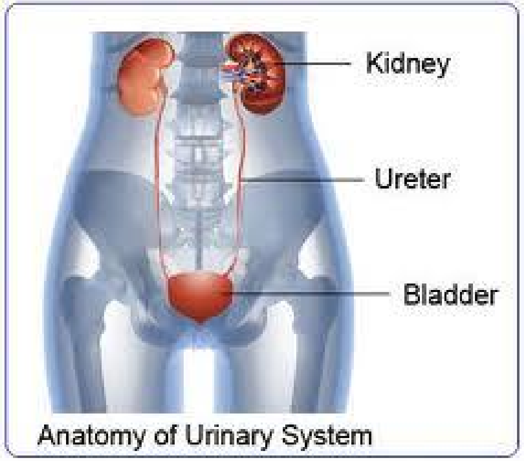
Chapter 15 腎臟生理

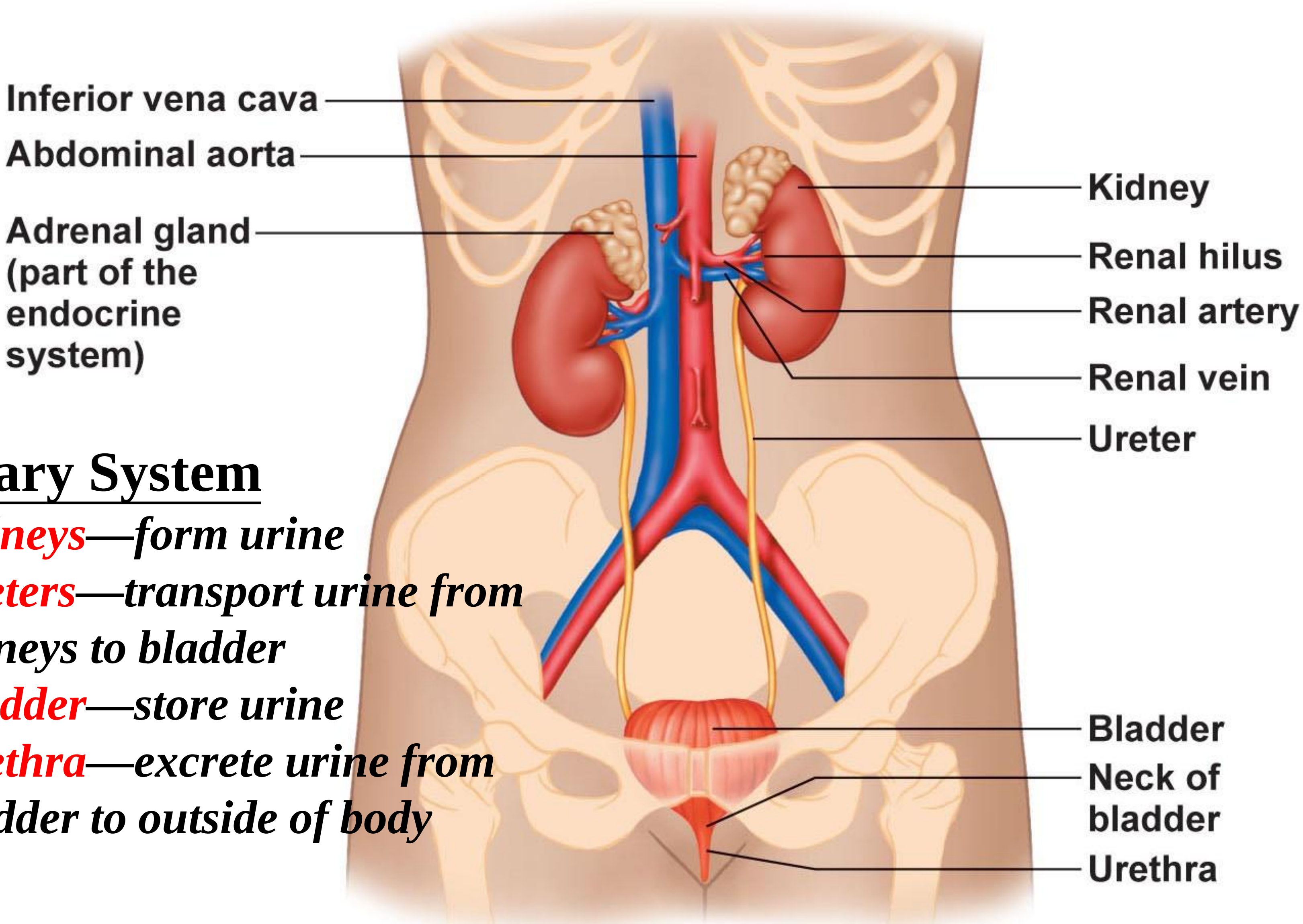
- ✓ 15-1　腎臟的構造及功能
- ✓ 15-2　尿液的形成
- ✓ 15-3　腎血漿清除率
- ✓ 15-4　排尿作用
- 15-5　電解質及酸鹼平衡的調節

Functions of the Urinary System



- Regulate ***plasma ionic composition***
- Regulate ***plasma volume (BP)***
- Regulate ***plasma osmolarity***
- Regulate ***plasma pH***
- Remove ***metabolic waste products*** ***(ammonia, bilirubin etc.)*** ***and foreign substances*** ***(drugs and environmental toxins)*** from plasma
- Secrete ***erythropoietin (EPO)***
- Secrete ***renin (RAAS--BP)***
- Activate ***vitamin D_3 to calcitriol***
- ***Gluconeogenesis***

Structures of the Urinary System

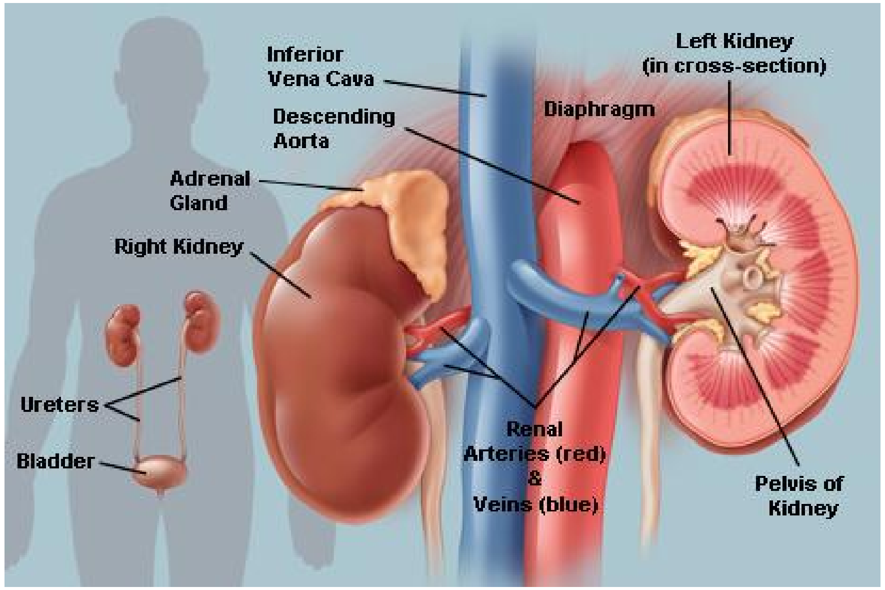


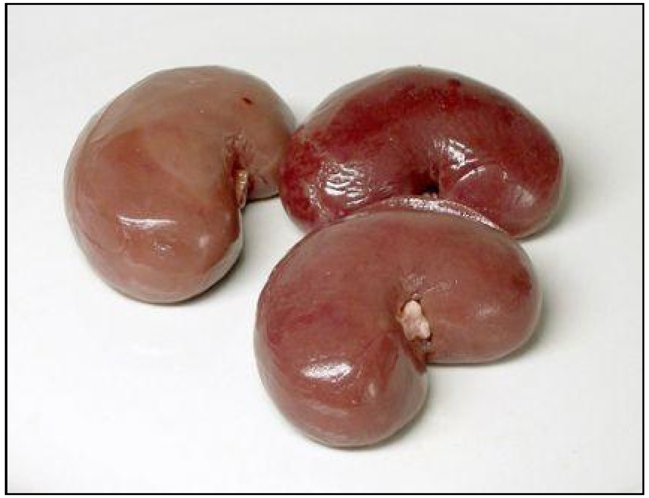
<u>**Urinary System**</u>

- ***Kidneys*—*form urine***
- ***Ureters*—*transport urine from kidneys to bladder***
- ***Bladder*—*store urine***
- ***Urethra*—*excrete urine from bladder to outside of body***

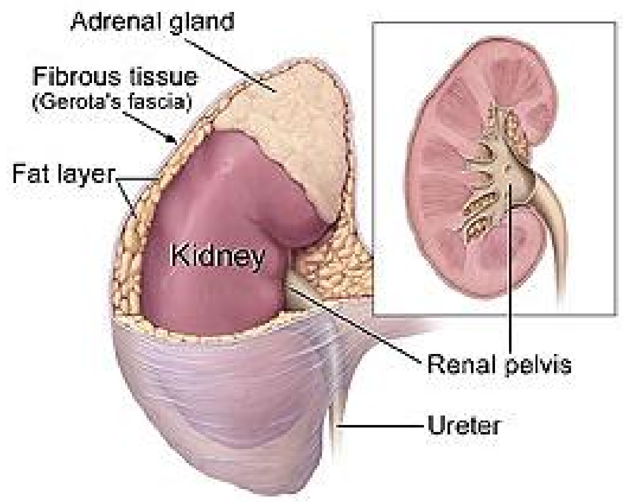
Gross Anatomy of the Kidneys

- **Paired**, **bean** shaped
- Approximate **size of fist**, **115–170 g**
- Each kidney is about 11-12 cm long, 5-6 cm width and 3-4 cm thickness
- **Retroperitoneal organs** that are normally located between the transverse processes of **T12-L2 vertebrae**
- The kidneys are located in right and left of the spine and below the diaphragm
- **Left kidney** typically somewhat **more superior** in position than the **right** **(liver oppression)**





Gross Anatomy of the Kidneys



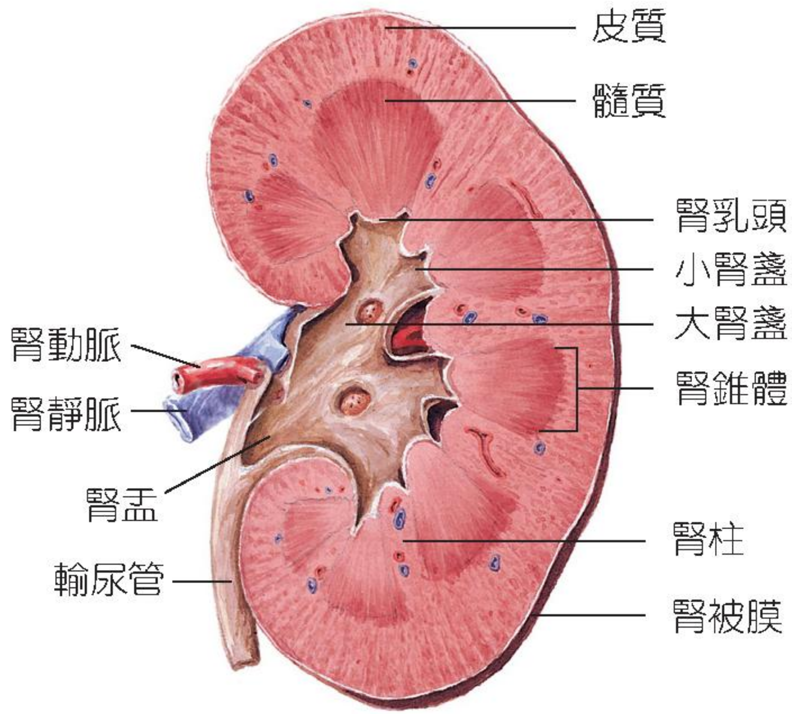
- **The kidneys are surrounded by three layers of tissue:**
  1. **The renal fascia (Gerota's fascia)** is a thin, outer layer of fibrous connective tissue that surrounds each kidney (and the attached adrenal gland) and **fastens it** to surrounding structures
  2. **The adipose capsule** is a middle layer of adipose (fat) tissue that **cushions the kidneys**
  3. **The renal capsule** is an inner fibrous membrane that **prevents the entrance of infections, barrier against trauma, and maintains kidney shape**

Anatomy of the Kidneys

- **Inside the kidney, three major regions:**

--The **renal cortex** borders the convex side

--The **renal medulla** lies adjacent to the renal cortex



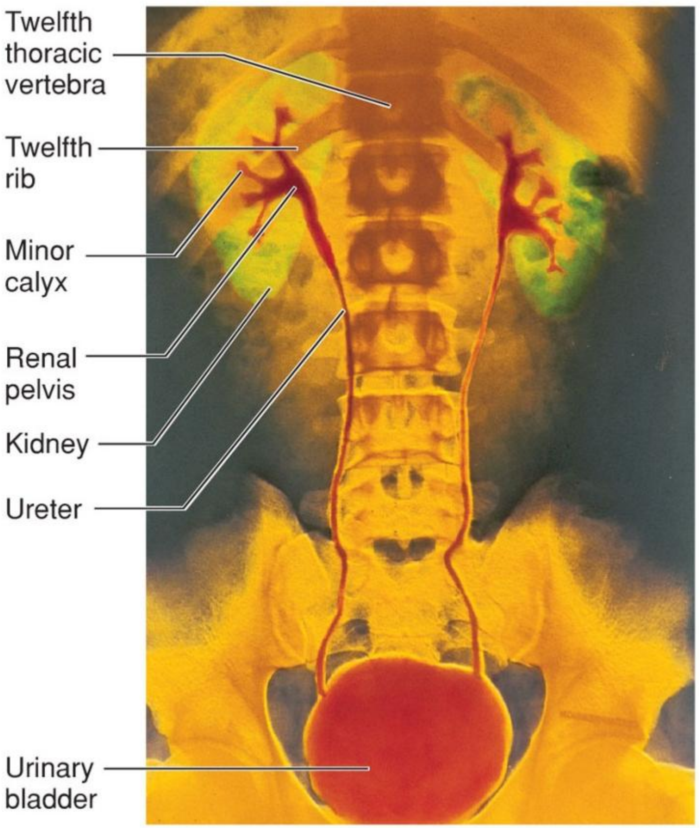
1. ***Renal pyramids*** (medullary pyramids): 8-12 striated, cone-shaped regions
2. ***Renal papillae***: peaks, face inward
3. ***Renal columns***: unstriated regions between the renal pyramids

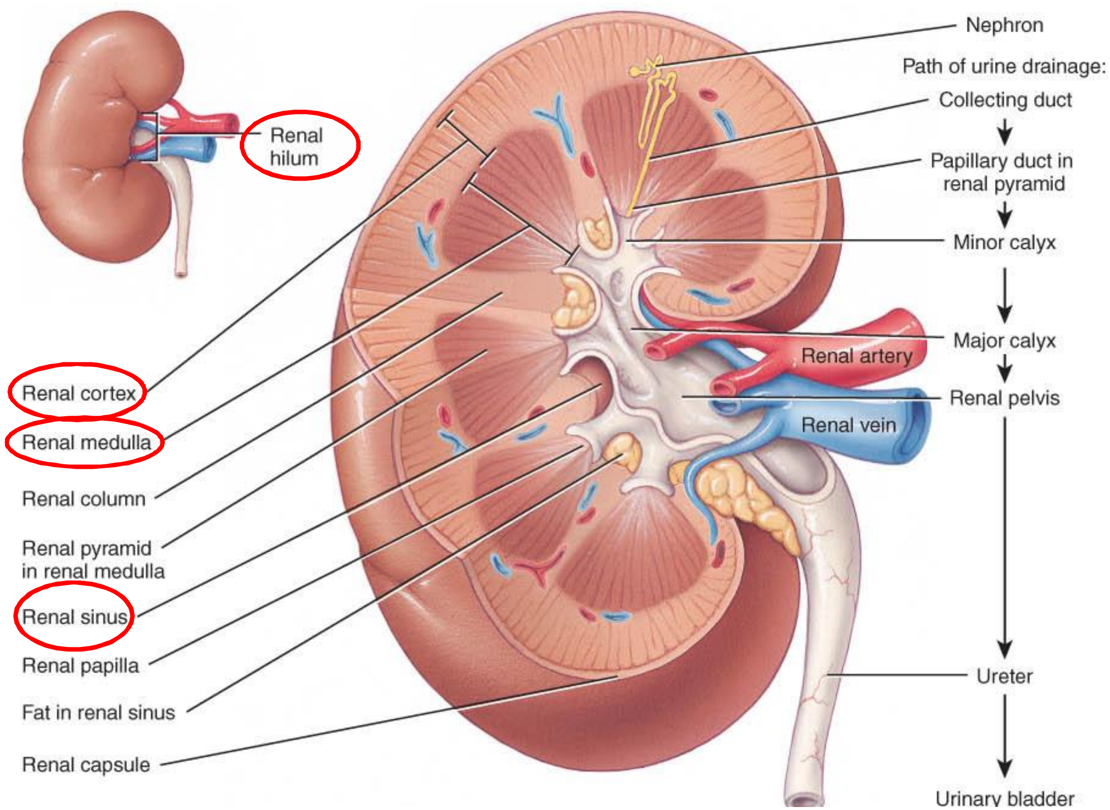
--The **renal sinus** is a cavity that lies adjacent to the renal medulla

1. ***Renal hilus***: ureter, nerves, and blood and lymphatic vessels enter the kidney on the concave surface through the renal hilus
2. ***Renal pelvis***: a funnel-shaped structure that merges with the ureter
3. ***Renal calyx***: a cavity that between the renal papillae and renal pelvis

Anatomy of the Kidneys

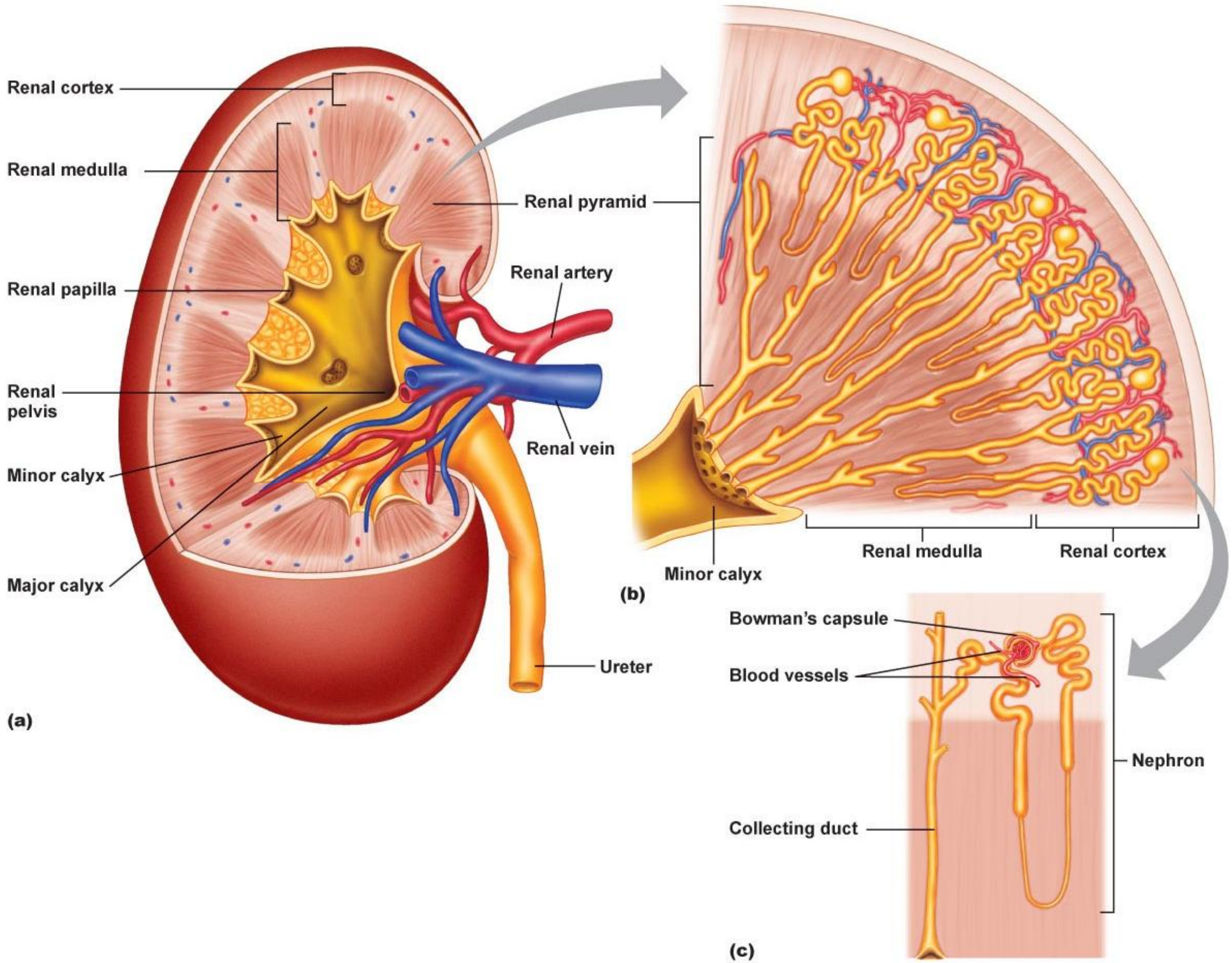
- **Parenchyma (functional portion)** of kidney = ***Renal cortex* + *Renal pyramids of medulla***
- **Nephron** – microscopic functional units of kidney





*Each **pyramid** (urine formed by nephron) → papillary ducts of the **papilla** → **minor calyx** → **major calyx** → **renal pelvis** → **ureter** → **urinary bladder***

Anatomy of the Kidneys



Blood Supply of the Kidneys

- **Renal arteries** ***enter*** kidney at hilus, **renal veins** ***exit*** at hilus
- Although kidneys constitute **< 0.5%** of body weight, receive **20-25%** of cardiac output at rest (1200 ml/min)

