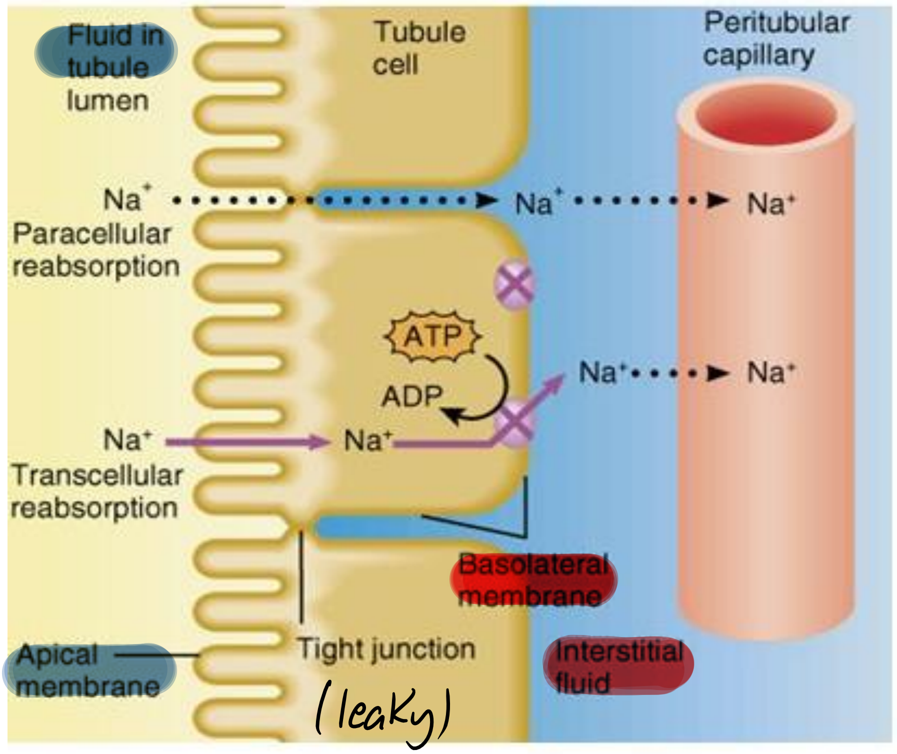
Reabsorption Routes

- Paracellular reabsorption
  - 50% of reabsorbed material moves between cells by diffusion in some parts of tubule
- Transcellular reabsorption
  - material moves through both the apical and basal membranes of the tubule cell by active transport



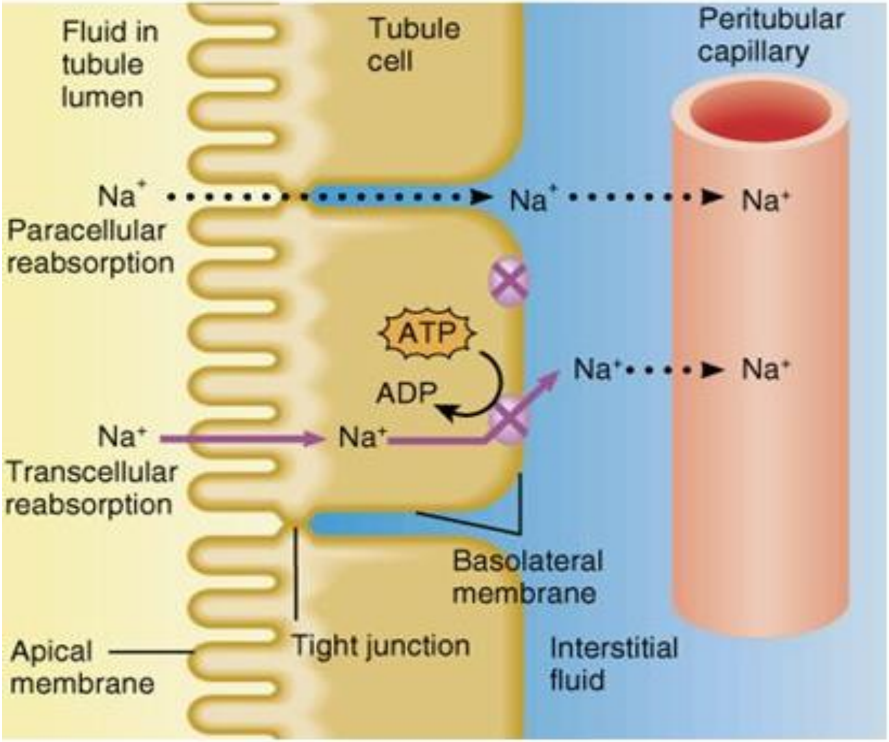
✓ **In the renal system, peritubular capillaries** are tiny blood vessels, supplied by the efferent arteriole, that travel alongside nephrons allowing reabsorption and secretion between blood and the inner lumen of the nephron.