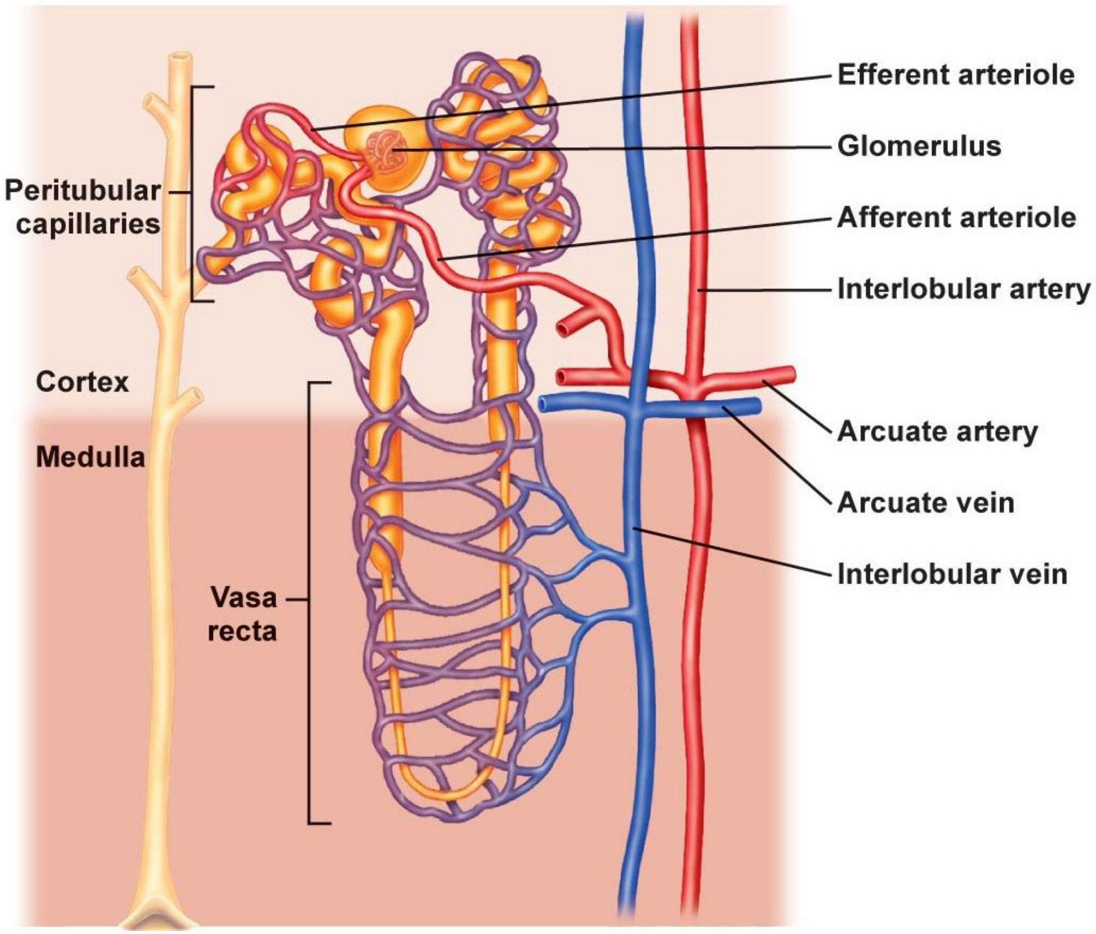
  --Renal cortex (>90% blood), renal medulla (<10% blood)

  --Utilize 16% of ATP usage by body

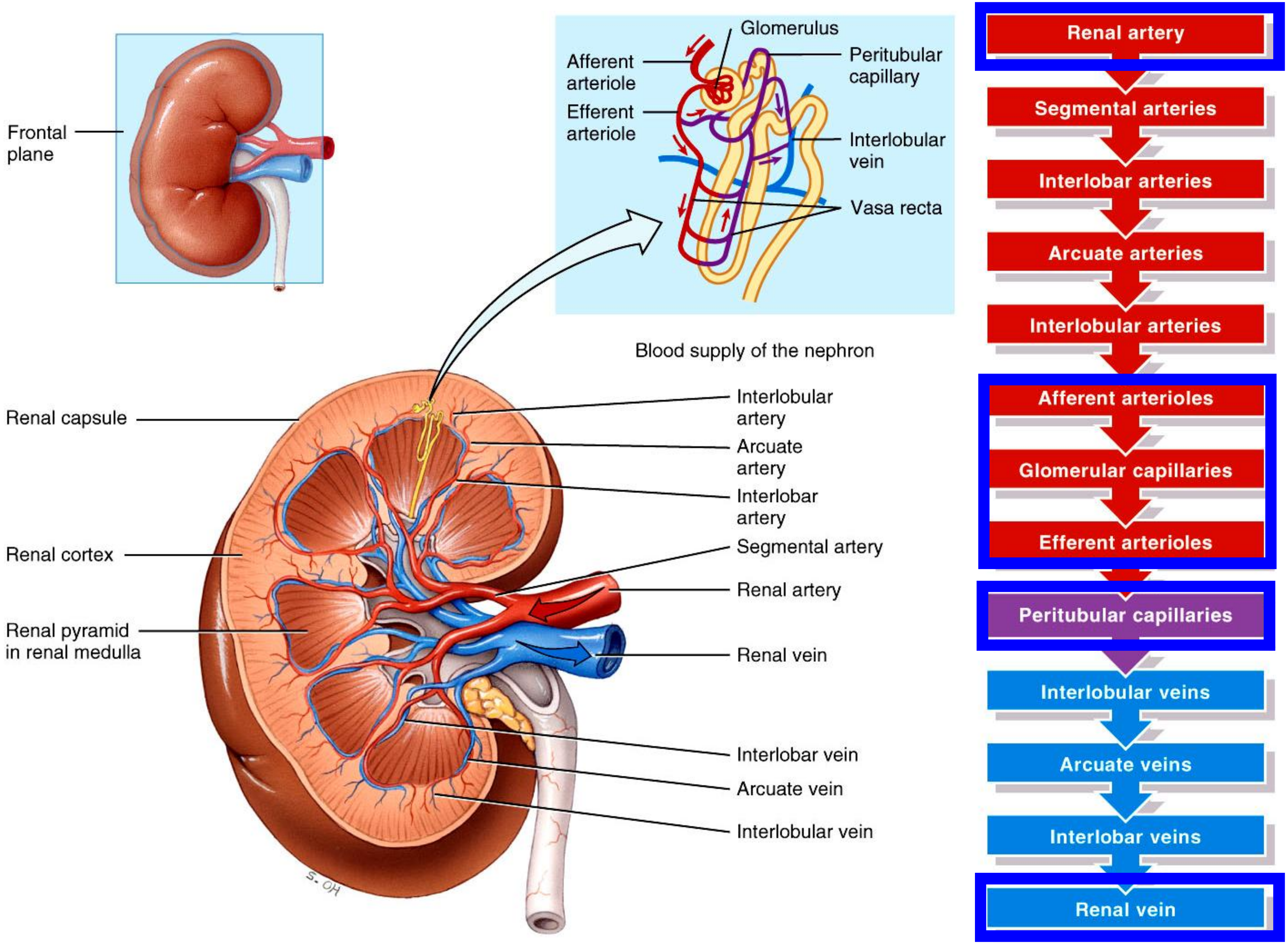
  --Function is to filter blood
- Branches into segmental, interlobar, arcuate, interlobular arteries
- Each nephron receives one ***afferent arteriole***
- Divides into glomerulus – ***capillary ball***
- Reunite to form ***efferent arteriole*** (unique)
- Divide to form peritubular capillaries or some have vasa recta
- Peritubular venule, interlobular, arcuate, interlobar vein and renal vein exits kidney

Nephron Blood Supply

- **Functions of different capillary beds**
  - --***Glomerular capillaries*** where filtration of blood occurs
    - ➢ Vasoconstriction & vasodilation of afferent & efferent arterioles produce large changes in renal filtration
  - --***Peritubular capillaries*** that carry away reabsorbed substances from filtrate
  - --***Vasa recta*** supplies nutrients to medulla without disrupting its osmolarity form



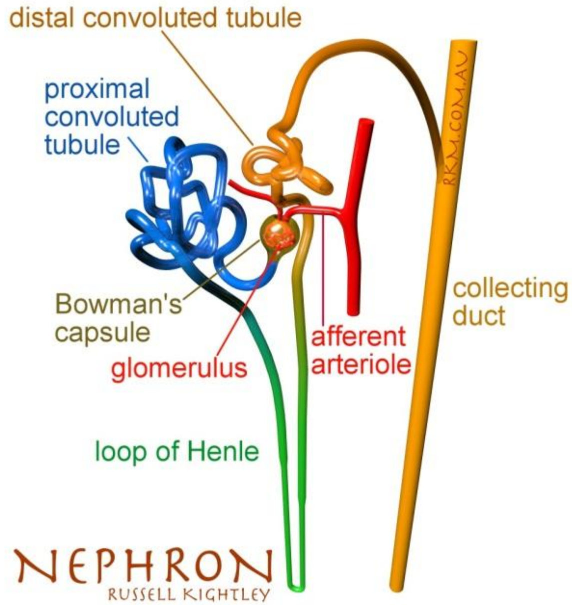
- ➢ *The nerve supply to the kidney: the renal plexus (**sympathetic** division of ANS)*
- ➢ *Sympathetic vasomotor nerves regulate **blood flow & renal resistance by altering arterioles***



(a) Frontal section of right kidney

(b) Path of blood flow

Nephron



- **Each kidney has more than a million nephrons**
- **2 parts**

  1. Renal corpuscle – filters blood plasma

  --**Glomerulus** = ***capillary network*** → **filtration**

  --**Glomerular (Bowman's) capsule** = ***double-walled cup surrounding glomerulus*** → **receives the filtrate and inflow to renal tubules**

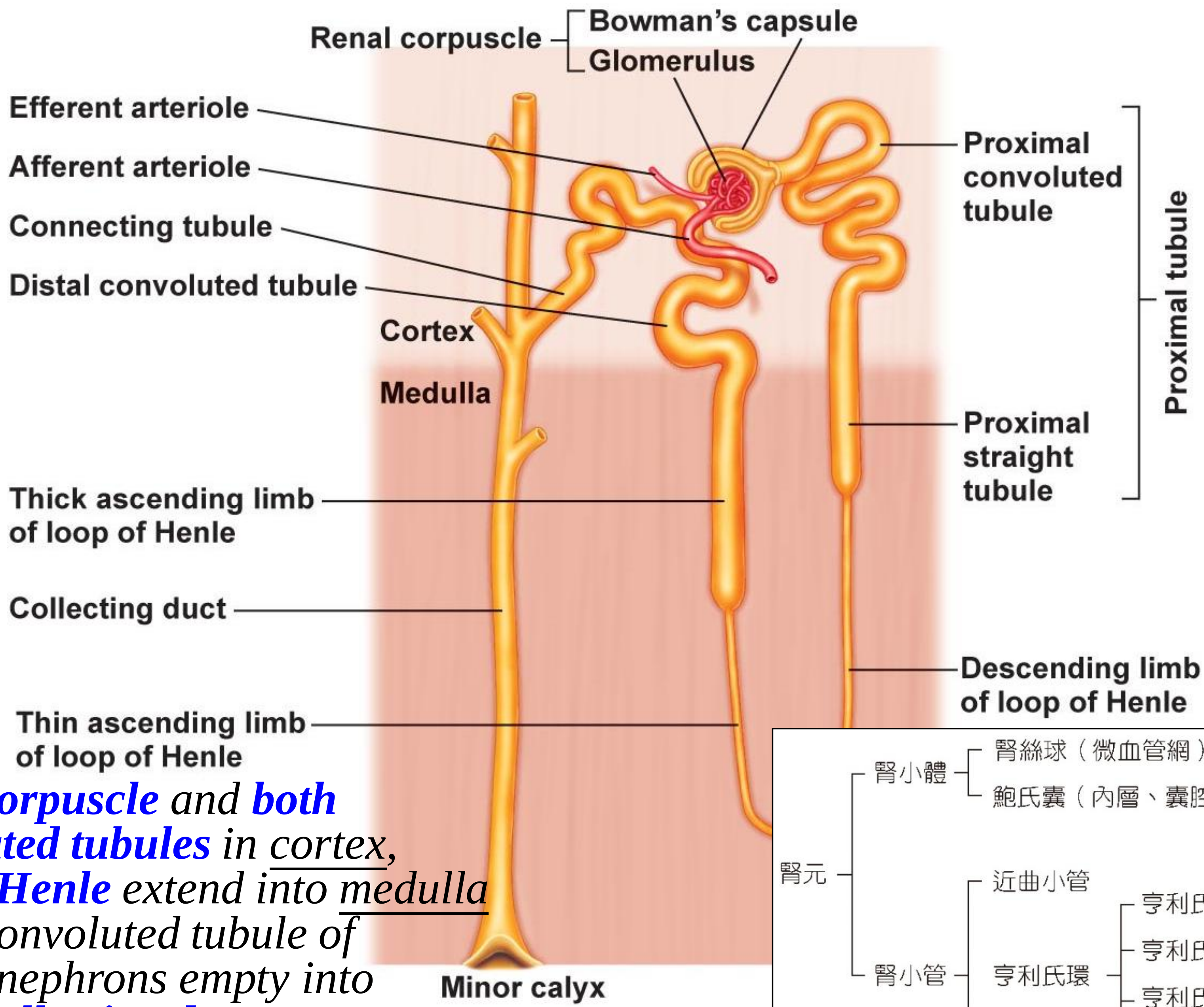
  2. Renal tubule – filtered fluid passes into

  --**Proximal convoluted tubule**

  --**Descending and ascending loop of Henle** (nephron loop)

  --**Distal convoluted tubule**

Anatomy of the Nephron



- ➤ ***Renal corpuscle*** *and* ***both convoluted tubules*** *in cortex,* ***loop of Henle*** *extend into medulla*
- ➤ *Distal convoluted tubule of several nephrons empty into* ***single collecting duct***

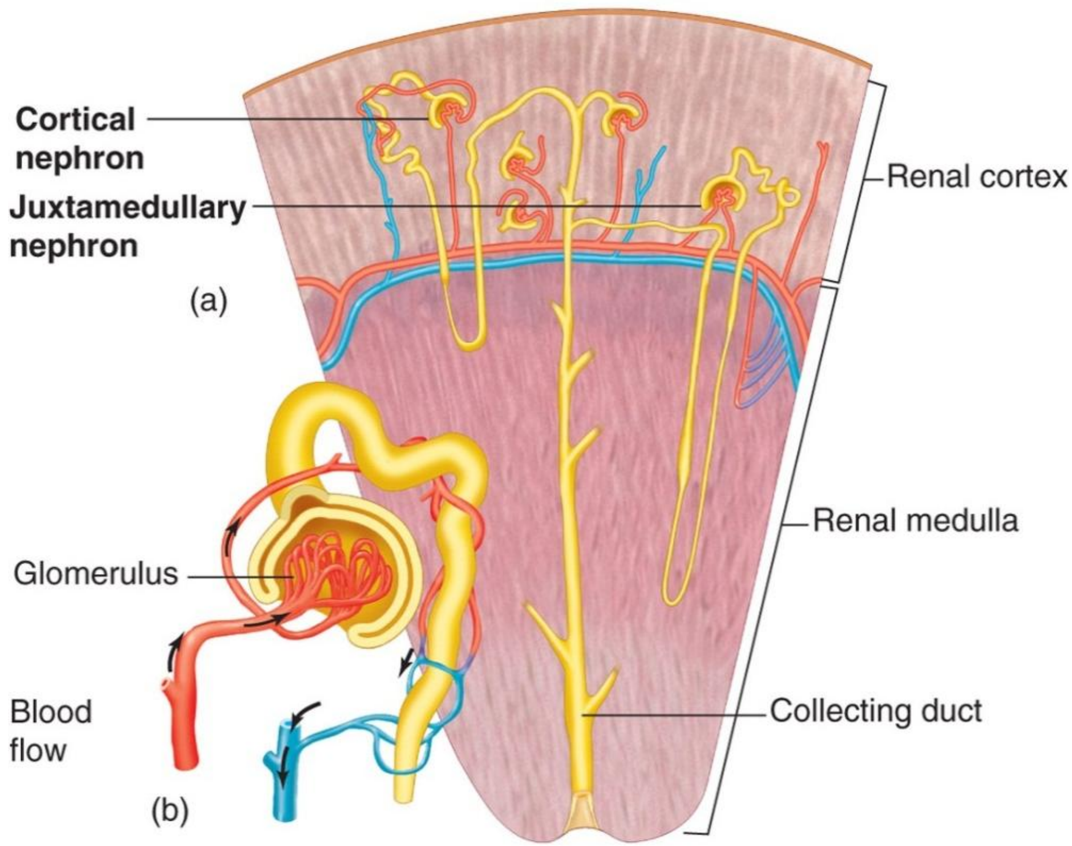
- 腎元
  - 腎小體
    - 腎絲球（微血管網）
    - 鮑氏囊（內層、囊腔、外層）
  - 腎小管
    - 近曲小管
    - 亨利氏環
      - 亨利氏環下降支粗段
      - 亨利氏環下降支細段
      - 亨利氏環上升支細段
      - 亨利氏環上升支粗段
    - 遠曲小管

Number of Nephrons

- Remains **constant** from birth
  - --Any increase in size of kidney is ***size increase of individual nephrons***, but not in number
- If injured, **no replacement** occurs
- Dysfunction is not evident until function declines by **25% of normal** (other nephrons handle the extra work)
- Removal of one kidney causes **enlargement** of the remaining until it can filter at 80% of normal rate of 2 kidneys

Two Types of Nephron

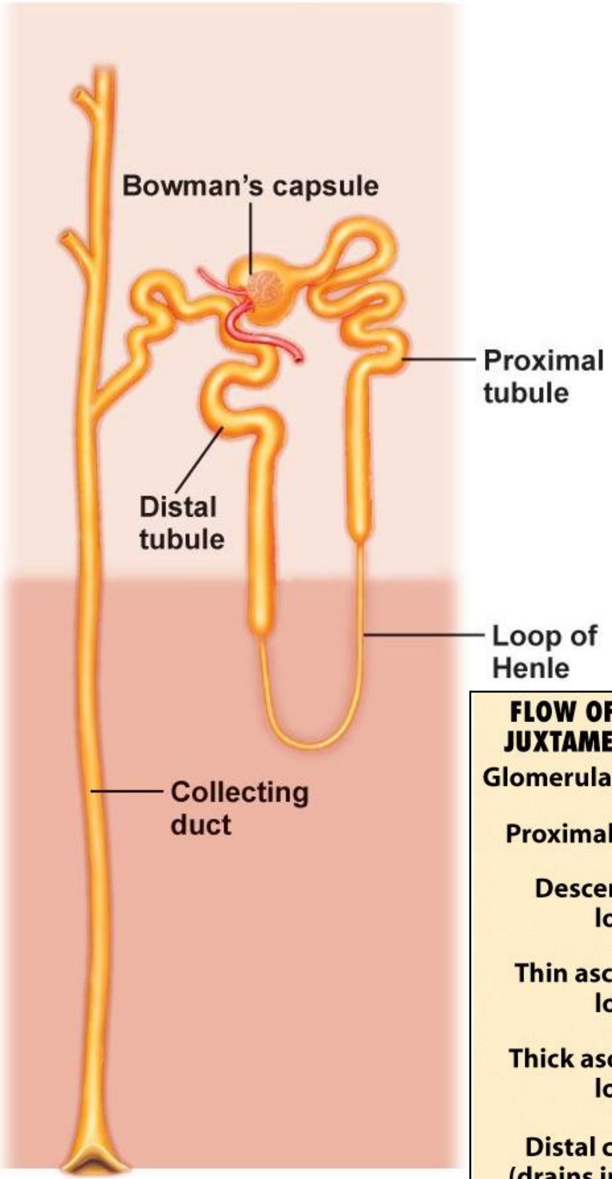
- **Cortical nephrons** – 80-85% of nephrons
  - --Renal corpuscle in outer portion of cortex and short loops of Henle extend only into outer region of medulla
- **Juxtamedullary nephrons** – other 25-20%
  - --Renal corpuscle deep in cortex and long loops of Henle extend deep into medulla
  - --Receive blood from peritubular capillaries and vasa recta
  - --Ascending limb has thick and thin regions
  - --Enable kidney to secrete very dilute or very concentrated urine



Cortical *vs.* Juxtamedullary Nephrons

FLOW OF FLUID THROUGH A CORTICAL NEPHRON

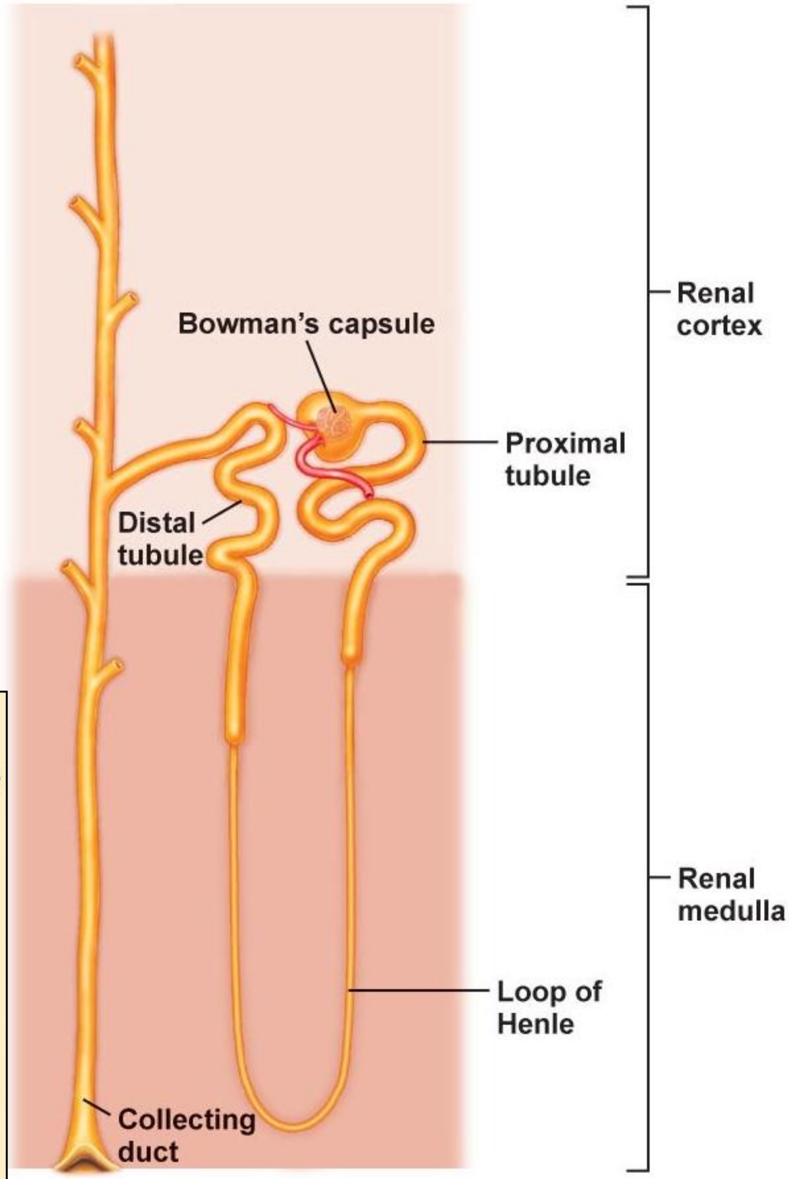
Glomerular (Bowman's) capsule
↓
Proximal convoluted tubule
↓
Descending limb of the loop of Henle
↓
Ascending limb of the loop of Henle
↓
Distal convoluted tubule (drains into collecting duct)



(a) Cortical nephron

FLOW OF FLUID THROUGH A JUXTAMEDULLARY NEPHRON

Glomerular (Bowman's) capsule
↓
Proximal convoluted tubule
↓
Descending limb of the loop of Henle
↓
Thin ascending limb of the loop of Henle
↓
Thick ascending limb of the loop of Henle
↓
Distal convoluted tubule (drains into collecting duct)

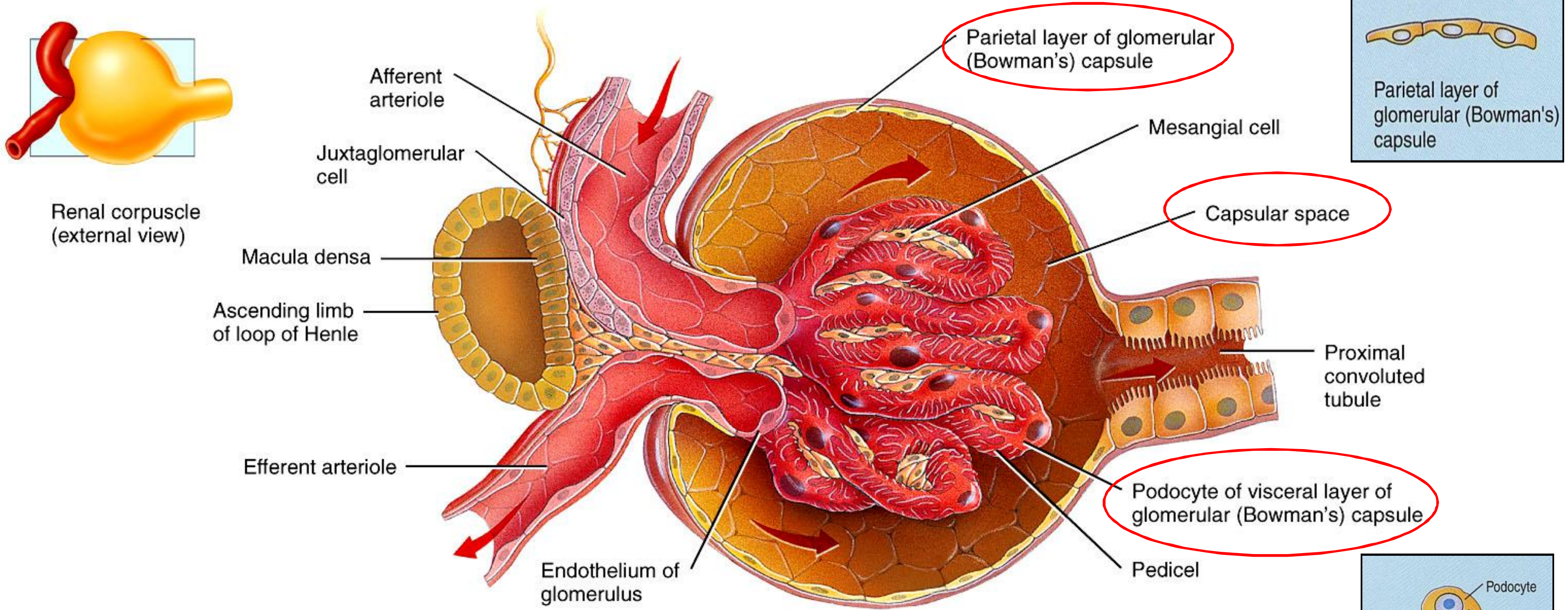


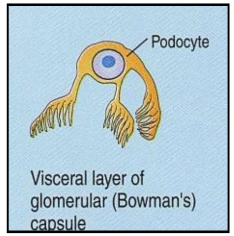
(b) Juxtamedullary nephron

Cortical *vs.* Juxtamedullary Nephrons

類 型	皮質腎元	近髓質腎元
部位	腎皮質的外及中層	腎皮質的內層
數量	85~90%	10~15%
腎絲球體積	小	大
入球小動脈與出球小動脈口徑比	2：1	1：1
出球小動脈分支	腎小管周圍	U 形直血管和腎小管周圍
亨利氏環長短	短	長
分泌腎素	有	無
交感神經支配	入球小動脈和緻密斑	出球小動脈
功能	1. 過濾、再吸收，生成尿液 2. 分泌腎素 3. 維持血容量和血壓穩定	1. 濃縮和稀釋尿液 2. 維持水平衡

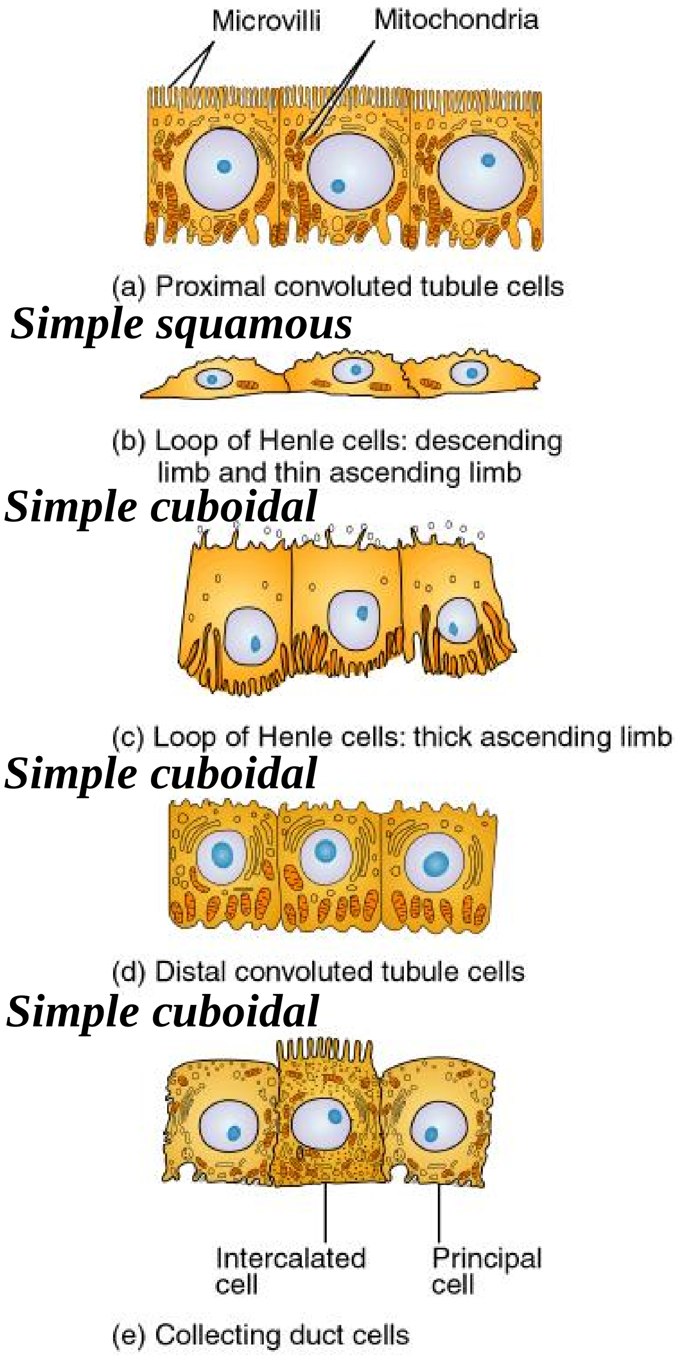
Histology of a Renal Corpuscle





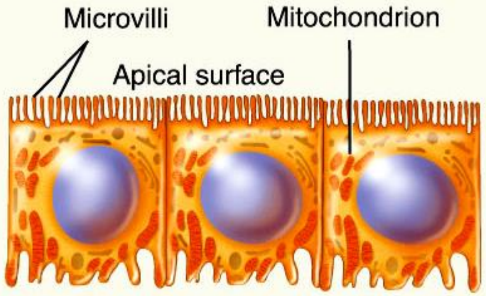
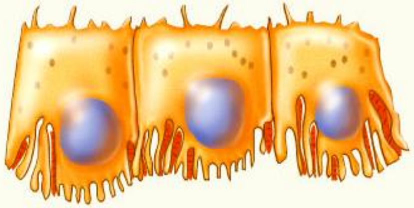
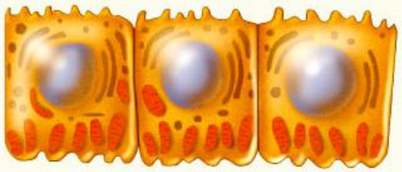
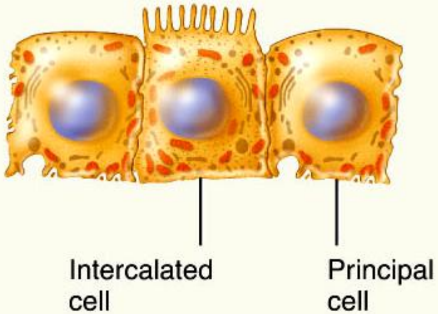
- **Glomerular (Bowman's) Capsule**
  - --***Visceral layer + capsular space + parietal layer***
  - --The visceral (inner) layer consists of modified simple squamous epithelial cells called ***podocytes***
  - --The parietal layer consists of simple squamous epithelium and forms the outer wall of the capsule
- Fluid filtered from the glomerular capillaries enters the ***capsular space***, the space between the two layers of the glomerular capsule

Histology of a Renal Tubule

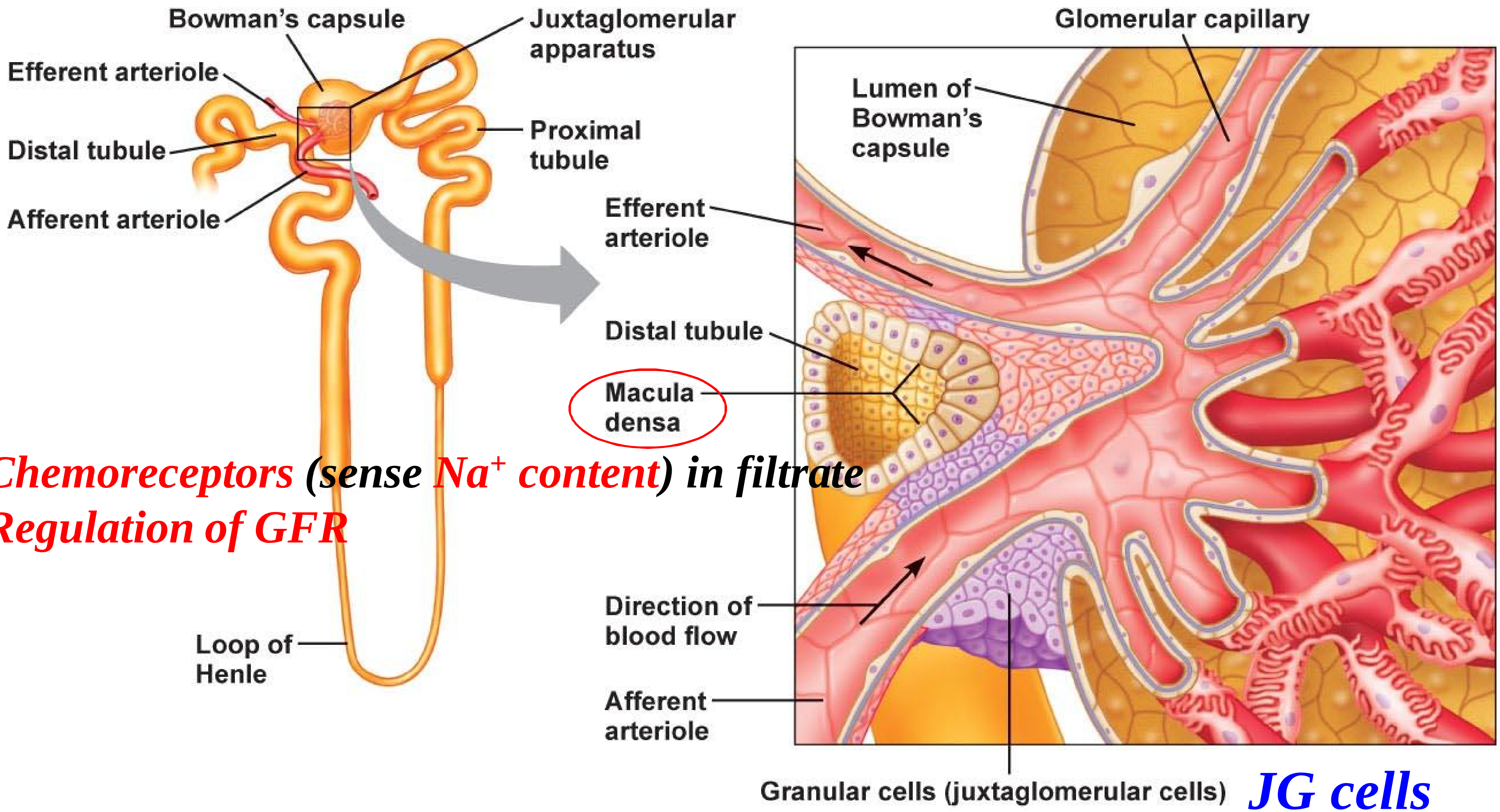


- **Proximal convoluted tubule cells** have **microvilli** with brush border – increases surface area
- **Juxtaglomerular appraratus** helps regulate blood pressure in kidney
  - --***Macula densa*** – cells in distal tubule and thick ascending loop of Henle
  - --***Juxtaglomerular (JG) cells*** – cells of afferent and efferent arterioles contain modified smooth muscle fibers
- **Last part of distal convoluted tubule** and **collecting duct**
  - --***Principal cells*** – receptors for antidiuretic hormone (ADH) and aldosterone
  - --***Intercalated cells*** – role in blood pH homeostasis

Histology of a Renal Tubule

REGION AND HISTOLOGY		DESCRIPTION
Proximal convoluted tubule (PCT)		Simple cuboidal epithelial cells with prominent brush borders of microvilli.
Loop of Henle: descending limb and thin ascending limb		Simple squamous epithelial cells.
Loop of Henle: thick ascending limb		Simple cuboidal to low columnar epithelial cells.
Most of distal convoluted tubule (DCT)		Simple cuboidal epithelial cells.
Last part of DCT and all of collecting duct (CD)		Simple cuboidal epithelium consisting of principal cells and intercalated cells.

Juxtaglomerular Apparatus



➢ ***Chemoreceptors*** ***(sense Na*$^{+}$ *content) in filtrate***

➢ ***Regulation of GFR***

JG cells

➢ ***Mechanoreceptors*** ***(sense blood pressure) in the afferent arteriole***

➢ ***Secrete renin and erythropoietin (EPO)***

Basic Renal Exchange Functions

1. **Glomerular filtration**

   --Blood water and most solutes ***from glomerulus to Bowman's capsule***

2. **Tubular reabsorption**

   --As filtered fluid moves along tubule and through collecting duct, about 99% of water and many useful solutes reabsorbed – ***from tubules to peritubular capillaries***

3. **Tubular secretion**

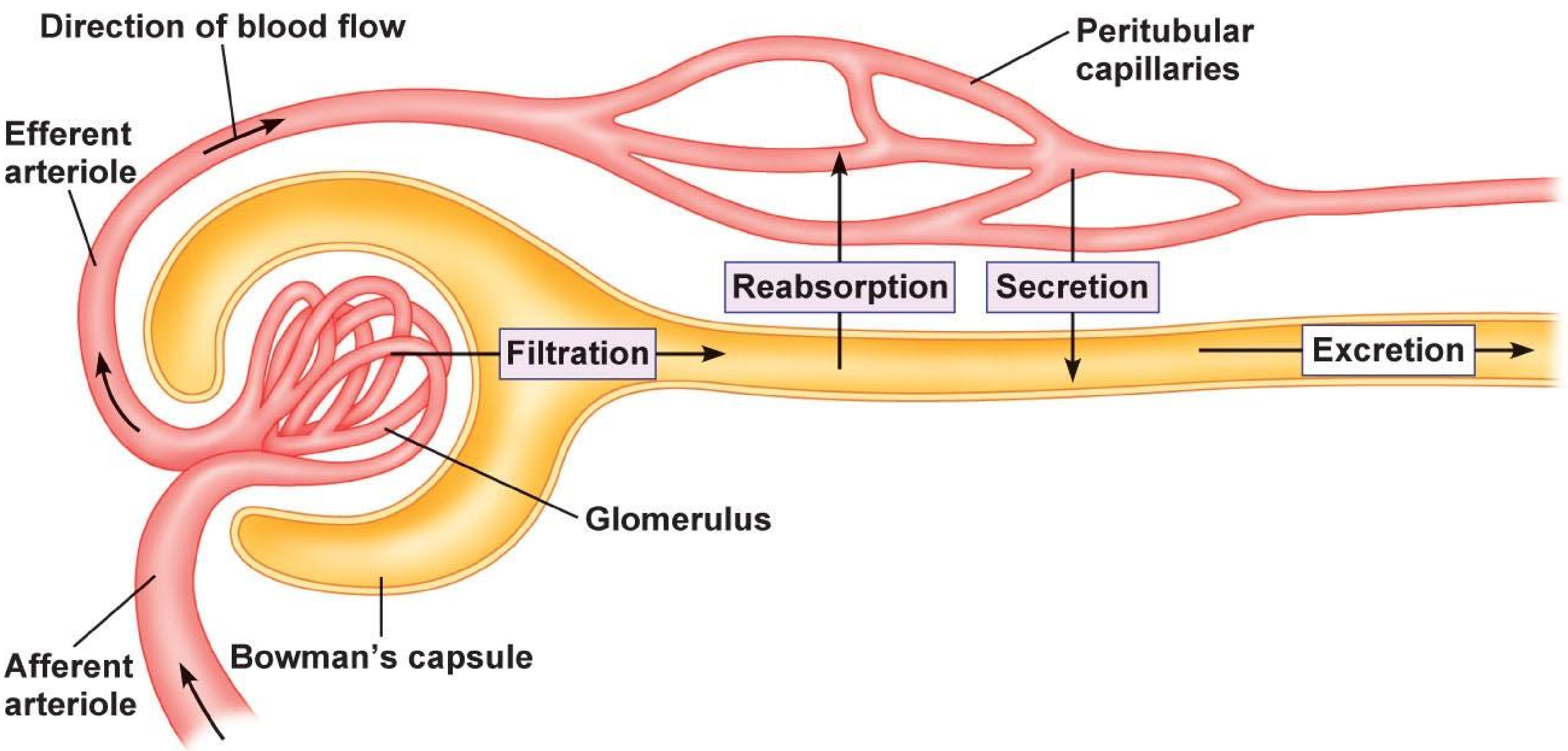
   --As filtered fluid moves along tubule and through collecting duct, other material secreted into fluid such as wastes, drugs, and excess ions – ***from peritubular capillaries to tubules***

4. **Tubular excretion**

   --Solutes in the fluid that drains into the renal pelvis remain in the fluid and are excreted – ***from tubules out of body***

   --**Excretion of any solute = glomerular filtration + secretion - reabsorption**

Basic Renal Exchange Functions



Glomerular Filtration

- **Glomerular filtrate** – fluid that enters capsular space
  - --**180 liters/day: > 99%** returned to blood plasma via tubular reabsorption
- **Filtration fraction** – the fraction of plasma in the afferent arterioles of the kidneys that becomes filtrate
- **Filtration membrane** – ***endothelial cells of glomerular capillaries*** and ***podocytes*** encircling capillaries
  - --Permits filtration of water and small solutes
  - --Prevents filtration of ***most plasma proteins, blood cells and platelets***
  - --3 barriers to cross – ***glomerular endothelial cells fenestrations (pores)***, ***basement membrane*** between endothelium and podocytes and ***slit membranes*** between pedicels of podocytes
  - --Volume of fluid filtered is large because of ***large surface area***, ***thin and porous membrane***, and ***high glomerular capillary blood pressure***

The Filtration Membrane

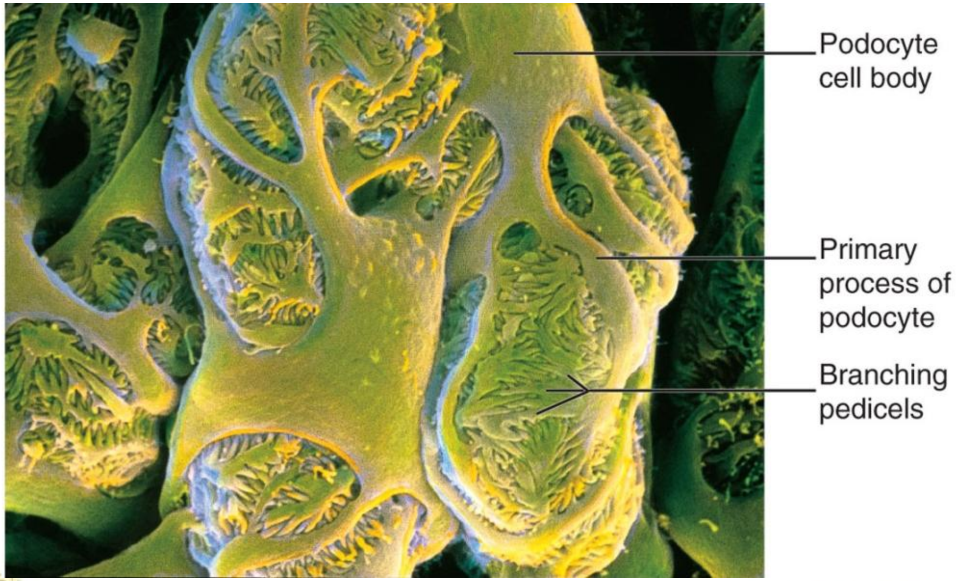
- **The filtering unit of a nephron is the *endothelial-capsular membrane* (three barriers)**

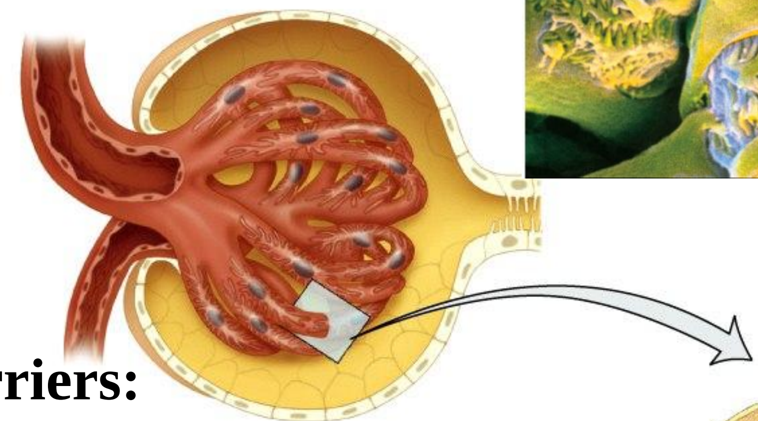
  --*Glomerular endothelium*

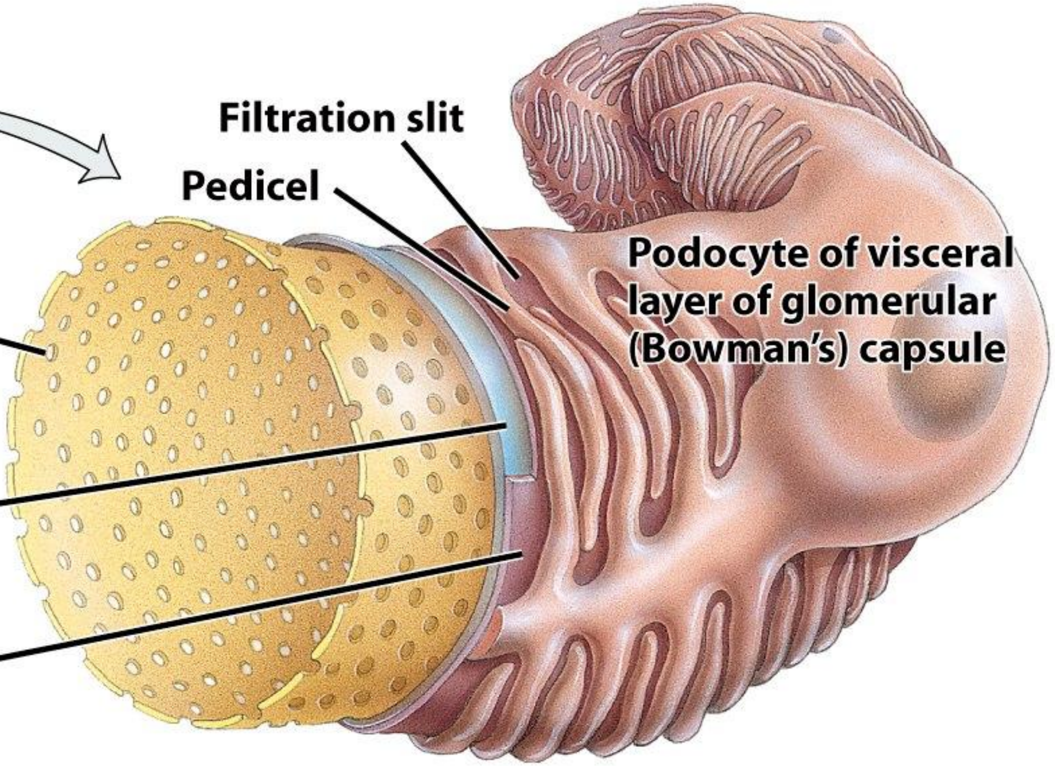
  --*Glomerular basement membrane (basal lamina)*