REABSORPTION ROUTES



- ✓ The apical membrane contacts the tubular fluid, and the basolateral membrane contacts interstitial fluid at the base and sides of the cell.
- ✓ Even though the epithelial cells are connected by tight junctions, the tight junctions between cells in the proximal convoluted tubules are "leaky" and permit some reabsorbed substances to pass between cells into peritubular capillaries.

TRANSPORT MECHANISMS

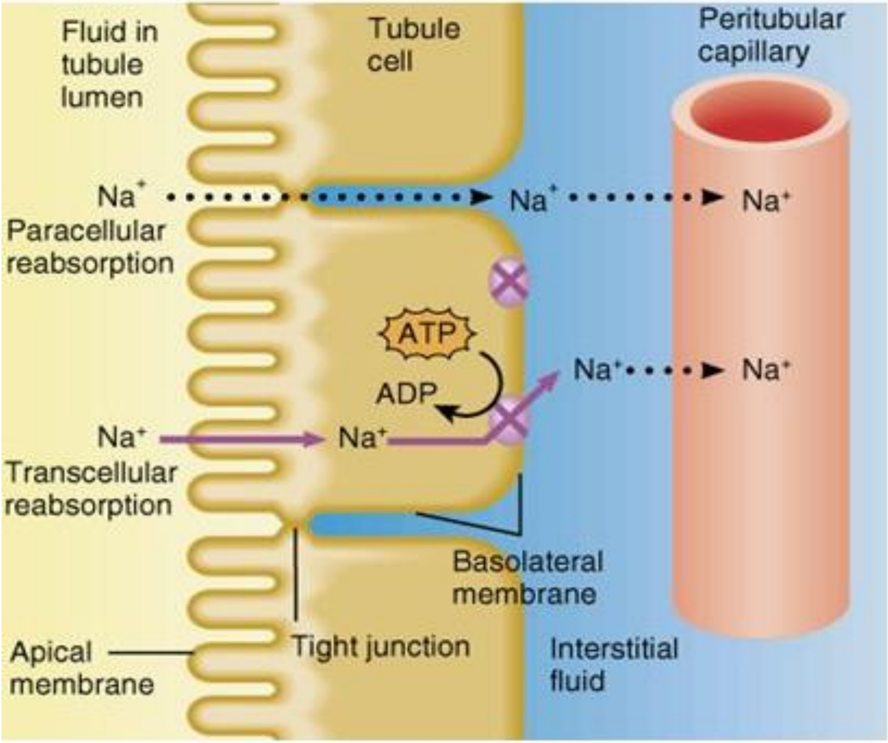


Active transport

- ✓ In transcellular reabsorption, a substance passes from the fluid in the tubular lumen through the apical membrane of a tubule cell, across the cytosol, and out into interstitial fluid through the basolateral membrane.

- ✓ When renal cells transport solutes out of or into tubular fluid, they move specific substances in one direction only. Not surprisingly, different types of transport proteins are present in the apical and basolateral membranes. The tight junctions form a barrier that prevents mixing of proteins in the apical and basolateral membrane compartments.

TRANSPORT MECHANISMS



- ✓ **Each type of transporter has an upper limit on how fast it can work**, just as an escalator has a limit on how many people it can carry from one level to another in a given period. **This limit, called the transport maximum (Tm), is measured in mg/min.**

- ✓ Cells lining the renal tubules, like other cells throughout the body, have a low concentration of sodium ions in their cytosol due to the activity of sodium–potassium pumps. These pumps are located in the basolateral membranes and eject sodium ions from the renal tubule cells. The absence of sodium–potassium pumps in the apical membrane ensures that reabsorption of sodium ions is a one-way process.

TUBULAR REABSORPTION

- ✓ Solute reabsorption drives water reabsorption because all water reabsorption occurs via osmosis. About 90% of the reabsorption of water filtered by the kidneys occurs along with the reabsorption of solutes such as sodium and chloride ions, and glucose.
  Na^+ Cl^-
- ✓ Water reabsorbed with solutes in tubular fluid is termed obligatory water reabsorption because the water is "obliged" to follow the solutes when they are reabsorbed. This type of water reabsorption occurs in the proximal convoluted tubule and the descending limb of the nephron loop.
- ✓ Reabsorption of the final 10% of the water, a total of 10–20 liters per day, is termed facultative water reabsorption. Facultative water reabsorption is regulated by antidiuretic hormone and occurs mainly in the collecting ducts.