  --*Slit membranes between pedicels of podocytes*
- **The principle of filtration -** to force fluids and solutes through a membrane by **net filtration pressure**
- During filtration it is important to keep **the plasma proteins in the plasma** to maintain **osmotic (oncotic) pressure**
- If you see blood cells or protein in the urine **(protinuria)** then there is a problem with the **filtration membrane** **(diabetes and hypertension → kidney damage → renal failure)**

The Filtration Membrane







Three barriers:

Glomerular endothelium

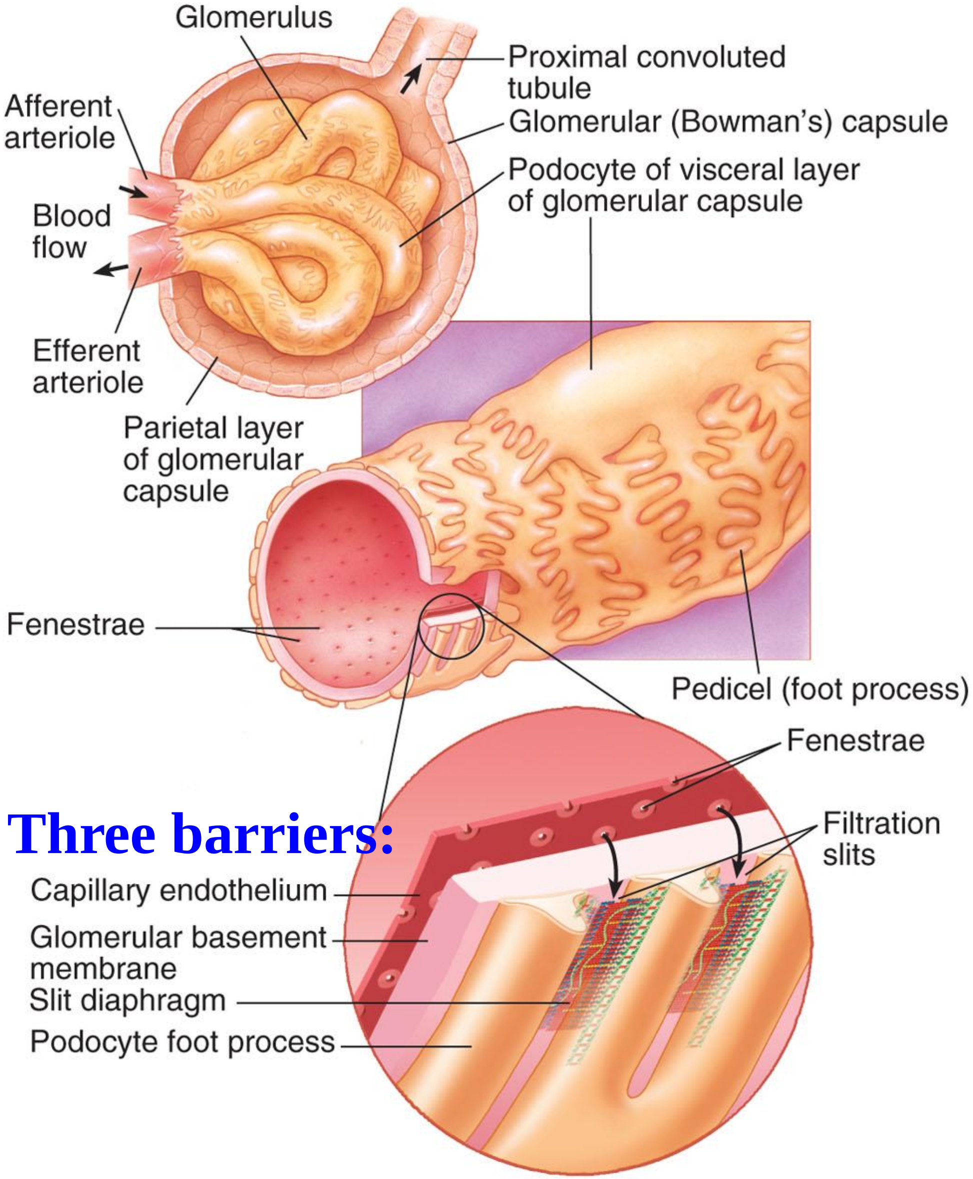
1. **Fenestration (pore) of glomerular endothelial cell: prevents filtration of blood cells but allows all components of blood plasma to pass through**

Glomerular basement membrane

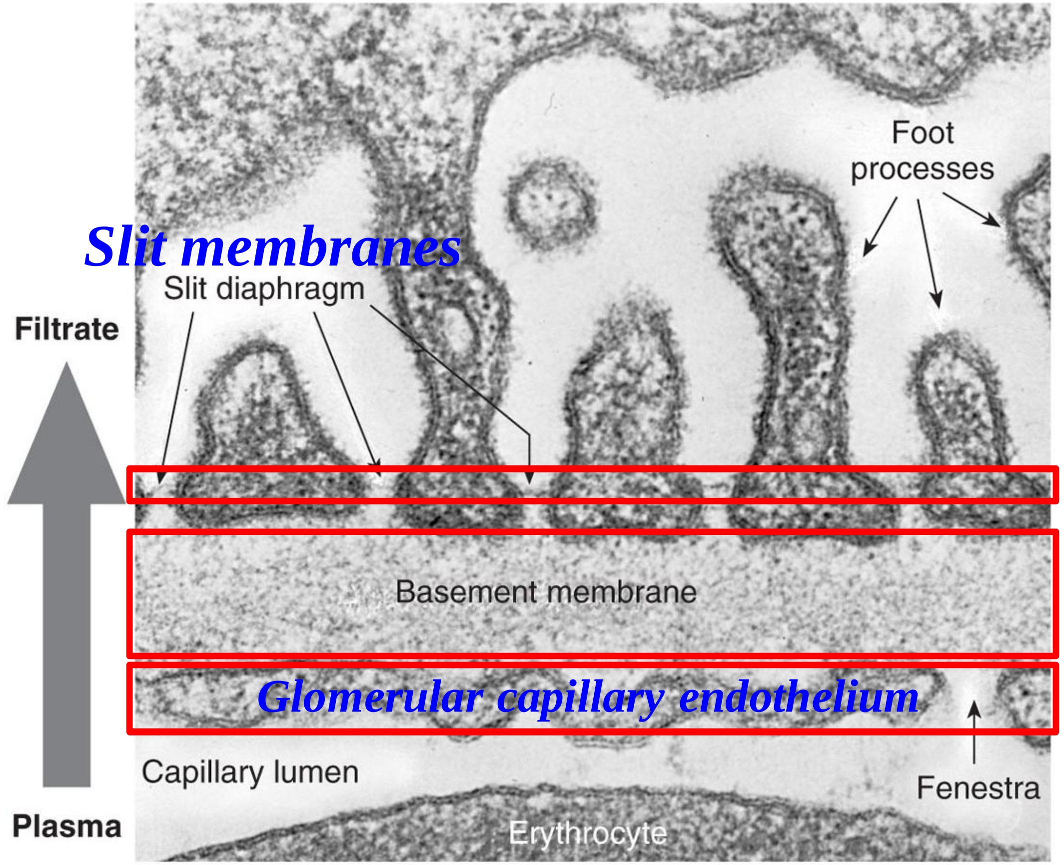
2. **Basal lamina of glomerulus: prevents filtration of larger proteins**

3. **Slit membrane between pedicels: prevents filtration of medium-sized proteins**

The Filtration Membrane

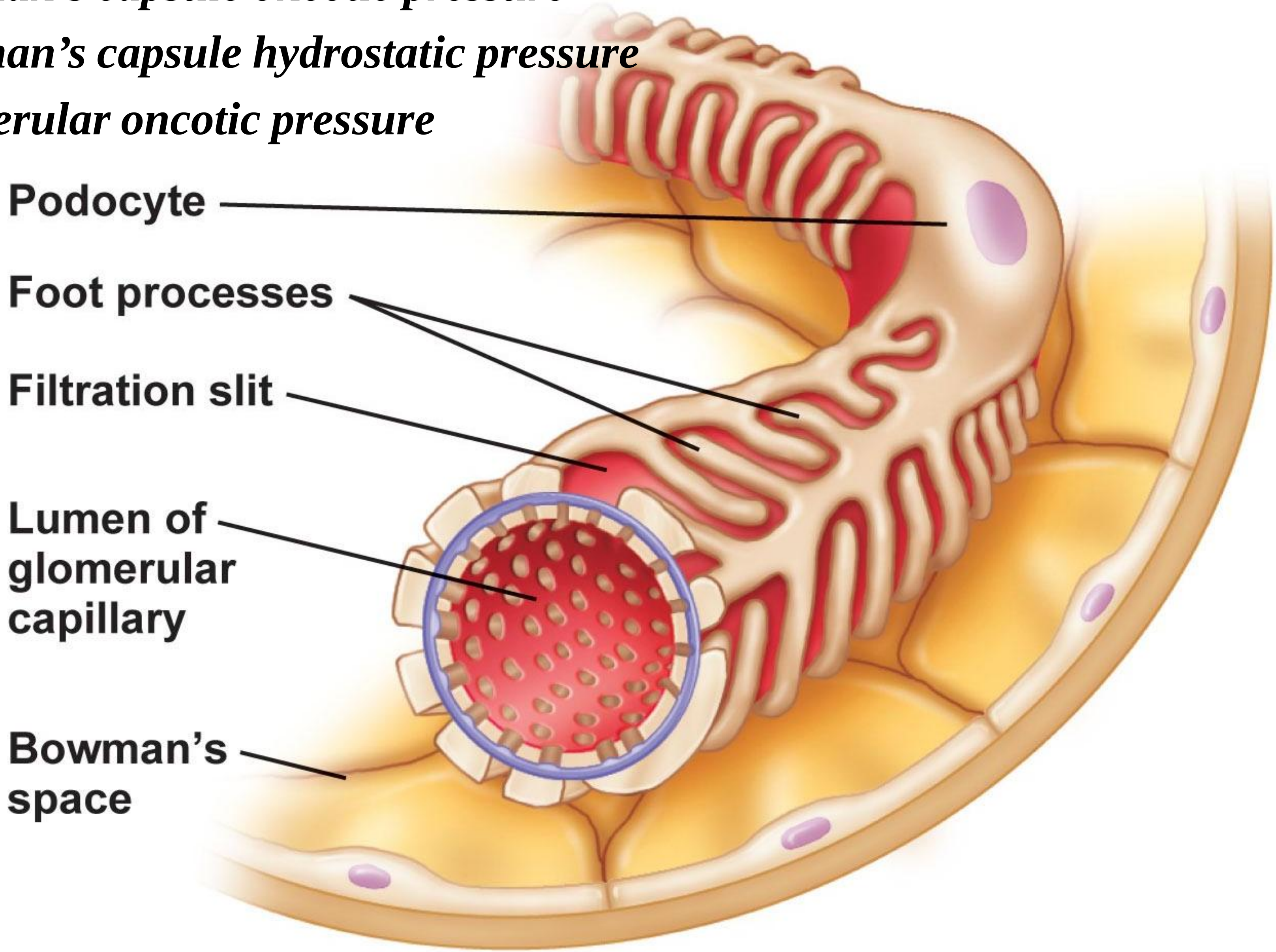


Three barriers:



Starling Forces for Glomerular Filtration

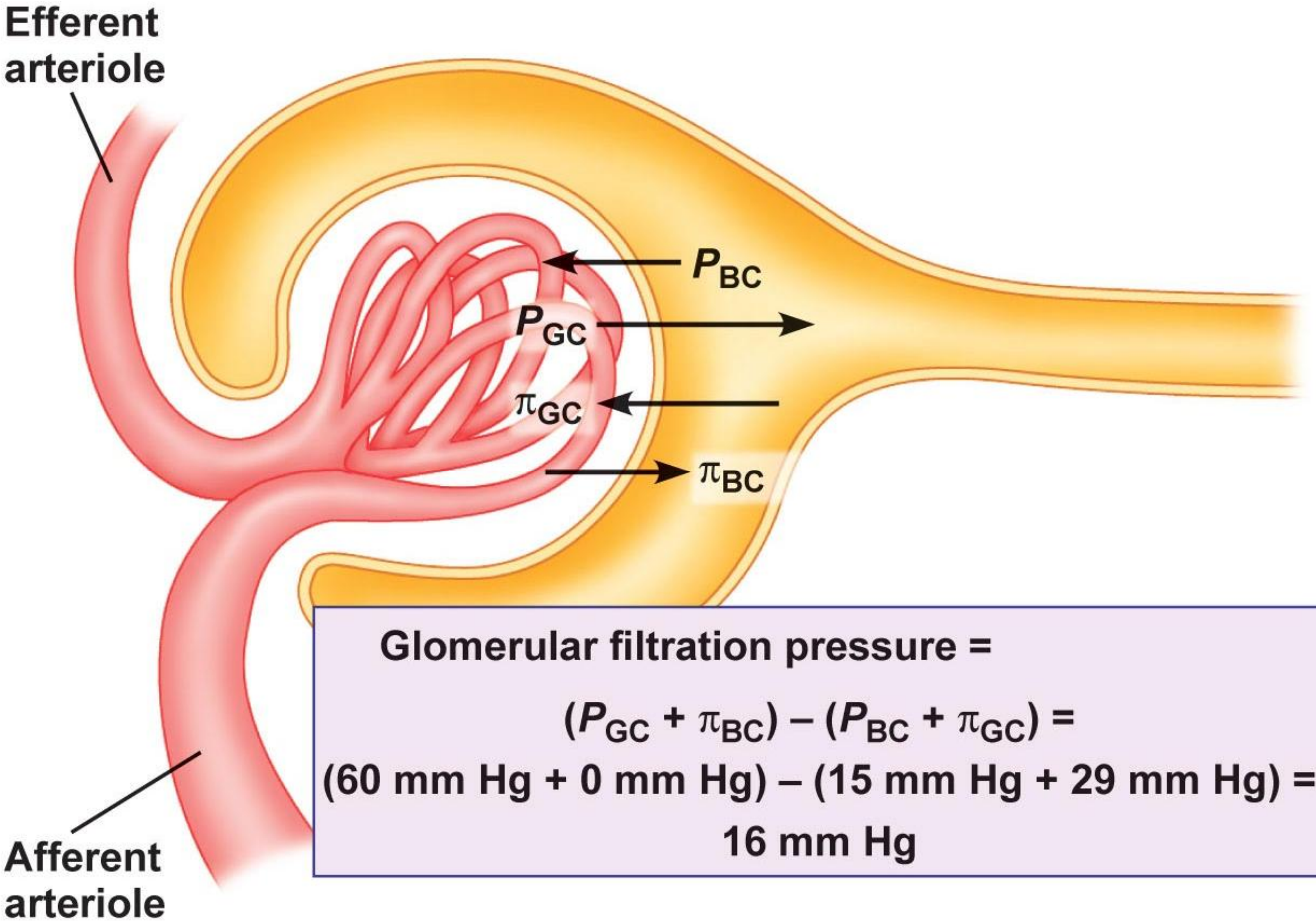
- *Glomerular capillary hydrostatic pressure*
- *Bowman's capsule oncotic pressure*
- *Bowman's capsule hydrostatic pressure*
- *Glomerular oncotic pressure*



Starling Forces for Glomerular Filtration

- **Starling Forces Favoring Filtration Across Glomerulus**
  - **--Glomerular capillary hydrostatic pressure**
    - **60 mm Hg**: High due to ***resistance of efferent arteriole***
  - **--Bowman's capsule oncotic pressure**
    - **0 mm Hg:** Low due to ***lack of protein in filtrate***
- **Starling Forces Opposing Filtration Across the Glomerulus**
  - **--Bowman's capsule hydrostatic pressure**
    - **15 mm Hg:** Relatively high (compared to systemic capillaries) due to ***large volume of filtrate in closed space***
  - **--Glomerular capillary oncotic pressure**
    - **29 mm Hg:** Higher than in systemic capillaries due to ***plasma proteins in smaller volume of plasma***

Glomerular Filtration Pressure



Glomerular filtration pressure =

$$(P_{GC} + \pi_{BC}) - (P_{BC} + \pi_{GC}) =$$

$$(60 \text{ mm Hg} + 0 \text{ mm Hg}) - (15 \text{ mm Hg} + 29 \text{ mm Hg}) =$$

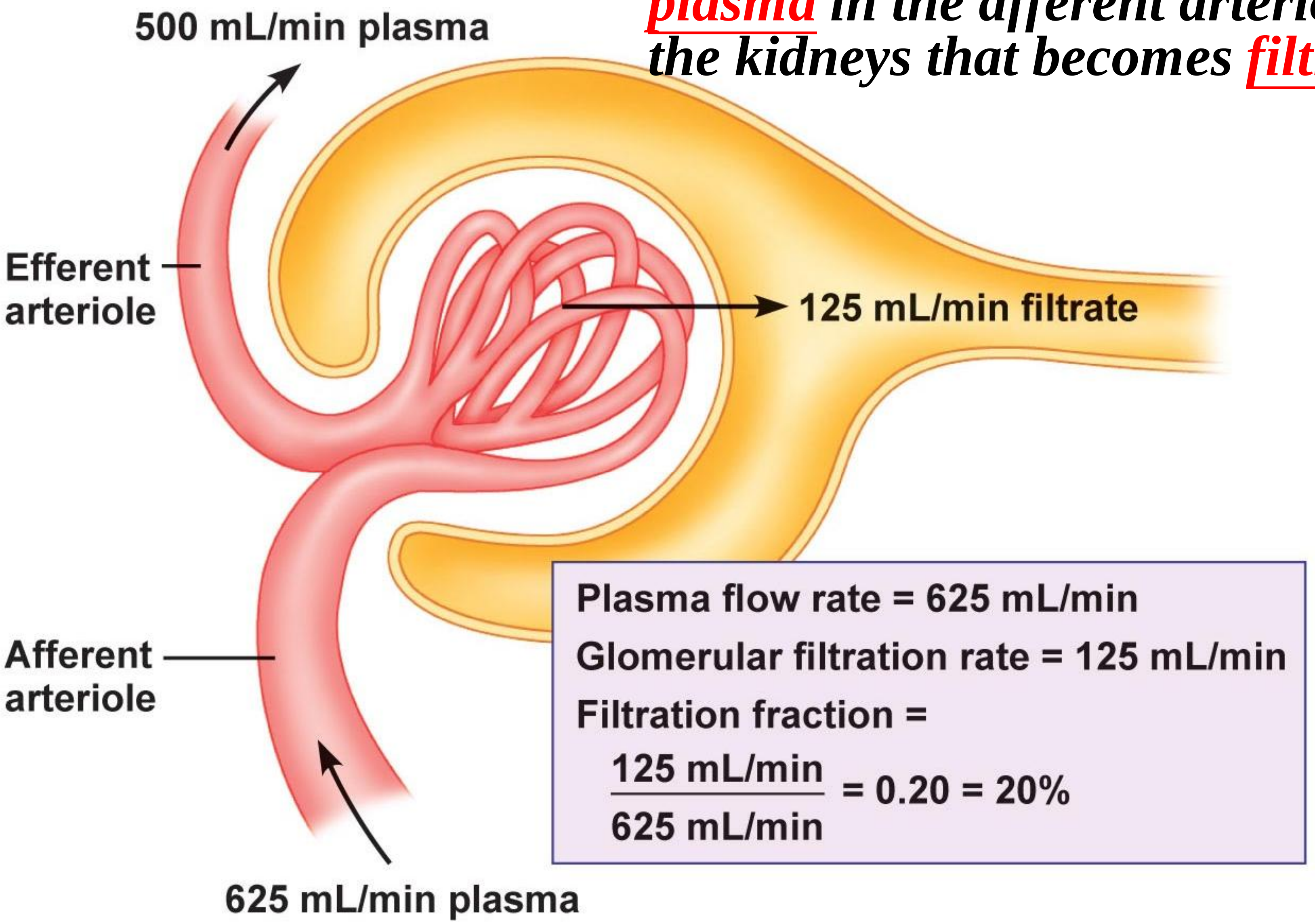
$$16 \text{ mm Hg}$$

Glomerular Filtration Rate

- **Filtration pressure** = $(P_{GC} + \pi_{BC}) - (P_{BC} + \pi_{GC})$ = (60 + 0) – (15 + 29) = **16 mm Hg**
- **Renal plasma flow = 625 mL/minute**
  - --Regulation of renal plasma flow
    - ➢ Associated to ***urinary function*** of the kidney ***(autoregulation--Intrinsic regulation)***
    - ➢ Associated to ***blood circulation (neuro- and humoral regulation--Extrinsic regulation)***
- **GFR = 125 mL/min = 180 liters/day**
- **Total blood volume** filtered **every 40 minutes**
- Compared to **systemic capillaries**
  - --Filtration pressure = **2 mm Hg**
  - --Filtration rate = **3 liters/day**

Glomerular Filtration Rate

- ***Filtration fraction:*** ***the fraction of plasma in the afferent arterioles of the kidneys that becomes filtrate***



Filtered Load of Glucose

- **Filtered load = Quantity filtered = GFR × Px**
- **Depends on plasma concentration of solute and GFR**