AND : late distal convoluted tubule

REABSORPTION AND SECRETION IN THE PROXIMAL CONVOLUTED TUBULE

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- ✓ **The largest amount of solute and water reabsorption from filtered fluid occurs in the proximal convoluted tubules.**

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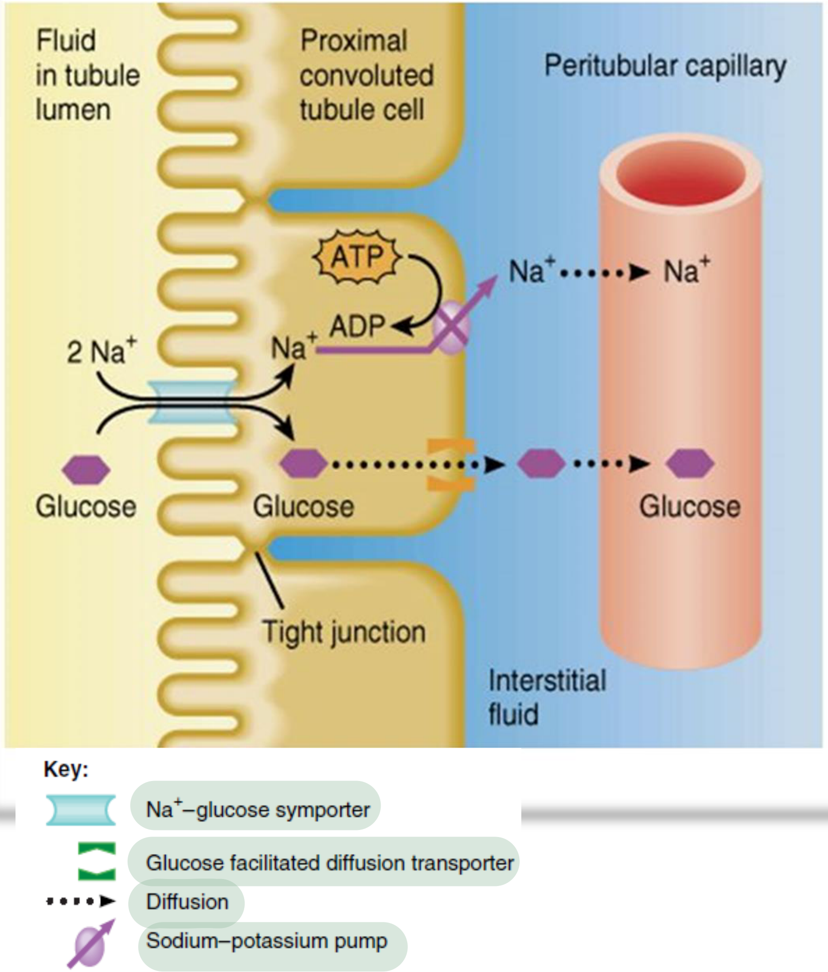
Reabsorption of Glucose in PCT

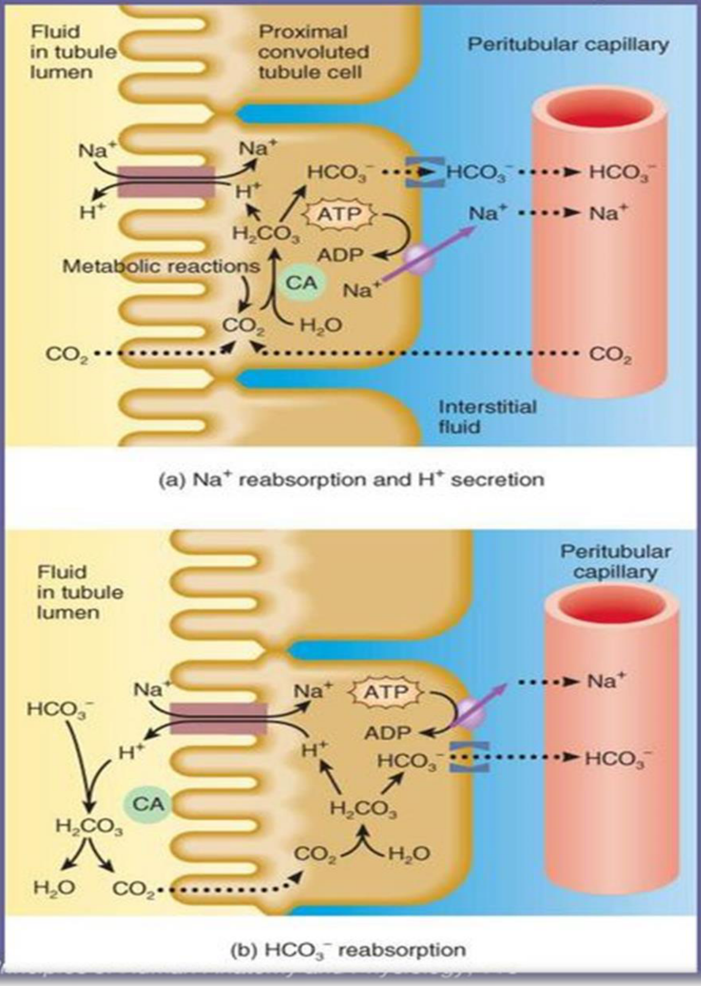
proximal convoluted tubule



- Intracellular sodium levels are kept low due to Na^+/K^+ ATPase pump on basolateral membrane
- Low intracellular Na+ creates concentration gradient
  - high in filtrate – low in cell
- Na^+ **symporters** on apical membrane use energy from gradient to bring in glucose
  - **Secondary active transport**
- 2 Na^+ and 1 glucose attach to symporter and enter cell together
- Glucose then diffuses out of cell and into peritubular capillaries