  --GFR = 125 mL/min

  --Plasma [glucose] =100 mg/dL = 1 mg/mL

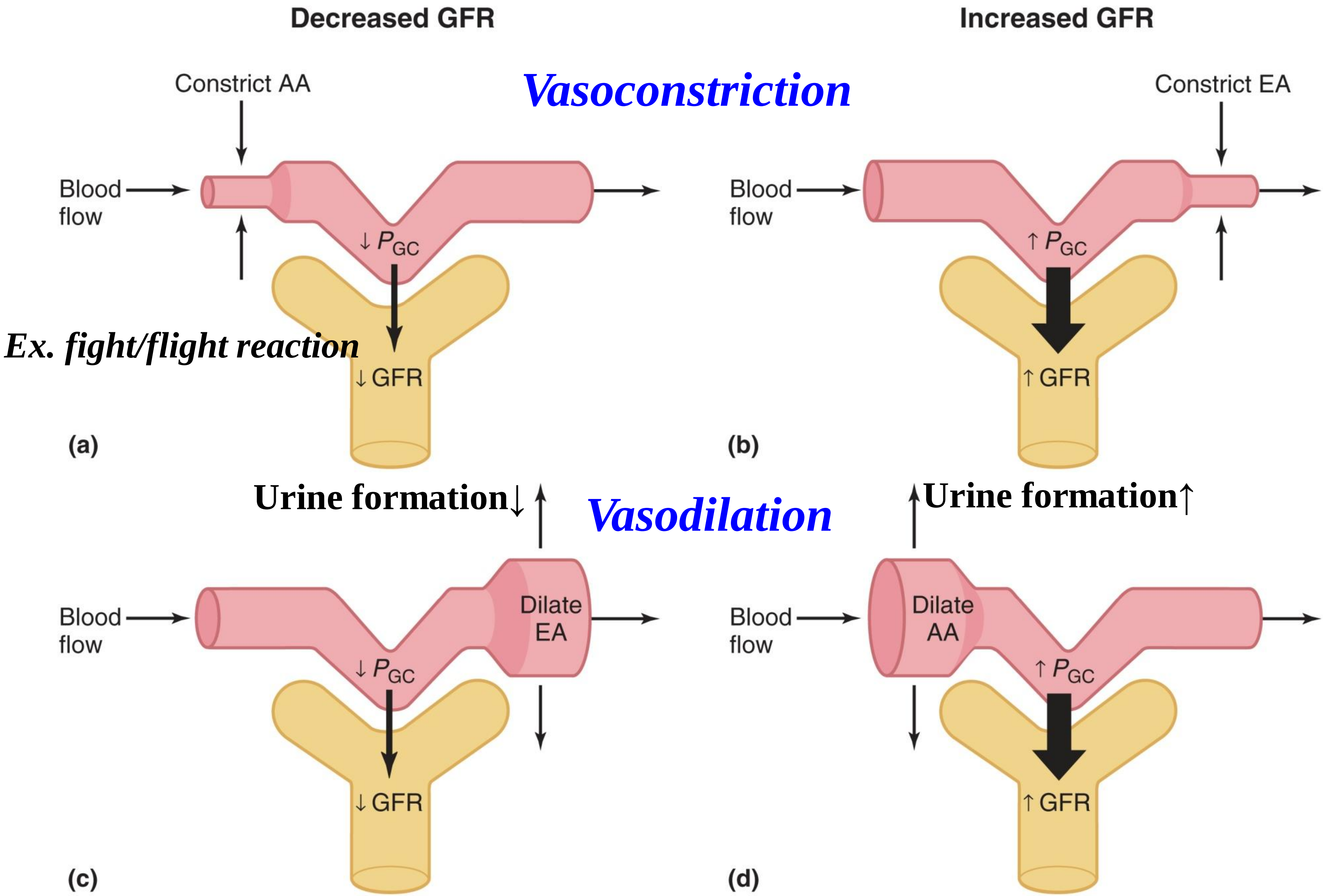
Filtered load of **glucose** =

(125 mL/min) × (1 mg/mL) = **125 mg/min**

Regulation of GFR

- **180 liters fluid filtered/day**
  - -- Only **1.5 liters** urine ***excreted***/day ($<1\%$)
  - -- **>99%** of filtered fluid is ***reabsorbed***
- ***Small*** increase in GFR → ***large*** increase volume fluid filtered and excreted
- **GFR highly regulated**
- **Two principal mechanisms:**
  - ***-- Intrinsic regulation (renal autoregulation)***
    - ➢**Myogenic regulation**
    - ➢**Tubuloglomerular feedback**
  - ***-- Extrinsic regulation (neural* and *hormonal regulation)***

Control of GFR by Vascular Changes



Renal Autoregulation of GFR

- Mechanisms that maintain **a constant GFR despite changes in arterial BP**

  --Myogenic regulation

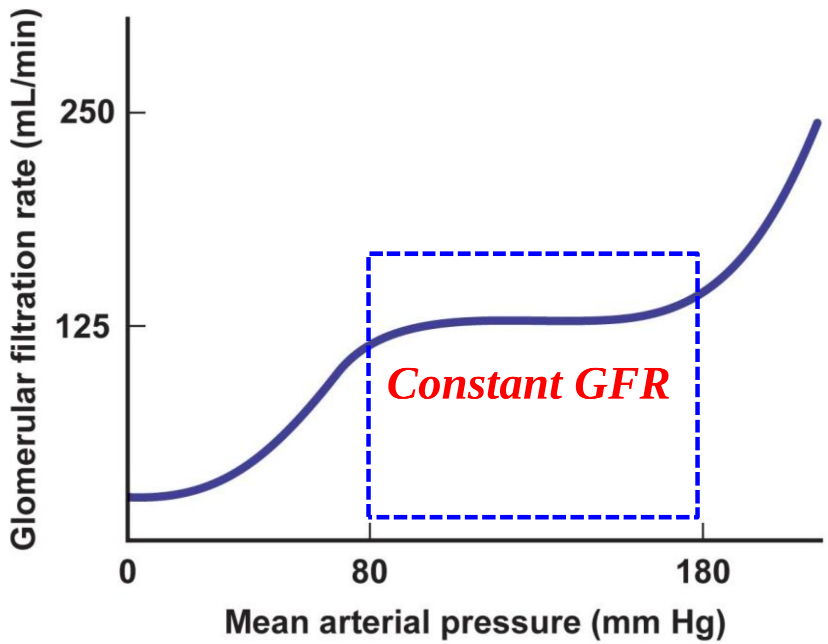
  - ➢Systemic increases in BP, stretch the afferent arteriole
  - ➢Smooth muscle contraction reduces the diameter of the arteriole returning the GFR to its previous level in seconds

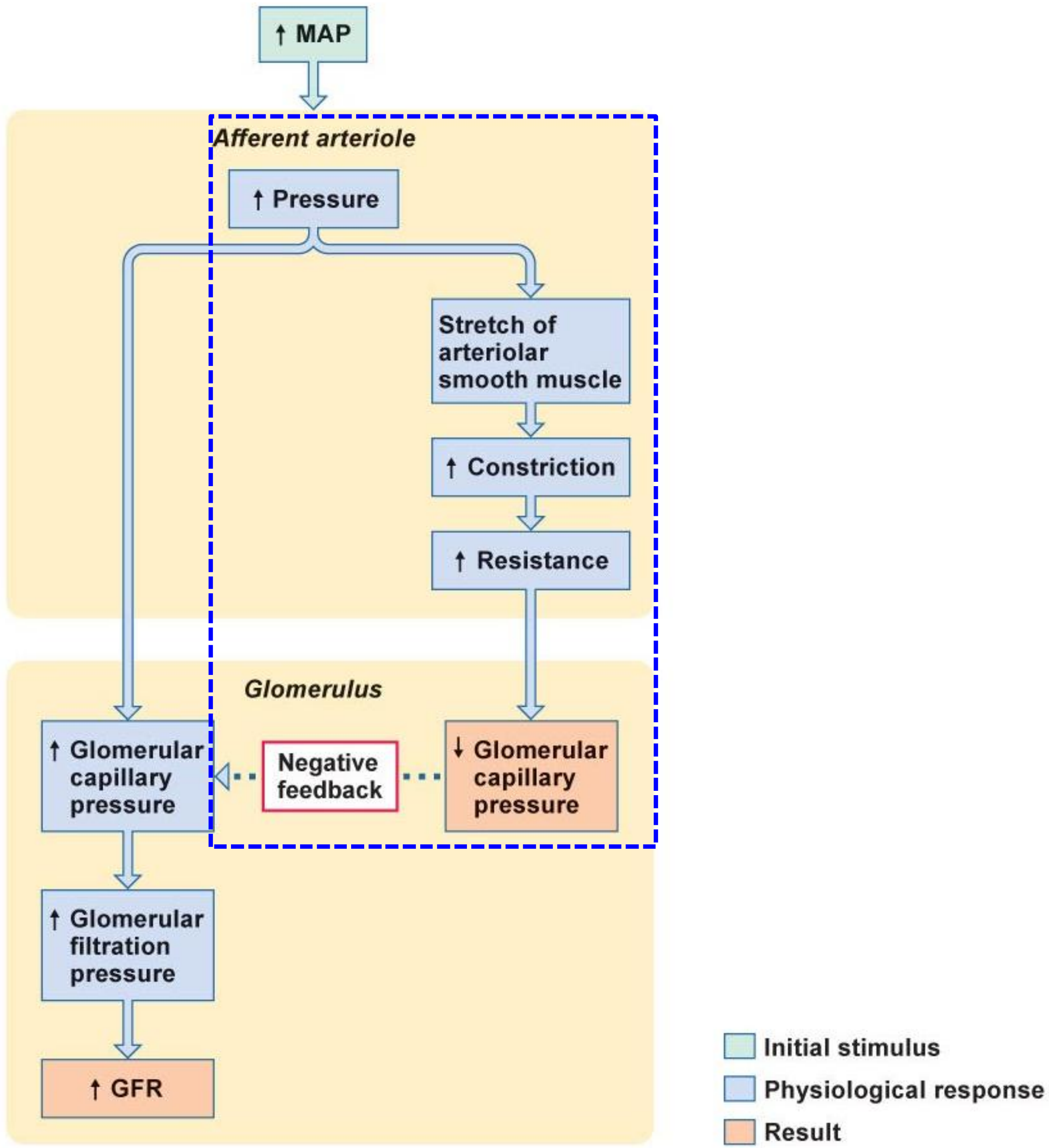
  --Tubuloglomerular feedback

  - ➢Elevated systemic BP raises the GFR so that fluid flows too rapidly through the renal tubule & Na^+, Cl^- and water are not reabsorbed
  - ➢Macula densa detects that difference & releases a vasoconstrictor (paracrine) from the juxtaglomerular apparatus
  - ➢Afferent arterioles constrict & reduce GFR

Renal Autoregulation of GFR

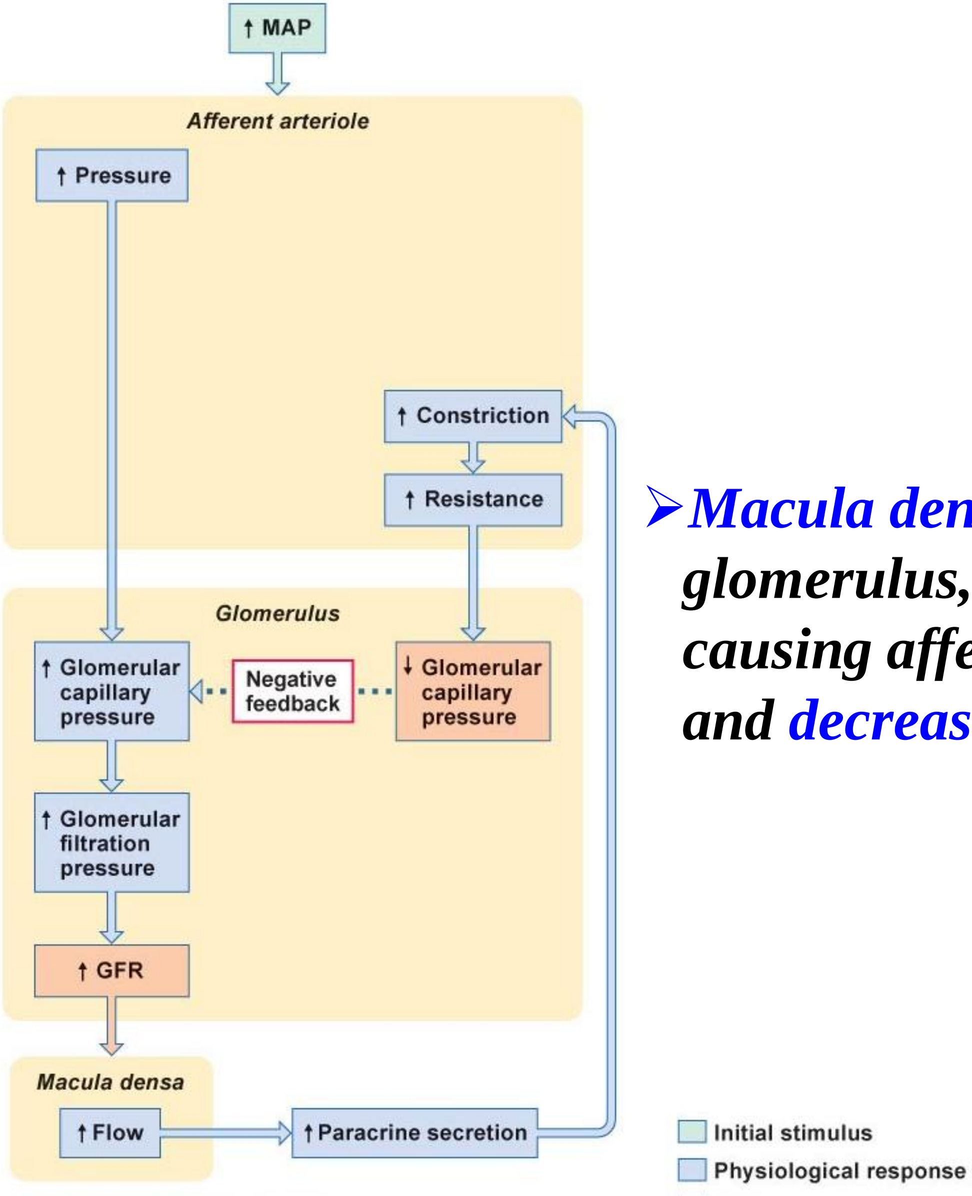
Myogenic Regulation





Renal Autoregulation of GFR

Tubuloglomerular feedback



(b) Tubuloglomerular feedback

- ***Macula densa* provides feedback to glomerulus, *inhibits release of NO* causing afferent arterioles to constrict and *decreasing GFR***

Extrinsic Regulation of GFR

Neural Regulation of GFR

- Blood vessels of the kidney are supplied by **sympathetic fibers** that cause ***vasoconstriction (NE) of afferent arterioles***
- **At rest**, renal BV are **maximally dilated** because sympathetic activity is minimal

  --***Renal autoregulation prevails***
- With **moderate sympathetic stimulation**, both afferent & efferent arterioles constrict equally

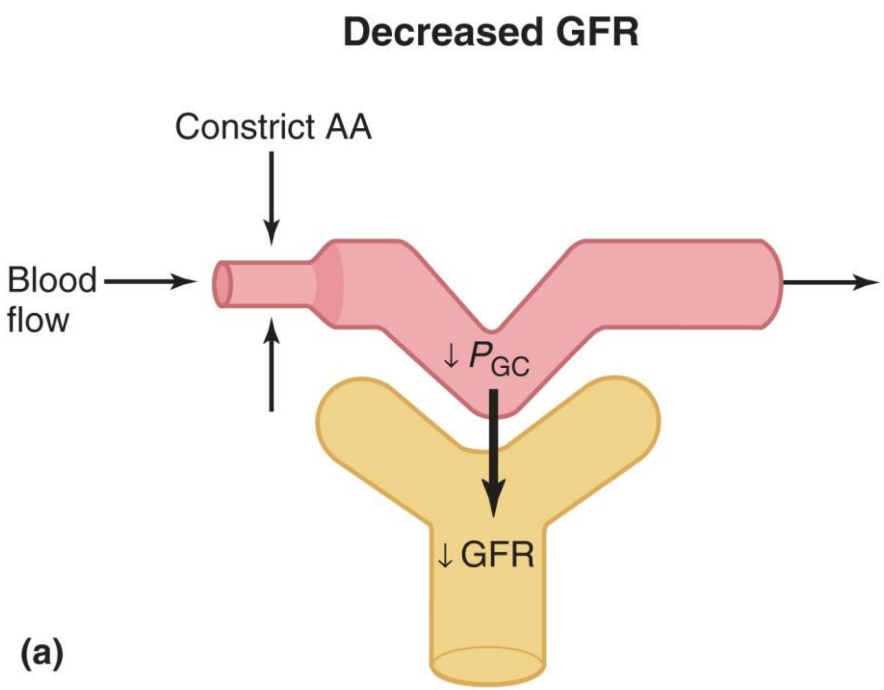
  --***Decreasing GFR equally***
- With **extreme sympathetic stimulation (exercise or hemorrhage)**, vasoconstriction of afferent arterioles