HCO_3^-

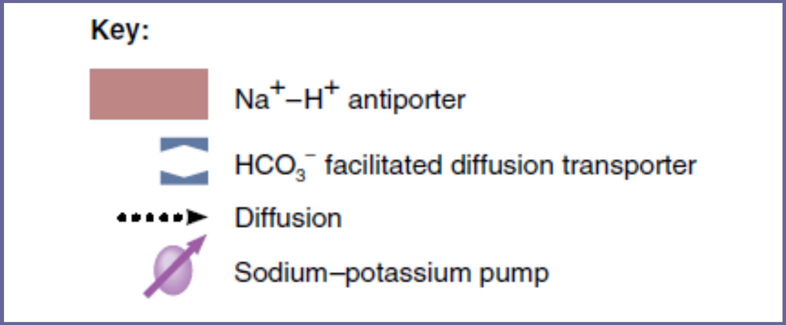
Reabsorption of Bicarbonate, Na+ & H+ Ions



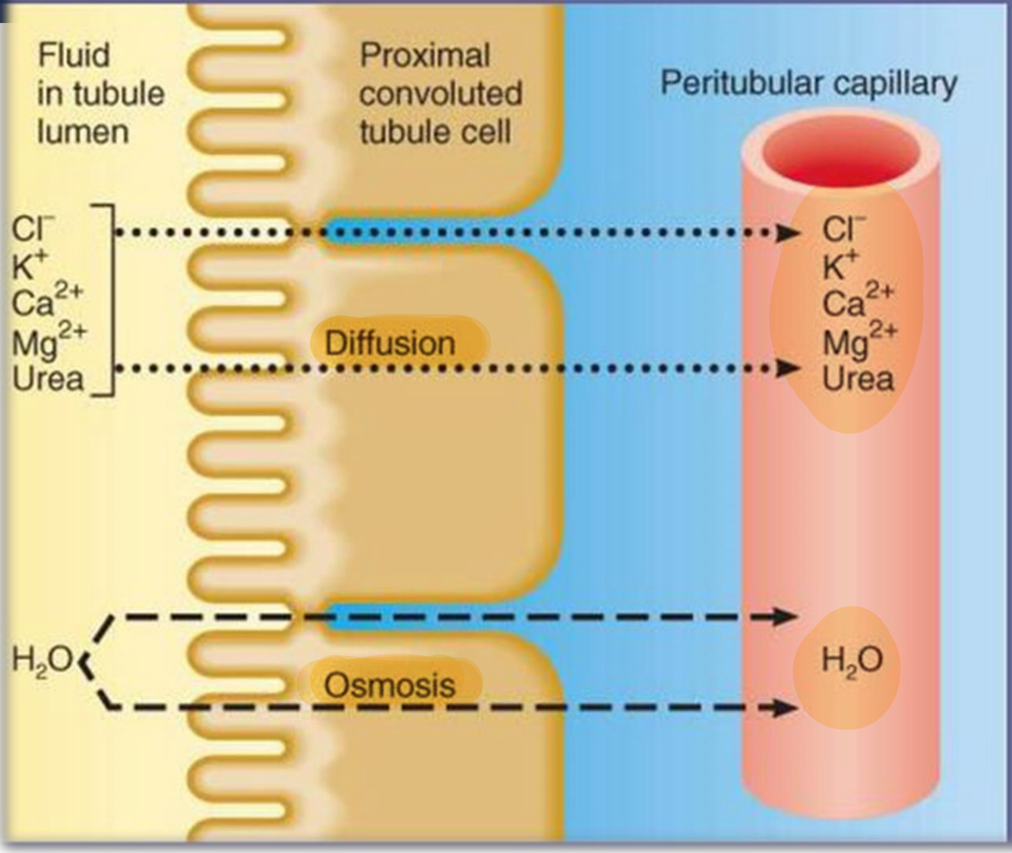
(a) Na^+ reabsorption and H^+ secretion

(b) HCO_3^- reabsorption

- Na+ antiporters reabsorb Na+ and secrete H+
  - PCT cells produce the H+ & release bicarbonate ion to the peritubular capillaries
  - important buffering system
- For every H+ secreted into the tubular fluid, one filtered bicarbonate eventually returns to the blood



Passive Reabsorption in the 2nd Half of PCT



- Electrochemical gradients produced by symporters & antiporters causes passive reabsorption of other solutes
- Cl-, K+, Ca+2, Mg+2 and urea passively diffuse into the peritubular capillaries
- Promotes osmosis in PCT (especially permeable due to aquaporin-1 channels

REABSORPTION IN THE NEPHRON LOOP

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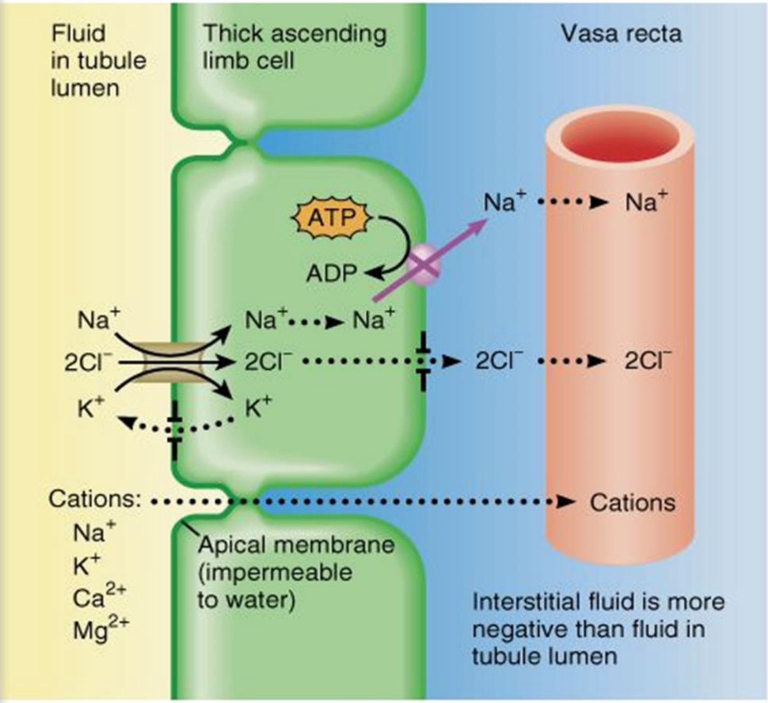
65%

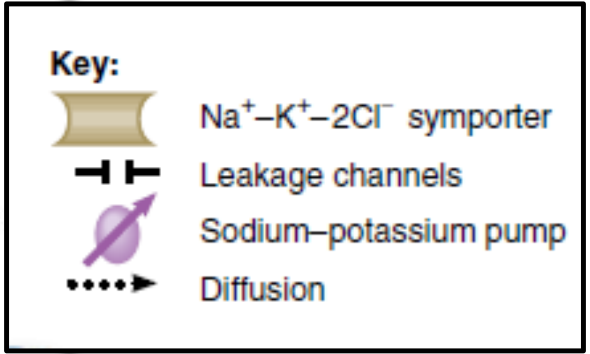
Because all of the proximal convoluted tubules reabsorb about 65% of the filtered water (about 80 mL/min), fluid enters the next part of the nephron, the nephron loop, at a rate of 40–45 mL/min.

decending loop of henle

Symporters in the Loop of Henle



- Thick limb of loop of Henle has Na+ K- Cl- symporters that reabsorb these ions
- K+ leaks through K+ channels back into the tubular fluid leaving the interstitial fluid and blood with a negative charge
- Cations passively move to the vasa recta



REABSORPTION IN THE EARLY DISTAL CONVOLUTED TUBULE

- **Fluid enters the distal convoluted tubules at a rate of about 25 mL/ min** because 80% of the filtered water has now been reabsorbed.

- **The early or initial part of the distal convoluted tubule (DCT)** reabsorbs about 10–15% of the filtered water, 5% of the filtered Na ions, and 5% of the filtered Cl ions.

- **Reabsorption of Na and Cl ions** occurs by means of Na–Cl ions symporters in the apical membranes.

REABSORPTION IN THE EARLY DISTAL CONVOLUTED TUBULE

- **Sodium–potassium pumps and Cl ions leakage channels in the basolateral membranes** then permit reabsorption of Na ions and Cl ions into the peritubular capillaries.
- **The early DCT also is a major site where parathyroid hormone (PTH) stimulates reabsorption of calcium ions.** The amount of calcium ions reabsorption in the early DCT varies depending on the body's needs.

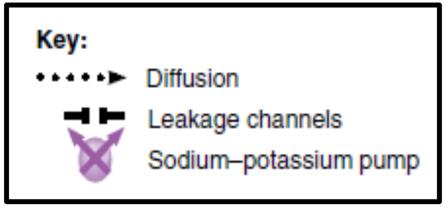
REABSORPTION AND SECRETION IN THE LATE DISTAL CONVOLUTED TUBULE AND COLLECTING DUCT