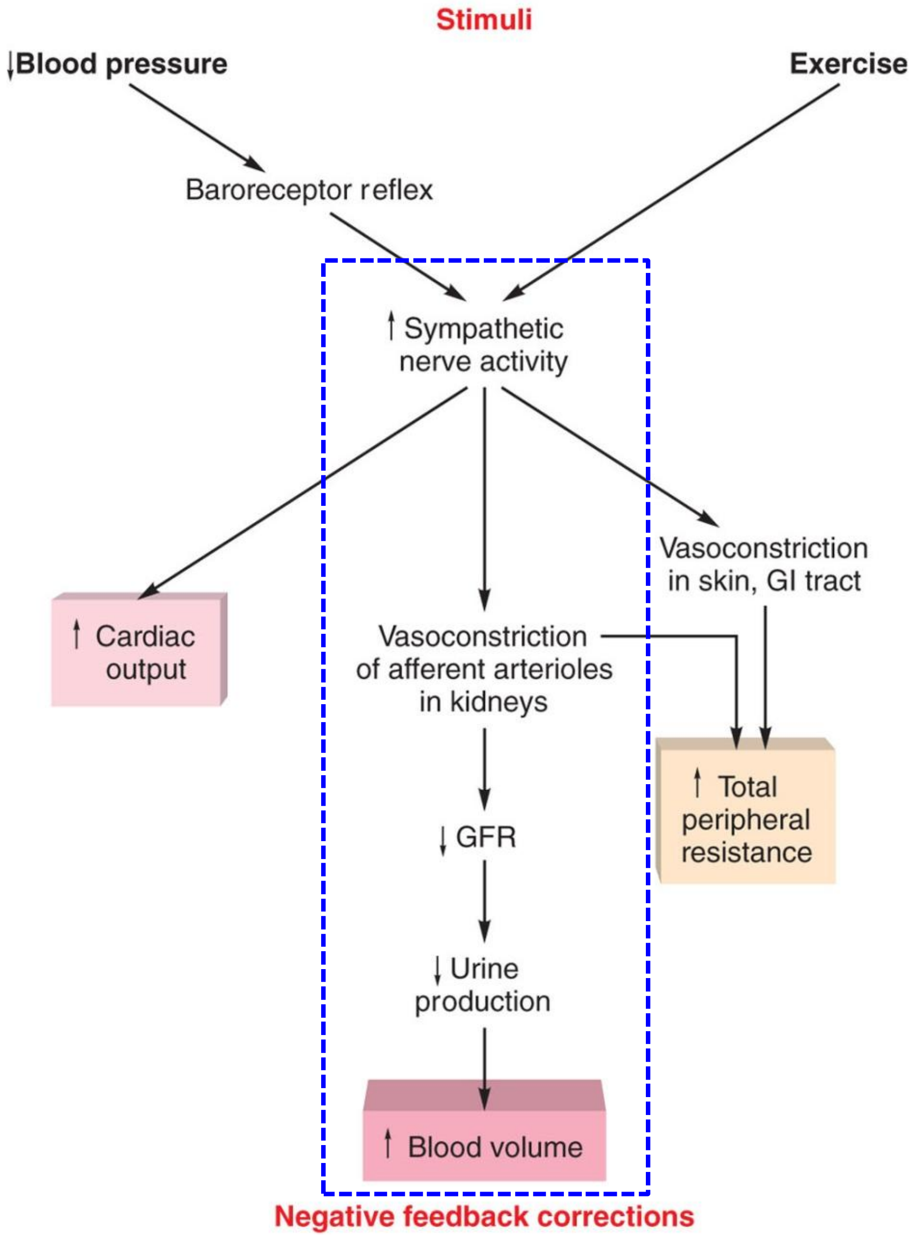
  --***Reduces GFR***

  --***Lowers urine output & permits blood flow to other tissues***

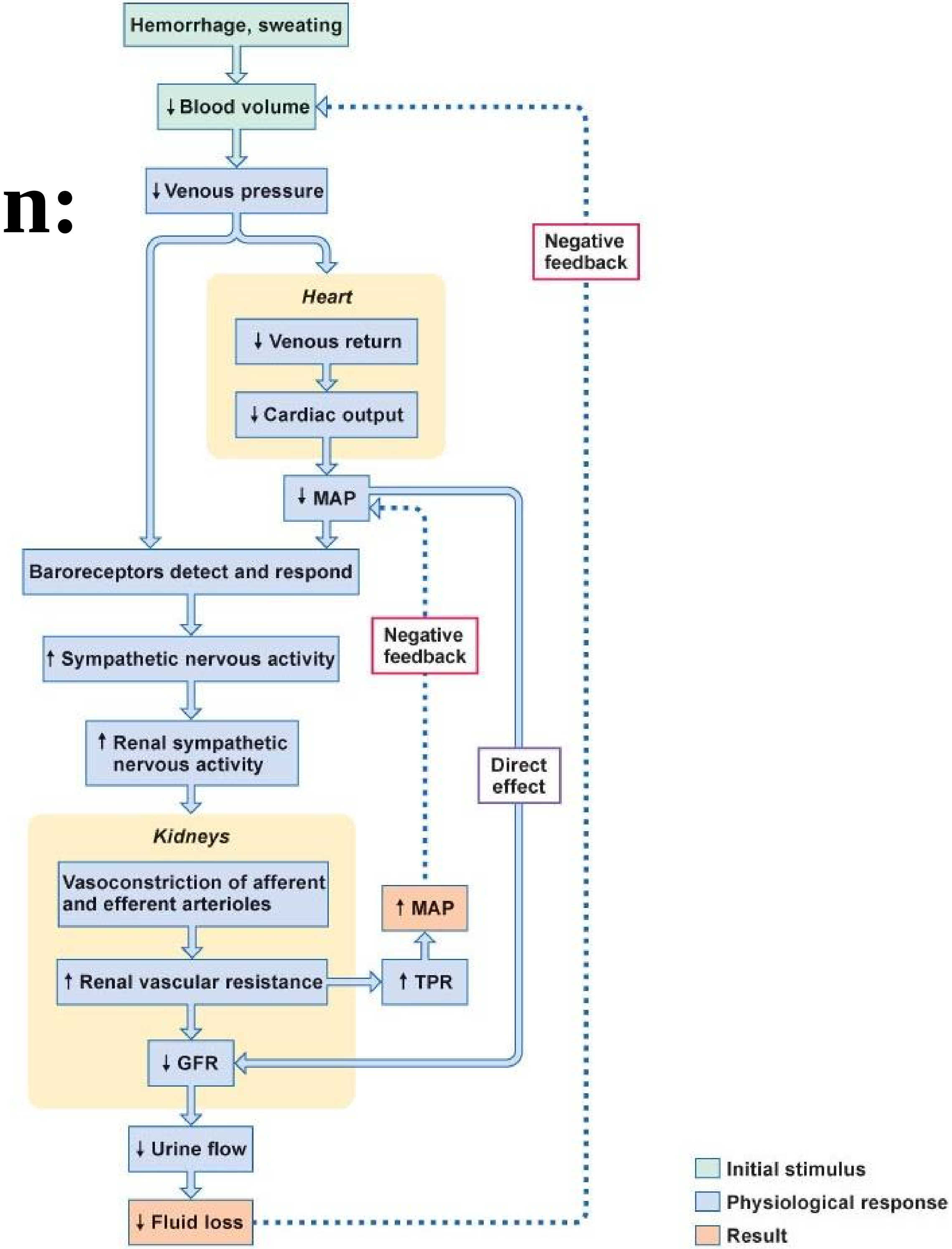
Extrinsic Regulation of GFR

Sympathetic Nerve Effects

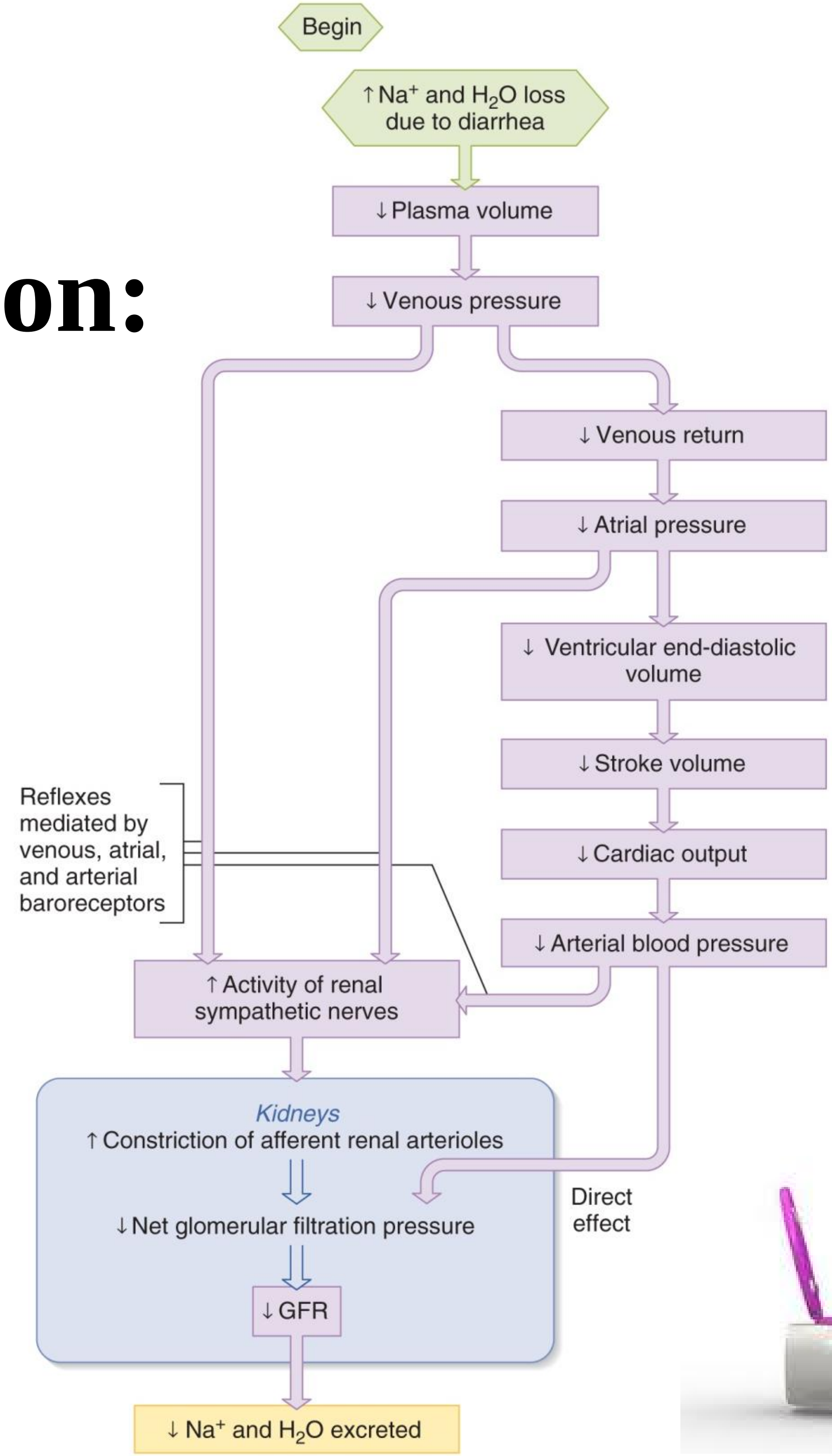




Clinical Application: Hemorrhage & Sweating



Clinical Application: Diarrhea



Hormonal Regulation of GFR

- **Atrial natriuretic peptide (ANP) <u>increases</u> GFR**

  --Stretching of the atria that occurs with an increase in blood volume causes hormonal release

  - Relaxes glomerular mesangial cells increasing capillary surface area → increasing GFR
  - AA dilation and EA constriction → increasing GFR

- **Angiotensin II & Epi <u>reduces</u> GFR**

  --Potent vasoconstrictor that narrows both afferent & efferent arterioles → reducing GFR

Regulation of GFR

TYPE OF REGULATION	MAJOR STIMULUS	MECHANISM AND SITE OF ACTION	EFFECT ON GFR
Renal autoregulation			
Myogenic mechanism	Increased stretching of smooth muscle fibers in afferent arteriole walls due to increased blood pressure.	Stretched smooth muscle fibers contract, thereby narrowing the lumen of the afferent arterioles.	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 the juxtaglomerular apparatus causes constriction of afferent arterioles.	Decrease.
Neural regulation	Increase in level of activity of renal sympathetic nerves releases norepinephrine.	Constriction of afferent arterioles through activation of α_1 receptors and increased release of renin.	Decrease.
Hormone regulation			
Angiotensin II	Decreased blood volume or blood pressure stimulates production of angiotensin II.	Constriction of both afferent and efferent arterioles.	Decrease.
Atrial natriuretic peptide (ANP)	Stretching of the atria of the heart stimulates secretion of ANP.	Relaxation of mesangial cells in glomerulus increases capillary surface area available for filtration.	Increase.

Tubular Reabsorption & Secretion

- **Reabsorption – return of most of the filtered water and many solutes to the bloodstream (movement from tubules into peritubular capillaries)**
  - --About **99%** of filtered water reabsorbed
  - --Most is **not regulated**
  - --**Proximal convoluted tubule cells** make largest contribution
    - ➢***Solutes** reabsorbed by **active & passive processes***
    - ➢***Water** follows by **osmosis***
    - ➢***Small proteins** by **pinocytosis***
- **Secretion – transfer of material from blood into tubular fluid**
  - --Helps control **blood pH** because of secretion of H^+
  - --Helps **eliminate certain substances** ($NH4^+$, creatinine, K^+)

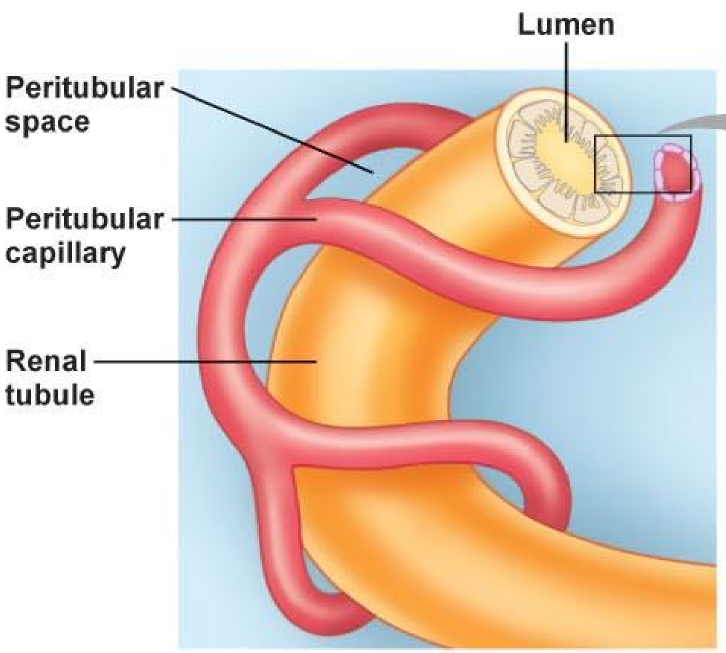
Normal Rates of Filtration and Reabsorption for Water and Solutes

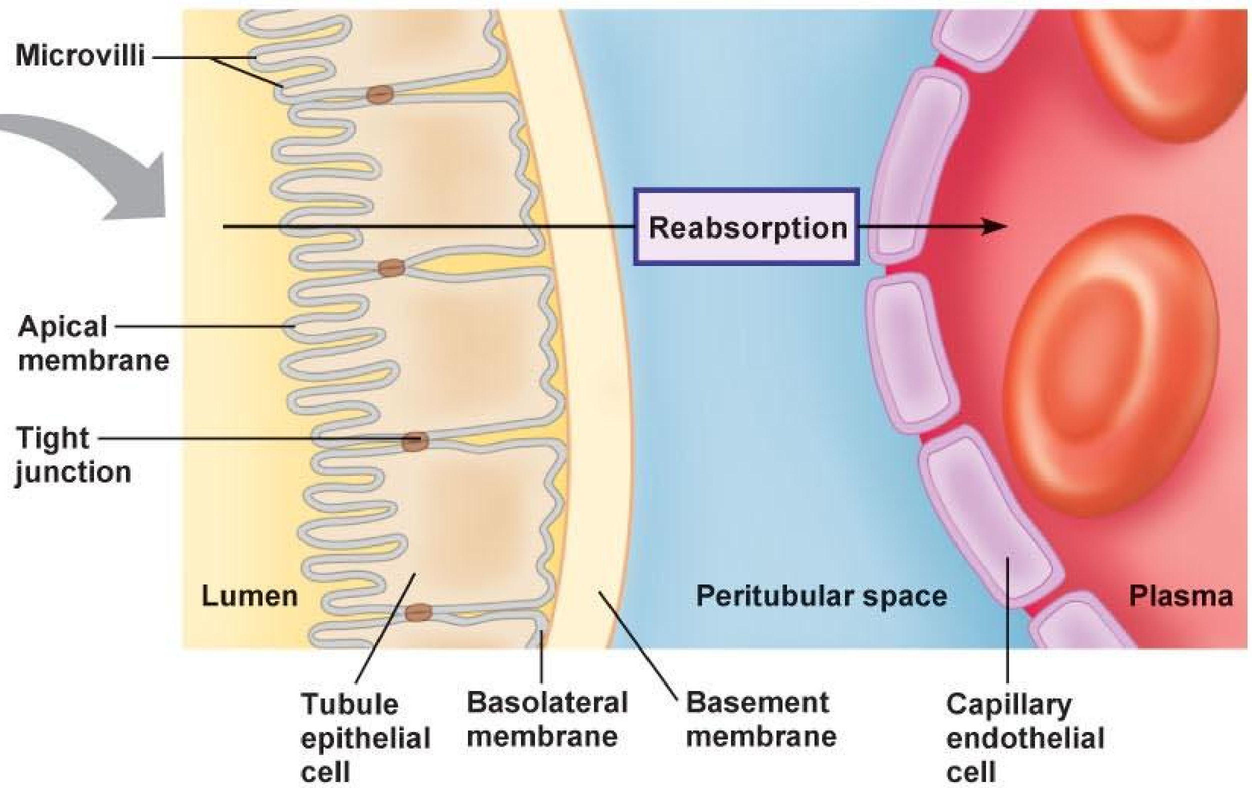
Substance	Filtration rate	Reabsorption rate	Percentage of filtered load reabsorbed
Water	180 liters/day	178.5 liters/day	99.2%
Glucose	800 millimoles/day	800 millimoles/day	100%
Urea	933 millimoles/day	467 millimoles/day	50%
Na^+	25.20 moles/day	25.05 moles/day	99.4%
K^+	720 millimoles/day	620 millimoles/day	86.1%
Ca^{2+}	540 millimoles/day	530 millimoles/day	98.1%
Cl^-	18.00 moles/day	17.85 moles/day	99.2%
HCO_3^-	4.320 moles/day	4.318 moles/day	$>$99.9%

Tubular Reabsorption

Reabsorption Barrier

Renal tubules → Peritubular capillaries





- **Solute Reabsorption**

  --Most occurs in **proximal convoluted tubule**

  --Some in distal convoluted tubule

  --**Barrier** for reabsorption

  Epithelial cells of renal tubules + Endothelial cells of capillary (minimal)

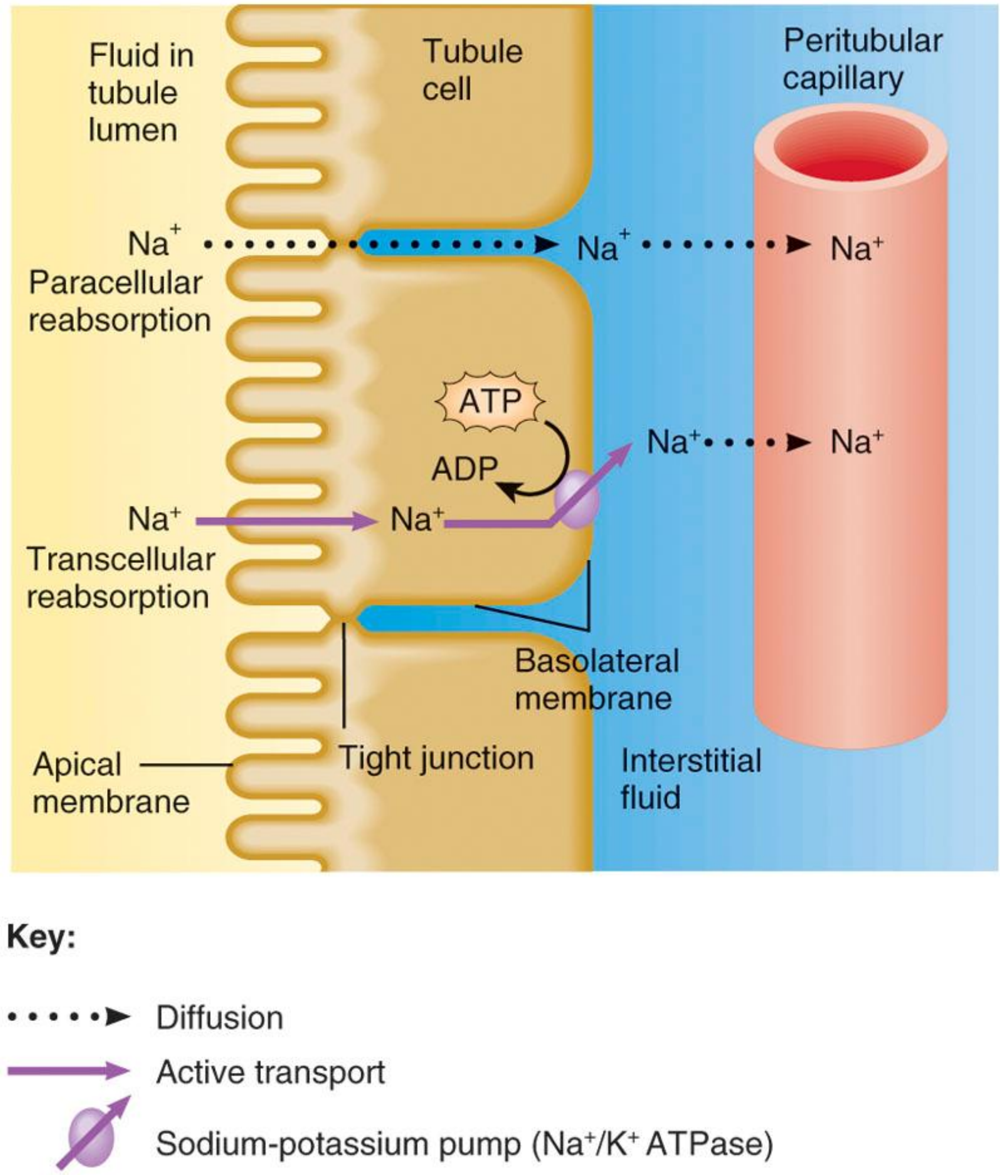
Reabsorption Routes

- **Paracellular reabsorption**

  --50% of reabsorbed material moves between cells (tight junction) by diffusion in some parts of tubule

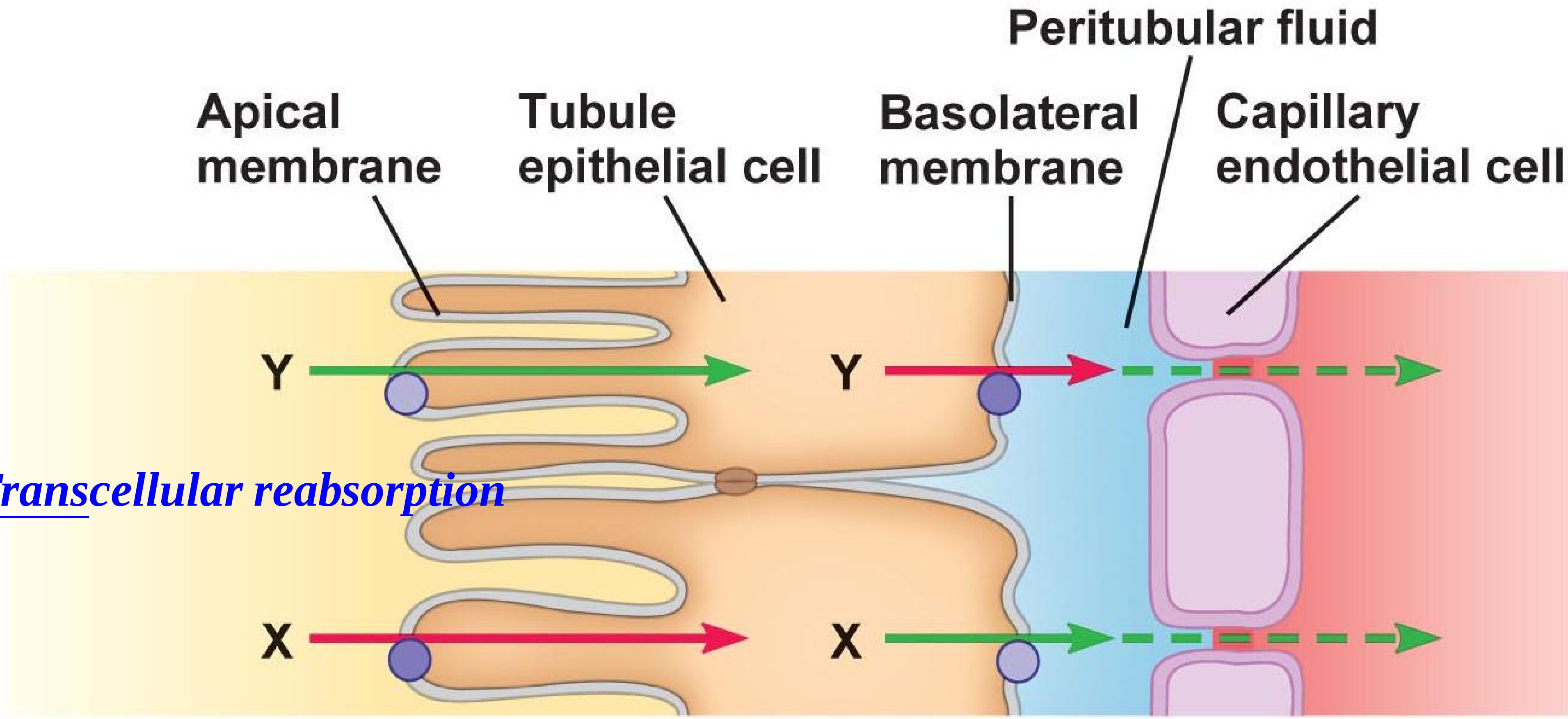
- **Transcellular reabsorption**

  --Material moves through both the apical and basal membranes of the tubule cell by active transport



Tubular Reabsorption

Active Solute (*Na*$^{+}$) Reabsorption/PCT

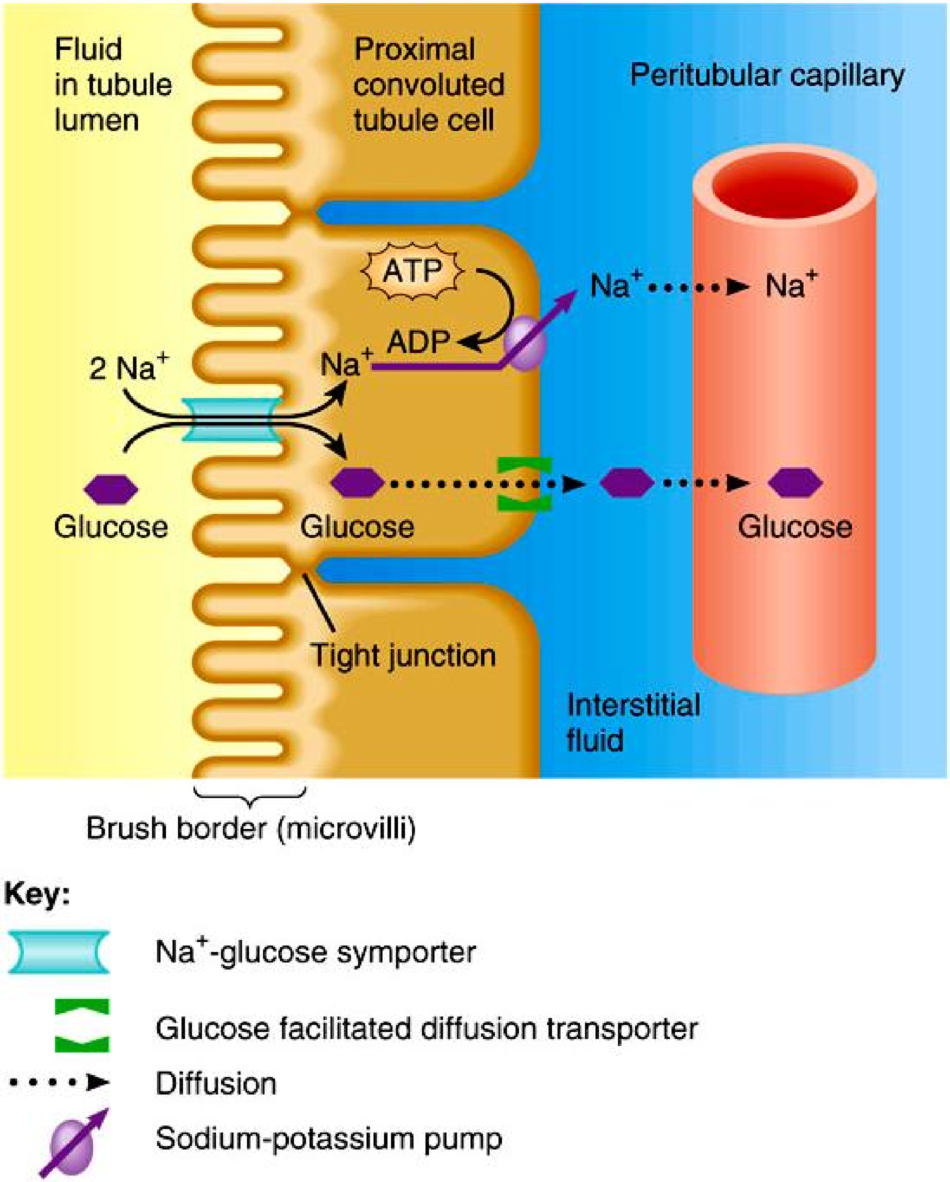


Transcellular reabsorption

- *Na*$^{+}$ ***is the most abundant cation in the filtrate***
- ***Reabsorption of*** *Na*$^{+}$ ***especially important (active transport)***
- ***Set up a concentration gradient to drive osmosis***

Tubular Reabsorption

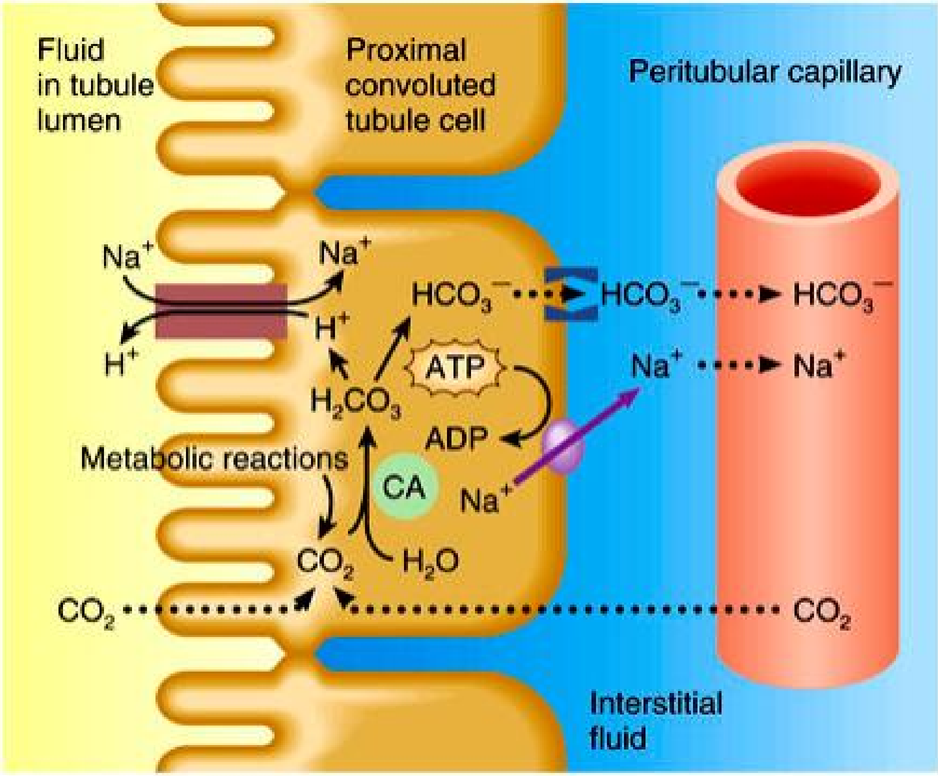
Active Solute (*Na^+ -Glu*) Reabsorption/PCT



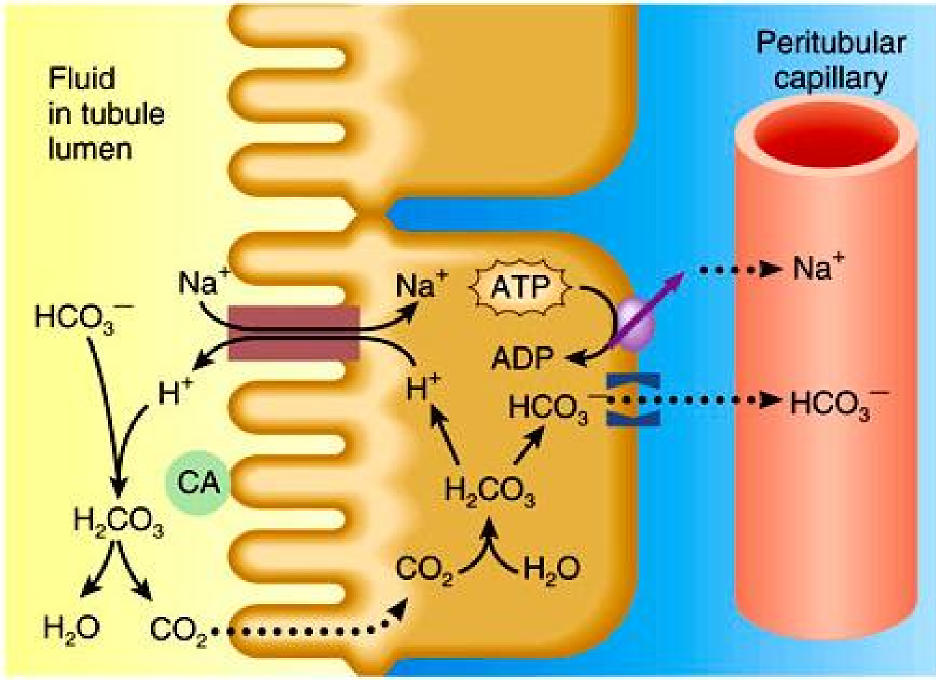
- **Most solute reabsorption involves Na⁺**
  - --***Symporters*** for ***glucose, amino acids, lactic acid, water-soluble vitamins, phosphate*** and ***sulfate***
  - --***Na^+ / H^+ antiporter*** causes Na^+ to be reabsorbed and H^+ to be secreted

Tubular Reabsorption

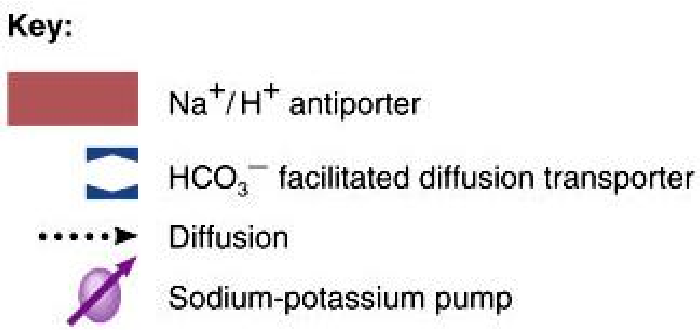
Active Solute (Na^+ -H^+) Reabsorption/PCT



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



(b) HCO_3^- reabsorption

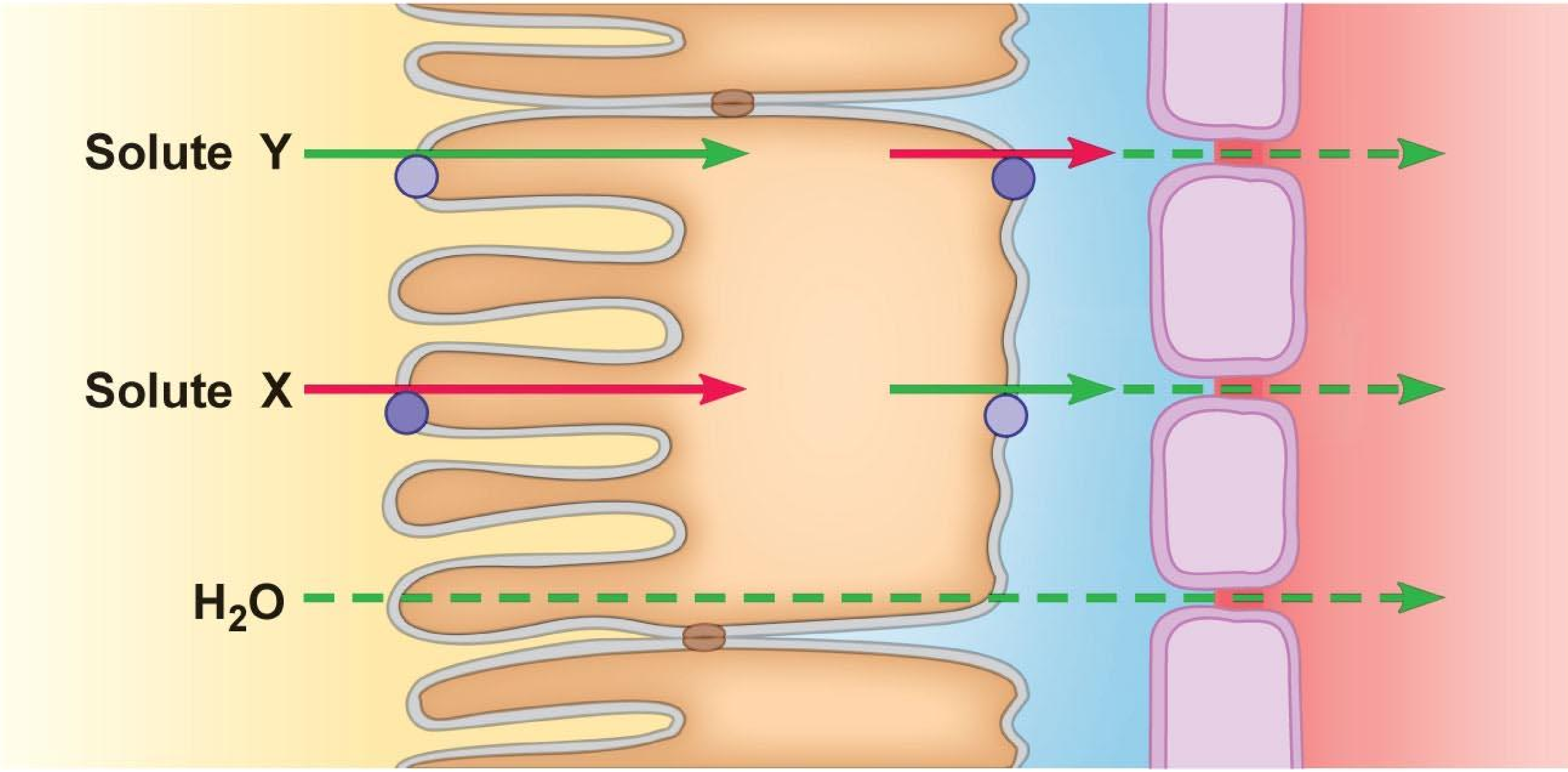


- PCT cells produce ***the H^+ & release bicarbonate ion*** to the peritubular capillaries
- ***Important buffering system***

CA: Carbonic Anhydrases

Tubular Reabsorption

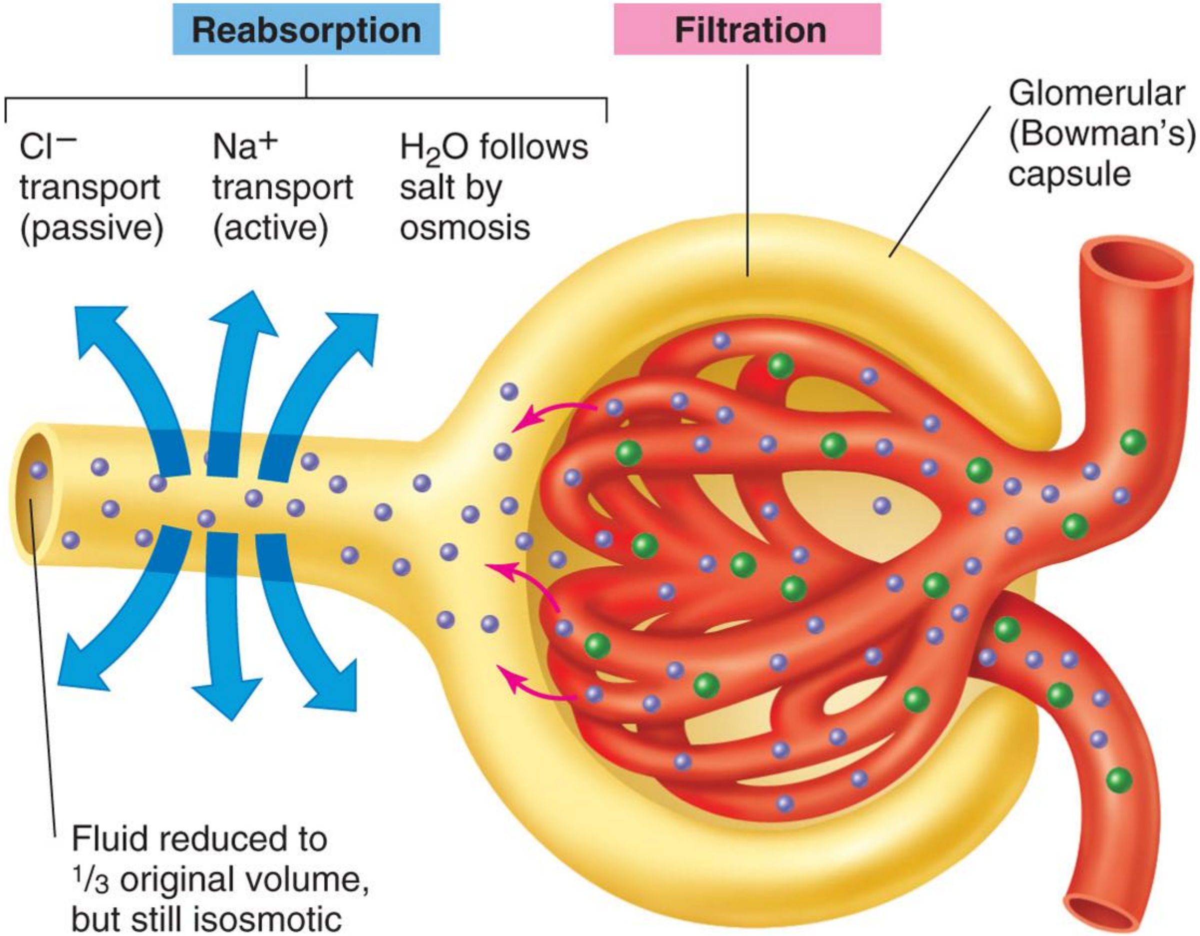
Passive Water Reabsorption/PCT



- ➢ *Na^+ concentration gradient (active)→ Cl^- reabsorption (passive) → Water reabsorption (osmosis--passive)*

Tubular Reabsorption

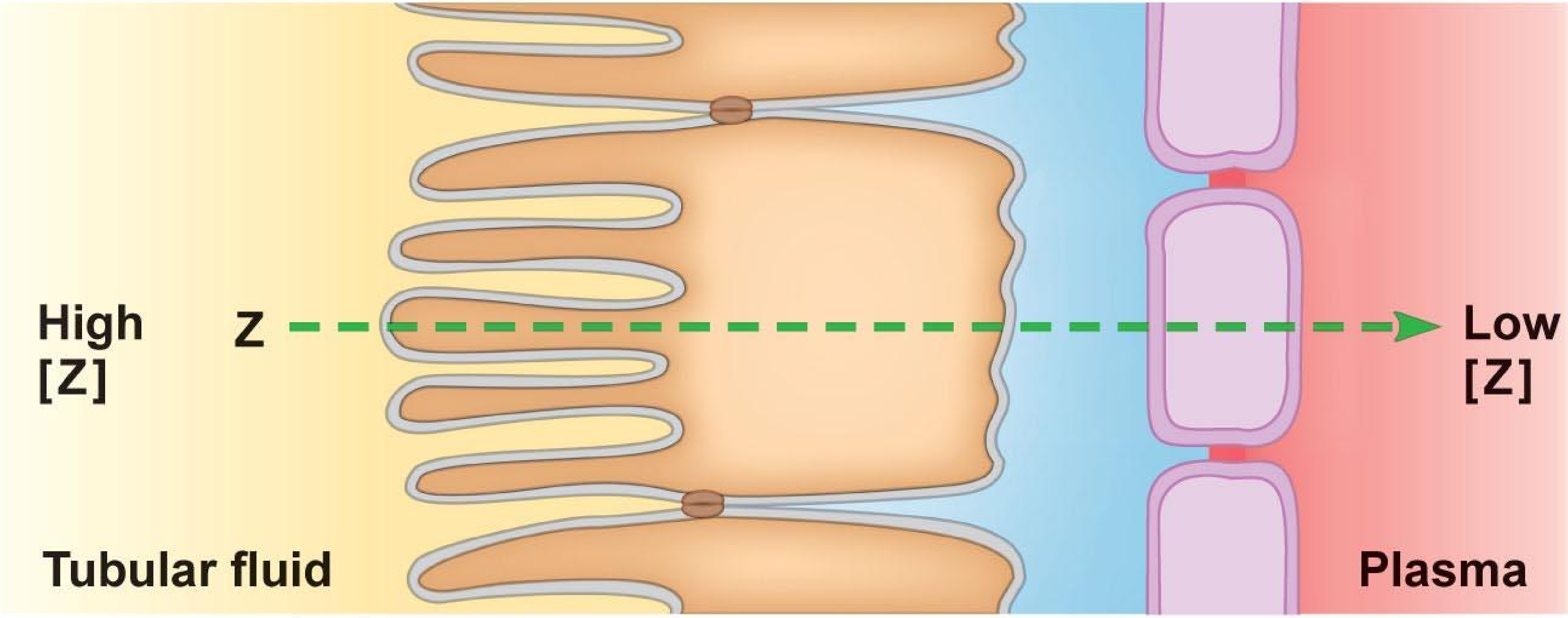
Passive Water Reabsorption/PCT



- ***Na^+ concentration gradient (active) → Cl^- reabsorption (passive) → Water reabsorption (osmosis--passive)***

Tubular Reabsorption

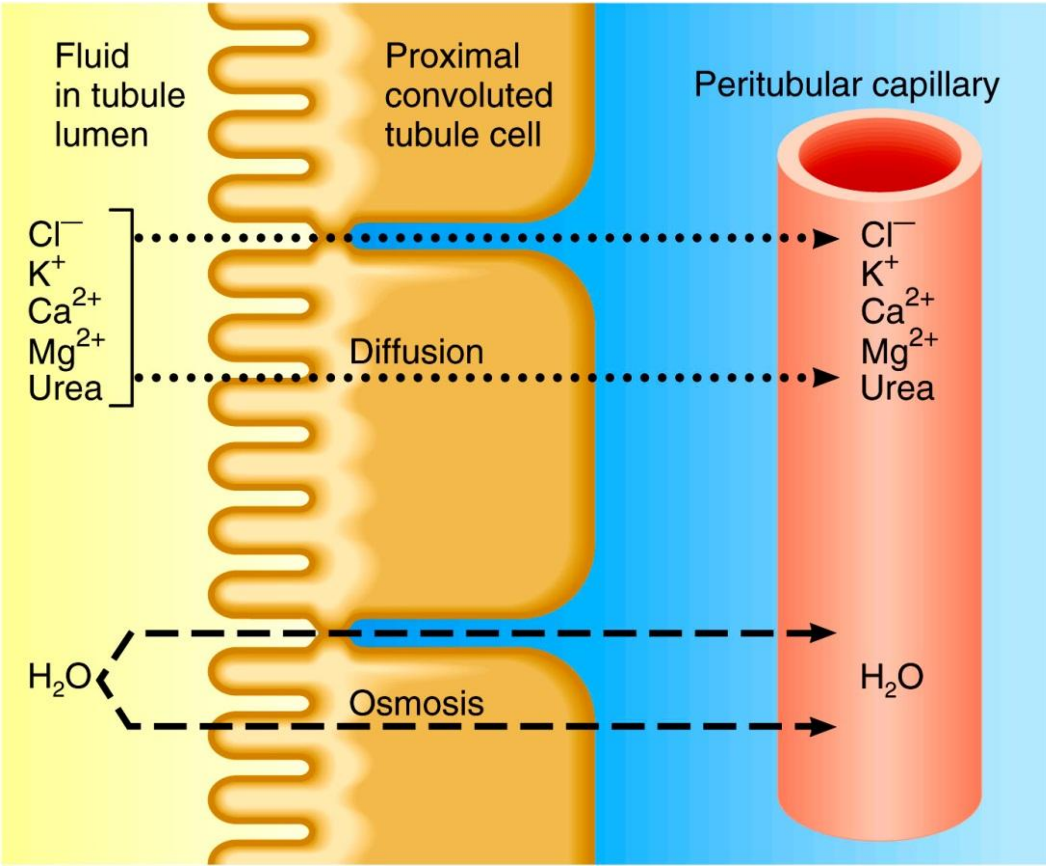
Passive Solute Reabsorption/PCT



- ***Passive solutes (Cl^-, K^+, urea etc.) reabsorption via diffusion***

Tubular Reabsorption

Passive Solute Reabsorption/PCT



- **Diffusion of Cl^-** into interstitial fluid via the **paracellular route** leaves tubular fluid more positive than interstitial fluid. This **electrical potential difference** promotes passive paracellular reabsorption of **Na^+, K^+, Ca^{+2}, and Mg^{+2}**

- ***Solute reabsorption promotes osmosis – creates osmotic gradient***
  - *--Aquaporin-1 in cells lining PCT and descending limb of loop of Henle*
  - *--As water leaves tubular fluid, solute concentration increases*
- ***Urea and ammonia in blood are filtered at glomerulus and secreted by proximal convoluted tubule cells***

Transport Maximum

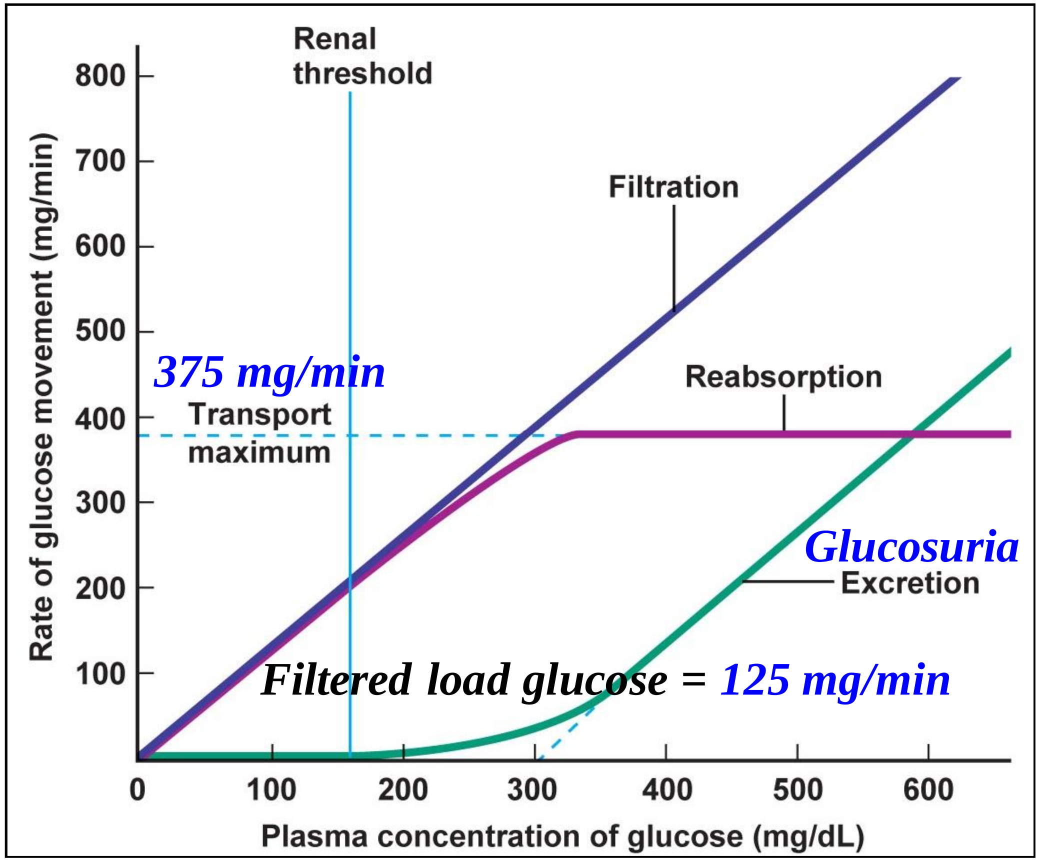
- Rate of transport when **carriers are saturated**
- When solute transported across epithelium by ***carrier protein***, saturation of carriers can occur
- **Renal Threshold**--For a solute which is normally 100% reabsorbed
  - --If solute in filtrate saturates carriers, then some solute excreted in urine
  - --Solute in plasma that causes solute in filtrate to saturate carriers and spillover into urine = renal threshold

➢ ***Theoretical renal threshold = 300 mg/dL***

(GFR × renal threshold = transport maximum)