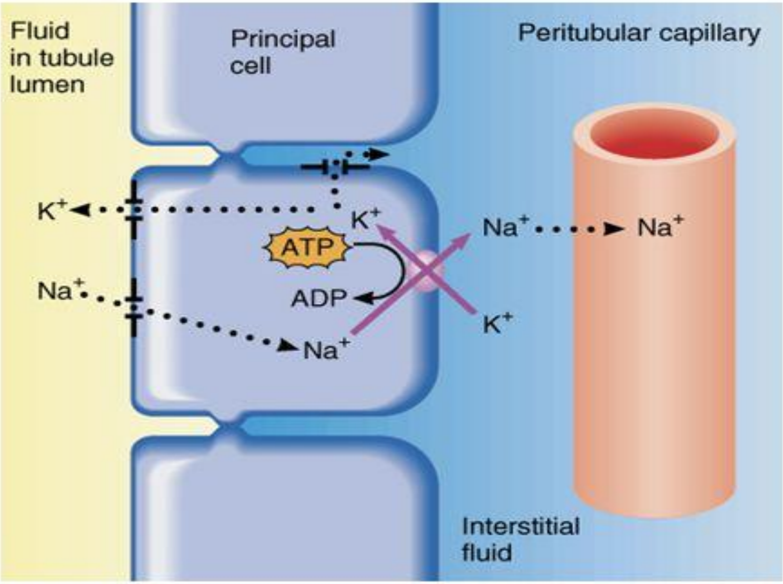
- ✓ **Two different types of cells—principal cells and intercalated cells**—are present at the late or terminal part of the distal convoluted tubule and throughout the collecting duct.

- ✓ **In contrast to earlier segments of the nephron**, sodium ions passes through the apical membrane of principal cells via sodium leakage channels rather than by means of symporters or antiporters.

- ✓ **In the apical membrane of principal cells,** sodium leakage channels allow entry of sodium ions while potassium ions leakage channels allow exit of potassium ions into the tubular fluid.

Actions of the Principal Cells





- Na+ enters principal cells through leakage channels
- Na+ pumps keep the concentration of Na+ in the cytosol low
- Cells secrete variable amounts of K+, to adjust for dietary changes in K+ intake
  - down concentration gradient due to Na+/K+ pump
- Aldosterone increases this Na+ reabsorption (and passive water reabsorption) & K+ secretion by principal cells by stimulating the synthesis of new pumps and channels.

HOMEOSTATIC REGULATION OF TUBULAR REABSORPTION AND TUBULAR SECRETION

- **Five hormones affect the extent of sodium, calcium and chloride ions, and water reabsorption as well as potassium ions secretion by the renal tubules. These hormones include: angiotensin II, aldosterone, antidiuretic hormone, atrial natriuretic peptide, and parathyroid hormone.**

TABLE 26.4

Hormonal Regulation of Tubular Reabsorption and Tubular Secretion

HORMONE	MAJOR STIMULI THAT TRIGGER RELEASE	MECHANISM AND SITE OF ACTION	EFFECTS
Angiotensin II	Low blood volume or low blood pressure stimulates renin-induced production of angiotensin II.	Stimulates activity of Na^+–H^+ antiporters in proximal tubule cells.	Increases reabsorption of Na^+, other solutes, and water, which increases blood volume and blood pressure.
Aldosterone	Increased angiotensin II level and increased level of plasma K^+ promote release of aldosterone by adrenal cortex. $K^+\uparrow$	Enhances activity of sodium–potassium pumps in basolateral membrane and Na^+ channels in apical membrane of principal cells in collecting duct.	Increases secretion of K^+ and reabsorption of Na^+, Cl^-; increases reabsorption of water, which increases blood volume and blood pressure.
Antidiuretic hormone (ADH)	Increased osmolarity of extracellular fluid or decreased blood volume promotes release of ADH from posterior pituitary gland.	Stimulates insertion of water channel proteins (aquaporin-2) into apical membranes of principal cells.	Increases facultative reabsorption of water, which decreases osmolarity of body fluids. osmolarity↓
Atrial natriuretic peptide (ANP)	Stretching of atria of heart stimulates ANP secretion.	Suppresses reabsorption of Na^+ and water in proximal tubule and collecting duct; inhibits secretion of aldosterone and ADH.	Increases excretion of Na^+ in urine (natriuresis); increases urine output (diuresis) and thus decreases blood volume and blood pressure. BP↓
Parathyroid hormone (PTH)	Decreased level of plasma Ca^{2+} promotes release of PTH from parathyroid glands.	Stimulates opening of Ca^{2+} channels in apical membranes of early distal tubule cells.	Increases reabsorption of Ca^{2+}.

- Regulation of GFR -

Autoregulation

- myogenic mechanism

من وظائفها لما BF ↑ stretch ↑

بدنا نرجع balance نعمل

afferent vasoconstriction

GFR ↓

- tubulaiglumerulal feedback

macula densa

موجودة ↩ distal convoluted tubule

→ sensitive to Na^+ / Cl^-

afferent vaso constriction

GFR ↓

neural regulation

(sympathetic effect)

- low dose (stimulation)

afferent dilation

efferent dilation

(No effect) يسيطر

Autoregulation dominate

- moderate dose (stimulation)

equal vasoconstriction

For afferent/efferent arteriole*

(same level)

GFR ↓ بشكل قليل

hormonal regulation

- Angiotensin II (4 functions)

efferent vasoconstriction

GFR ↓

↓ بشكل أقوى

- Atriel natriutic peptide (ANP)

afferent vasodilation

GFR ↑

- high dose (stimulation)

severe / extreme

afferent vasoconstriction

reduce GFR ↓ بكمية كبيرة

كمان efferent vasoconstriction

بس ال afferent أكبر بكثير

GFR ↓ → GF ↓

↓

urine output ↓

BF ↑ → systemic circulation للأطراف

ة الاكثر

GR ↓ كمية قليلة

EVALUATION OF KIDNEY FUNCTION:

1- URINALYSIS

TABLE 26.5

Characteristics of Normal Urine

CHARACTERISTIC	DESCRIPTION
Volume	One to two liters in 24 hours; varies considerably.
Color	Yellow or amber; varies with urine concentration and diet. Color due to urochrome (pigment produced from breakdown of bile) and urobilin (from breakdown of hemoglobin). Concentrated urine is darker in color. Color affected by diet (reddish from beets), medications, and certain diseases. Kidney stones may produce blood in urine.
Turbidity	Transparent when freshly voided; becomes turbid (cloudy) on standing.
Odor	Mildly aromatic; becomes ammonia-like on standing. Some people inherit ability to form methylmercaptan from digested asparagus, which gives characteristic odor. Urine of diabetics has fruity odor due to presence of ketone bodies.
pH	Ranges between 4.6 and 8.0; average 6.0; varies considerably with diet. High-protein diets increase acidity; vegetarian diets increase alkalinity.
Specific gravity (density)	Specific gravity (density) is ratio of weight of volume of substance to weight of equal volume of distilled water. In urine, 1.001–1.035. The higher the concentration of solutes, the higher the specific gravity.

داخل

معكر

معتدل

عصارة صفراوية bile / urochrome

urobilin / hemoglobin

high protein acidity ↑

vegetarian alkalinity ↑

- patho ال في ما نحتاج -

TABLE 26.6

مكونات

Summary of Abnormal Constituents in Urine

ABNORMAL CONSTITUENT	COMMENTS
Albumin	Normal constituent of plasma; usually appears in only very small amounts in urine because it is too large to pass through capillary fenestrations. Presence of excessive albumin in urine—**albuminuria** (al′-bū-mi-NOO-rē-a)—indicates increase in permeability of filtration membranes due to injury or disease, increased blood pressure, or irritation of kidney cells by substances such as bacterial toxins, ether, or heavy metals.
Glucose → stress	Presence of glucose in urine—**glucosuria** (gloo-kō-SOO-rē-a)—usually indicates diabetes mellitus. Occasionally caused by stress, which can cause excessive epinephrine secretion. Epinephrine stimulates breakdown of glycogen and liberation of glucose from liver.
Red blood cells (erythrocytes)	Presence of red blood cells in urine—**hematuria** (hēm-a-TOO-rē-a)—generally indicates pathological condition. One cause is acute inflammation of urinary organs due to disease or irritation from kidney stones. Other causes: tumors, trauma, kidney disease, contamination of sample by menstrual blood.
Ketone bodies	High levels of ketone bodies in urine—**ketonuria** (kē-tō-NOO-rē-a)—may indicate diabetes mellitus, anorexia, starvation, or too little carbohydrate in diet.

TABLE 26.6

Summary of Abnormal Constituents in Urine

ABNORMAL CONSTITUENT	COMMENTS
Bilirubin	When red blood cells are destroyed by macrophages, the globin portion of hemoglobin is split off and heme is converted to biliverdin. Most biliverdin is converted to bilirubin, which gives bile its major pigmentation. Above-normal level of bilirubin in urine is called **bilirubinuria** (bil′-ē-roo-bi-NOO-rē-a).
Urobilinogen	Presence of urobilinogen (breakdown product of hemoglobin) in urine is called **urobilinogenuria** (ū′-rō-bi-lin′-ō-je-NOO-rē-a). Trace amounts are normal, but elevated urobilinogen may be due to hemolytic or pernicious anemia, infectious hepatitis, biliary obstruction, jaundice, cirrhosis, congestive heart failure, or infectious mononucleosis.
Casts	Casts are tiny masses of material that have hardened and assumed shape of lumen of tubule in which they formed, from which they are flushed when filtrate builds up behind them. Casts are named after cells or substances that compose them or based on appearance (for example, white blood cell casts, red blood cell casts, and epithelial cell casts that contain cells from walls of tubules).
* **Microbes**	Number and type of bacteria vary with specific urinary tract infections. One of the most common is *E. coli.* (bactiria) Most common fungus is yeast *Candida albicans*, cause of vaginitis. Most frequent protozoan is *Trichomonas vaginalis*, cause of vaginitis in females and urethritis in males.

vaginitis → vagina inflammation

bactiria — E. coli
Fungus — yeast (candida albicans)
protozoa — trichomonas vaginalis

EVALUATION OF KIDNEY FUNCTION:
2- BLOOD TESTS

- Two blood-screening tests can provide information about kidney function:-

1. Blood urea nitrogen (BUN) test.
2. Plasma creatinine.

BLOOD UREA NITROGEN (BUN) TEST

N

- It **measures the blood nitrogen that is part of the urea resulting from catabolism and deamination of amino acids.**

GFR ↓ BUN ↑

- **When glomerular filtration rate decreases severely**, as may occur with renal disease or obstruction of the urinary tract, **BUN rises steeply**.

بشكل حاد

- **One strategy in treating such patients is to minimize their protein intake**, thereby reducing the rate of urea production.

Nitrogen amino acid proteins

PLASMA CREATININE

- It results from catabolism of creatine phosphate in skeletal muscle.
- Normally, the blood creatinine level remains steady because the rate of creatinine excretion in the urine equals its discharge from muscle.
- A creatinine level above 1.5 mg/dL (135 mmol/liter) usually is an indication of poor renal function.

pharma

Kinetics

RENAL PLASMA CLEARANCE

❖ **Renal plasma clearance** is **the volume of blood that is "cleaned" or cleared of a substance per unit of time, usually expressed in units of milliliters per minute.**

low clearance → inefficient excretion

❖ ***Low clearance*** **indicates** ***inefficient excretion*****. For example, the clearance of glucose normally is zero because it is completely reabsorbed; therefore, glucose is not excreted at all.**

zero clearance

RENAL PLASMA CLEARANCE

- **Knowing a drug's clearance is essential for determining the correct dosage. If clearance is high (one example is penicillin), then the dosage must also be high, and the drug must be given several times a day to maintain an adequate therapeutic level in the blood.**

high clearance
"pencillin"
high dose

The following equation is used to calculate clearance:

$$\text{Renal plasma clearance of substance S} = \left(\frac{U \times V}{P}\right)$$

urine
urine flow rate
mL / min
UFR
plasma

where U and P are the concentrations of the substance in urine and plasma, respectively (both expressed in the same units, such as mg/mL), and V is the urine flow rate in mL/min.

RENAL PLASMA CLEARANCE

❖ **The clearance of a solute depends on the three basic processes of a nephron:**

1. **Glomerular filtration.**
2. **Tubular reabsorption.**
3. **Tubular secretion.**

- Formation of urine -

osmolarity : concentration of solutes in water .

↑ osmolarity (in water) Cl^- / Na^+ كل ما زادت نسبة

- In proximal convoluted tubule : reabsorption for water / Na^+ sodium

osmolarity ↑ urine concentration ↑

Ascending loop of henle : impermeable to water غير منفذة للماء

reabsorption of Na^+ / Cl^- osmolarity ↑

→ permeable to urea

distal convoluted tubule / collecting duct : BV↓ → activation of osmoreceptors in hypothalamus → produce (ADH) osmolarity ↑ urine concentration ↑ ↲ يعمل reabsorption الـ water

↳ For systemic circulation

- diluted urine -

BF ↑ 90% sodium / water reabsorption

(excess) لن يتم أفراز (ADH) لأنه % ال water طالعها secretion

- characteristics of normal urine -

- **volume**: 1-2 liter in 24h
- **color**: yellow/amber
  - diet
  - medications
- **turbidity**: transparent
- **odor**: mild aromatic
  - diabetics urine has Fruity odor
- **PH**: average 6
  - high protein diets acidity ↑
  - vegetarian diets

alkalinity ↑

- Abnormal constituents - مكونات غير طبيعية
  - Albumin → albuminuria "مطلوب بس نعرف اسمائهم"
  - glucose → glucosuria (due to stress) "في ال patho رح نعرف أمراضهم"
  - red blood cells (erythrocytes) → hematuria
  - Ketone bodies → Ketonuria
  - bilirubin → bilirubinuria
  - microbes

Evaluation of Kidney Function

- urinalysis
  - normal urine
  - abnormal constituents
- blood tests - الأهم إلنا -
  - plasma creatinine
  - Blood urea nitrogen test (BUN

- result from creatine phosphate in skeletal muscle

above 1.5 mg/dL

↳ poor renal function

- directly related to GFR

GFR ↓ BUN ↑

↳ secretion يصيرلها

- reduce protein intake

- renal plasma clearance - → معدل تخلص الجسم من دواء معين أو مادة

penicillin → High clearance

↳ high excretion / low reabsorption

- مطلوب ع الامتحان - more frequent / higher dose نعطي -

U concentration of drug/substance in urine.

The following equation is used to calculate clearance:

$$\text{Renal plasma clearance of substance S} = \left(\frac{U \times V}{P}\right)$$

where U and P are the concentrations of the substance in urine and plasma, respectively (both expressed in the same units, such as mg/mL), and V is the urine flow rate in mL/min.

↳ urine output

P concentration of drug/substance in plasma