➢ ***Actual renal threshold = 160–180 mg/dL***

Filtered load = 225 mg/min



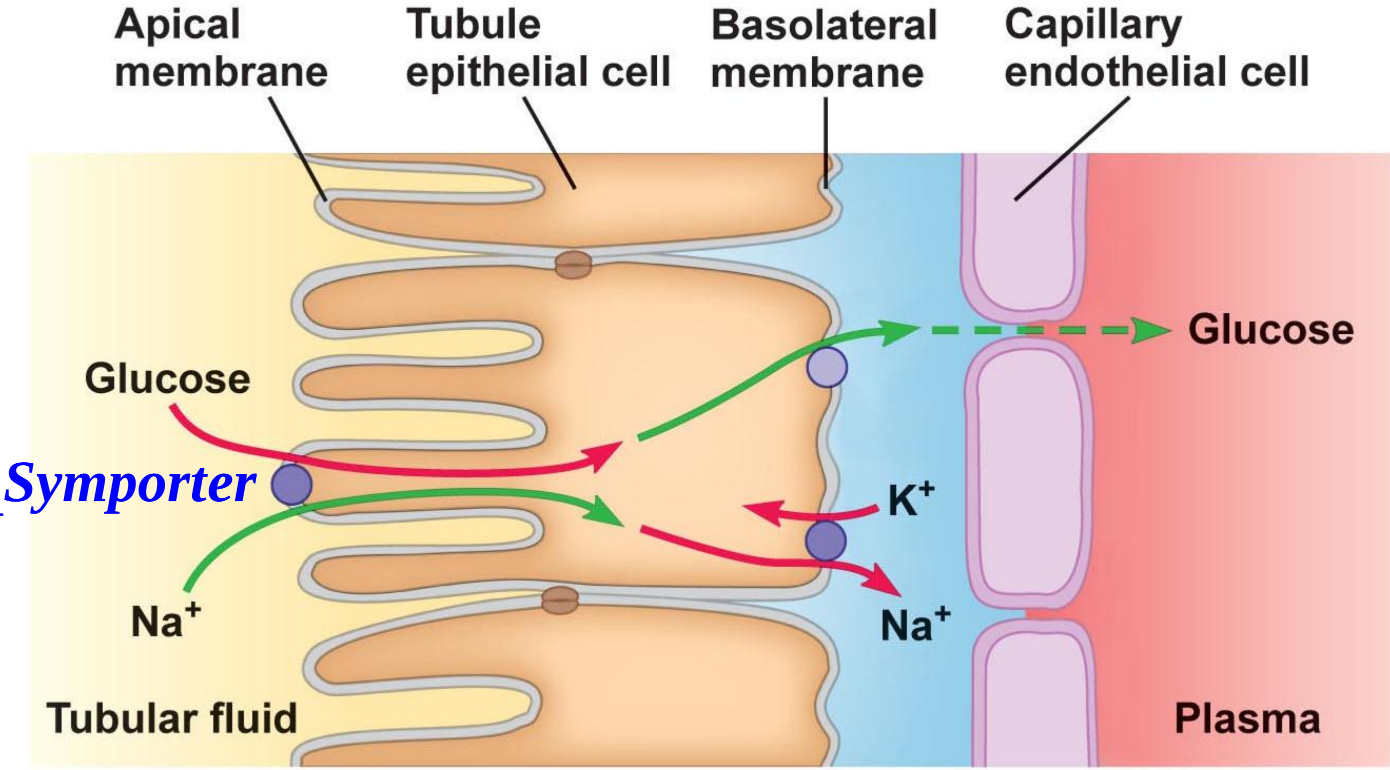
Plasma [glucose] = 100 mg/dL

Glucose Renal Curve

Transport Maximum: Glucose Reabsorption

- **Freely filtered** at glomerulus
- Normally **100% actively** reabsorbed in **proximal tubule**
- Normally, **no glucose** appears in urine

Na+ -Glu Symporter



- ***Carrier proteins for glucose reabsorption***

  --Apical membrane: secondary active transport

  --Basolateral membrane: facilitated diffusion

Tubular Reabsorption

Solute Reabsorption/Loop of Henle

- **Osmolarity still close to that of blood**

  --Reabsorption of water and solutes balanced

- **For the first time reabsorption of water is NOT automatically coupled to reabsorption of solutes**

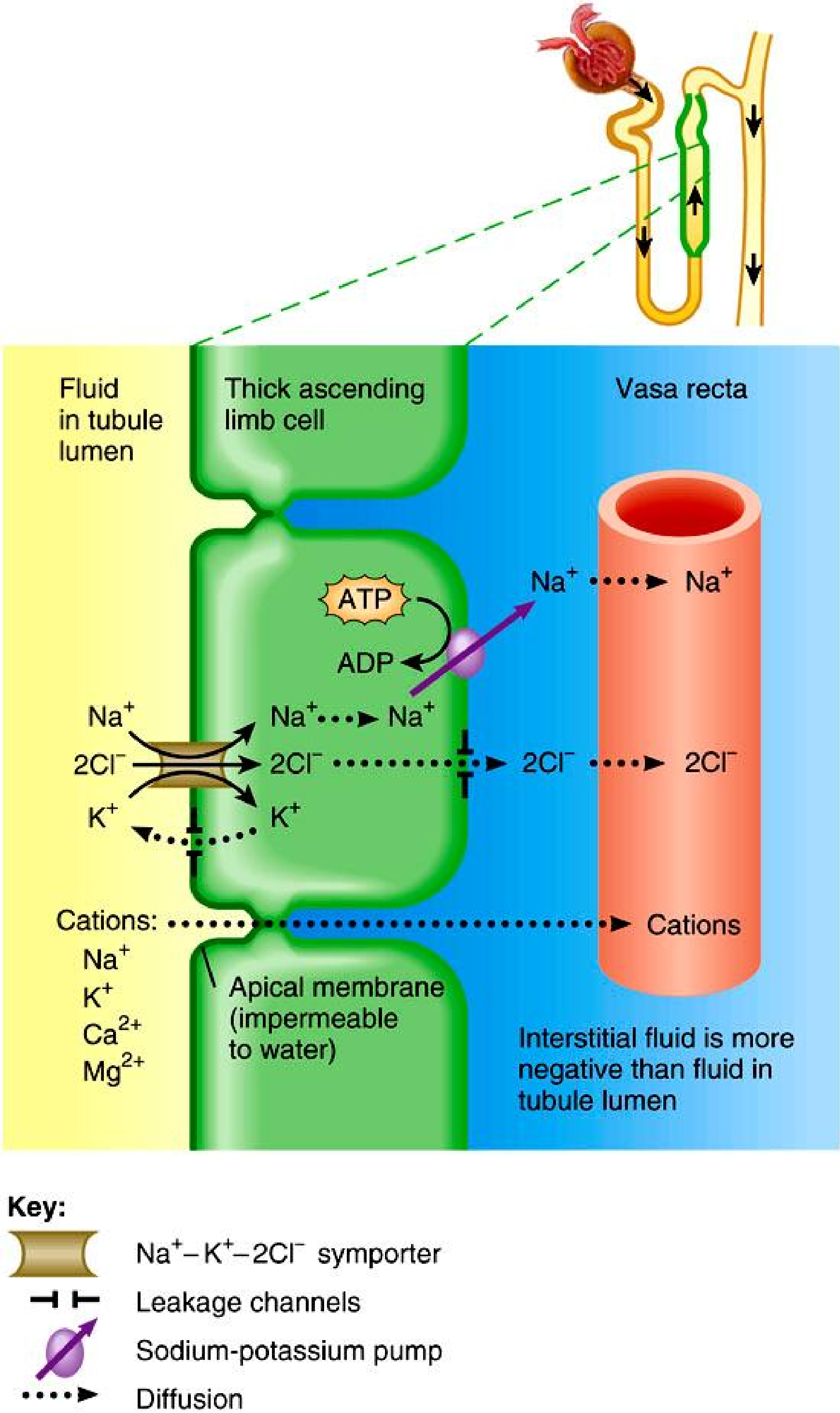
  --Independent regulation of both volume and osmolarity of body fluids

- **Na^+-K^+-$2Cl^-$ symporters** function in ***Na^+ and Cl^- reabsorption*** – promotes reabsorption of cations

- Although about **15%** of the filtered water is reabsorbed in the **descending limb (*Is not*** permeable to salt**)**, **little or no water is reabsorbed in ascending limb** – osmolarity decreases

Tubular Reabsorption

Solute Reabsorption/Loop of Henle



Na^+-K^+-$2Cl^-$ Symporter in Thick Ascending Limb of 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**

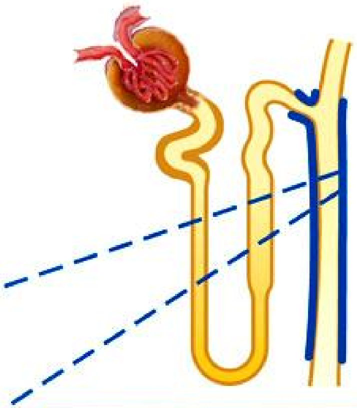
Tubular Reabsorption

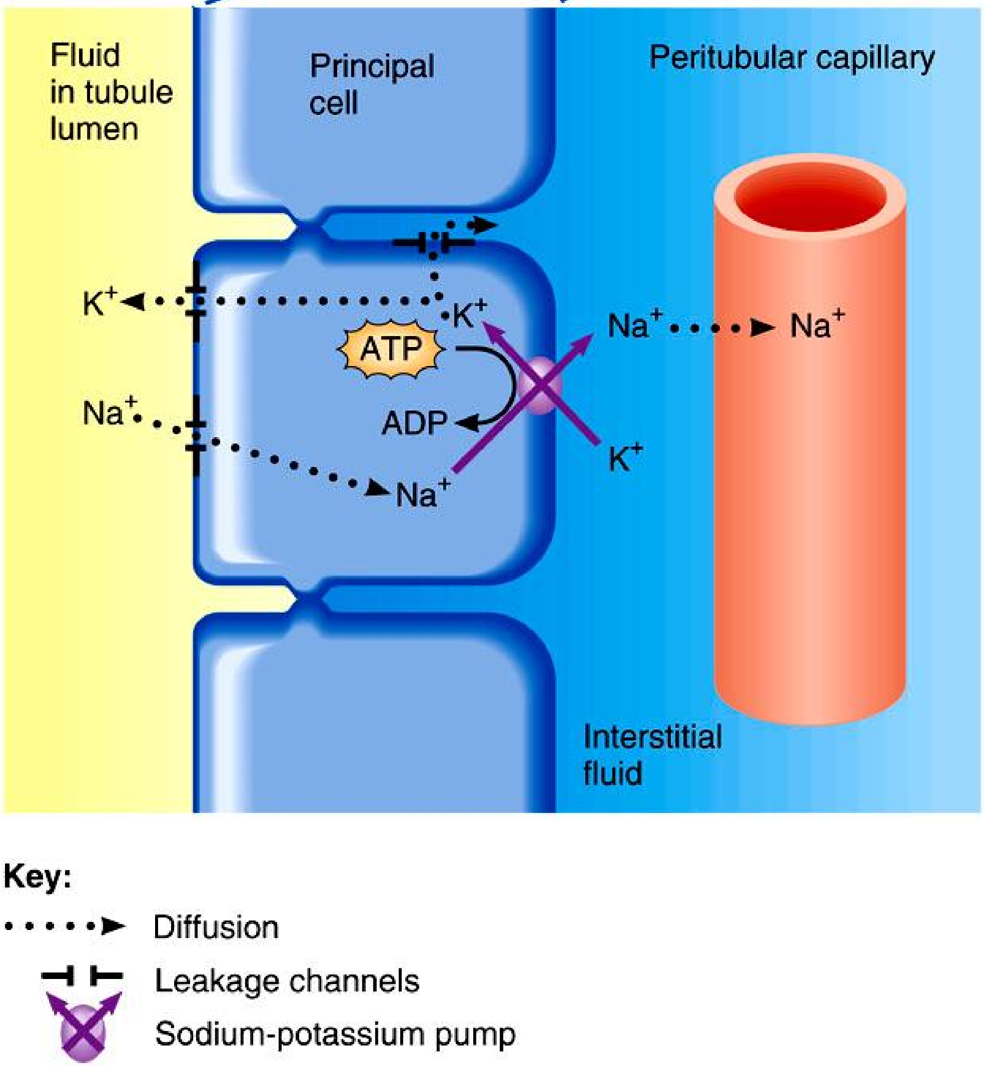
Solute Reabsorption/DCT & Collecting Duct

- Reabsorption on the **early distal convoluted tubule**
  - --***Na^+-Cl^- symporters*** reabsorb Na^+ and Cl^-
  - --Major site where ***parathyroid hormone (PTH)*** stimulates reabsorption of ***Ca^+*** depending on body's needs
  - --**early DCT** is not very permeable to ***water*** so the solutes are reabsorbed with little accompanying water
- Reabsorption and secretion in the **late distal convoluted tubule and collecting duct**
  - --**90-95%** of filtered solutes and fluid have been returned to the bloodstream
  - --**Principal cells** ***reabsorb Na^+ and secrete K^+***
  - --**Intercalated cells** ***reabsorb K^+ and HCO_3^- and secrete H^+***
  - --Amount of water reabsorption and solute reabsorption and secretion depends on body's needs

Actions of the Principal Cells/Collecting Duct

✓ ***Reabsorb Na⁺***
✓ ***Secrete K⁺***



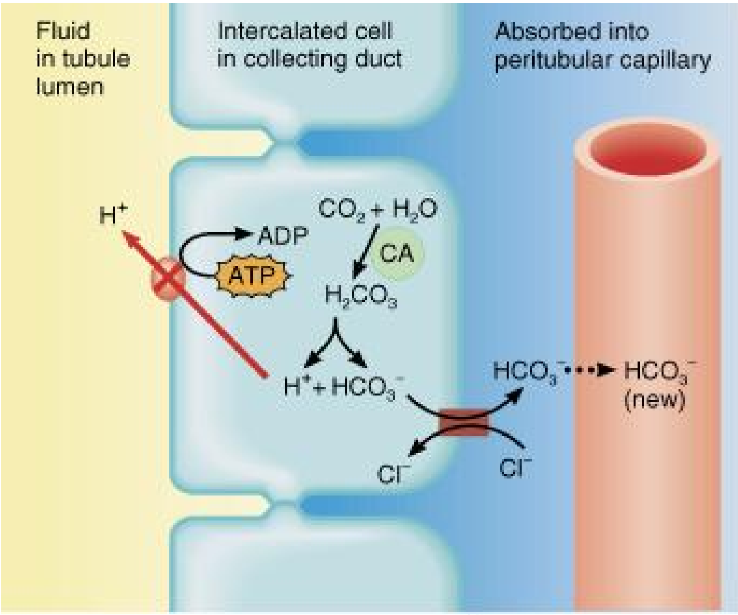


- Na^+ enters principal cells through ***leakage channels***
- ***Na^+ pumps*** keep the concentration of Na^+ in the cytosol low
- Cells secrete variable amounts of K^+, to adjust for ***dietary changes in K^+ intake***

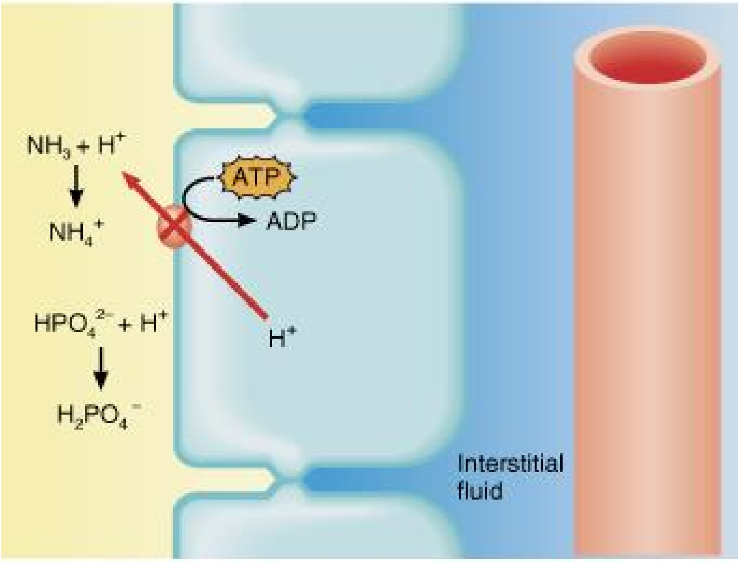
  --Down concentration gradient due to ***Na^+/K^+ pump***

- **Aldosterone increases *Na^+ and water reabsorption & K^+ secretion*** by principal cells by stimulating the synthesis of new pumps and channels

Secretion of H^+ and Absorption of Bicarbonate by Intercalated Cells/Collecting Duct



(a) Secretion of H^+

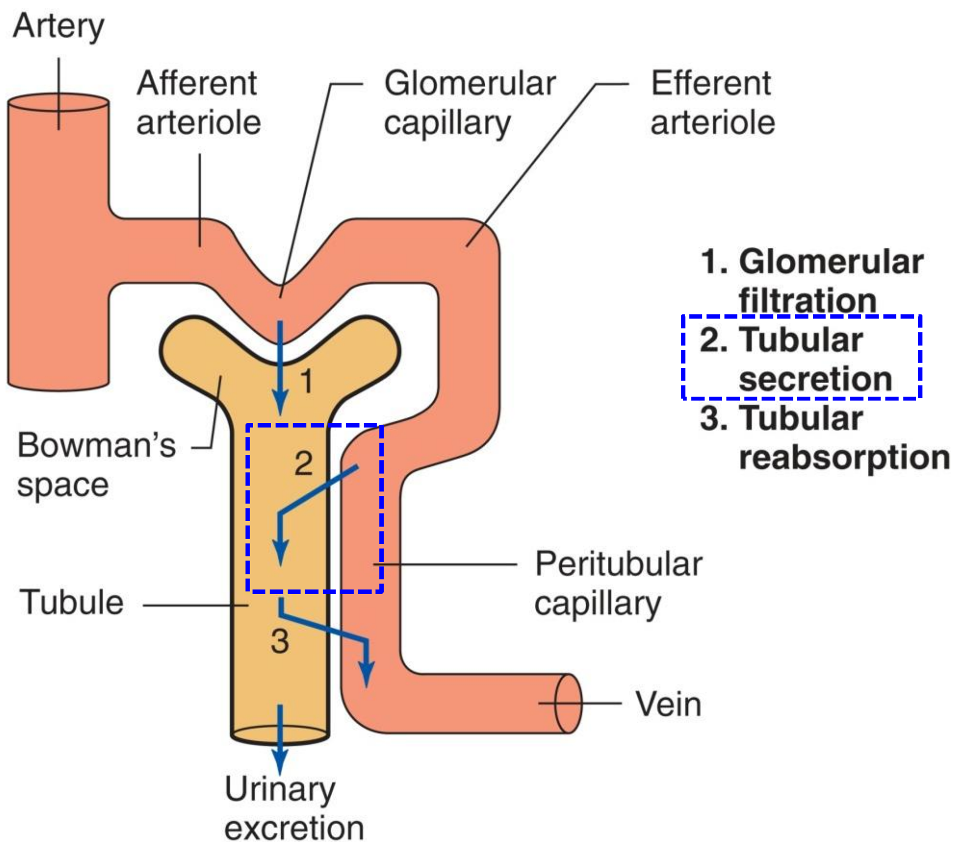


(b) Buffering of H^+ in urine

- ***Proton pumps (H^+ATPases)*** secrete H^+ into tubular fluid
  - --Can secrete against a concentration gradient so urine can be 1000 times ***more acidic*** than blood
- ***$Cl^-/HCO3^-$ antiporters*** move bicarbonate ions into the blood
  - --Intercalated cells help regulate ***pH of body fluids***
- Urine is buffered by ***HPO_4^{2-} and ammonia***, both of which combine irreversibly with H^+ and are excreted

Tubular Secretion

- Solutes move from **the peritubular capillaries into the tubular lumen**
- **Barriers (3) same** as for reabsorption
- Transport mechanisms same but **opposite direction**
- Secreted substances such as potassium, hydrogen ions, choline, creatinine, and penicillin etc.
- Tubular secretion is an important mechanism for:

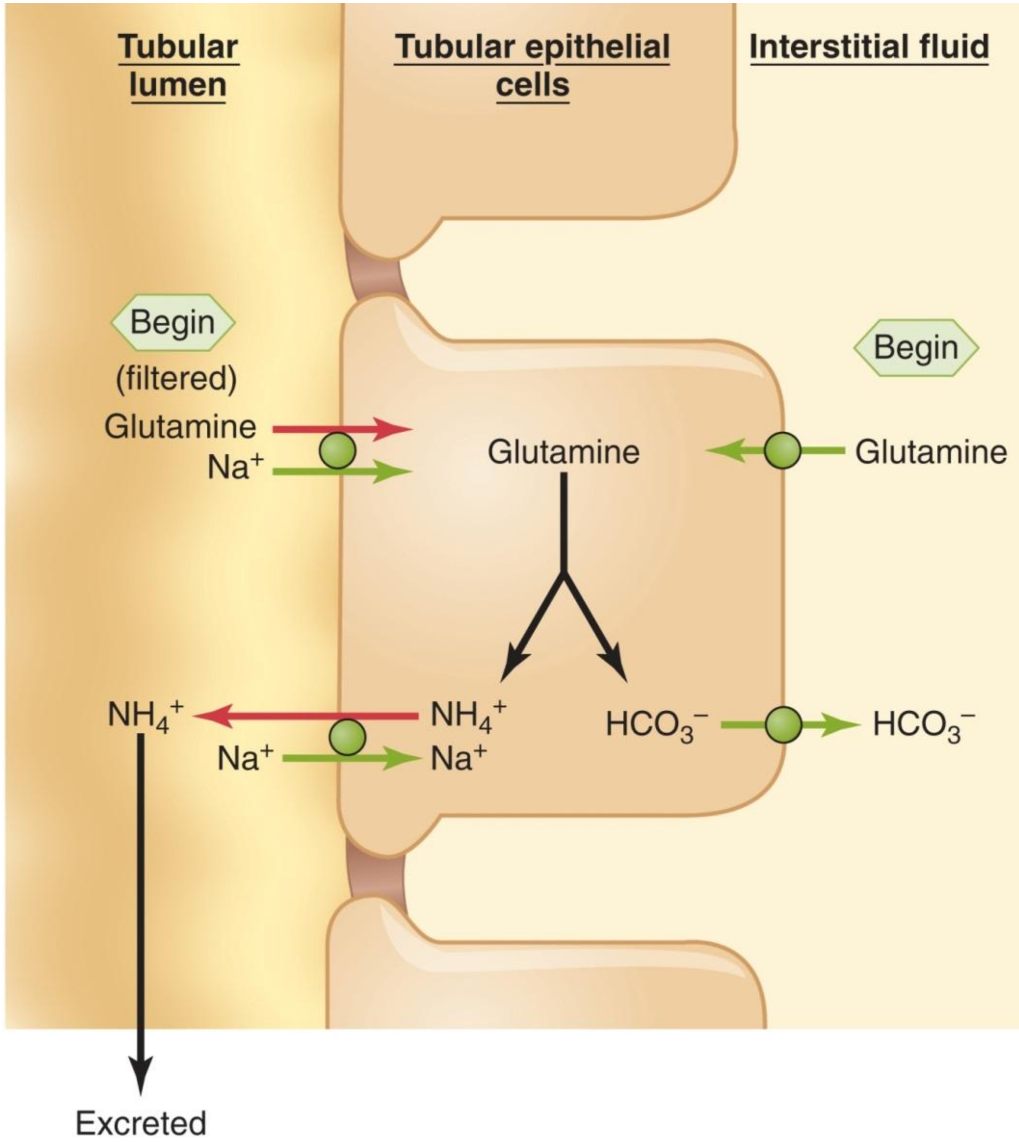


1. ***Disposing of drugs and drug metabolites***
2. ***Eliminating undesired substances or end products that have reabsorbed by passive processes (urea and uric acid)***
3. ***Removing excess K^+***
4. ***Controlling blood pH***

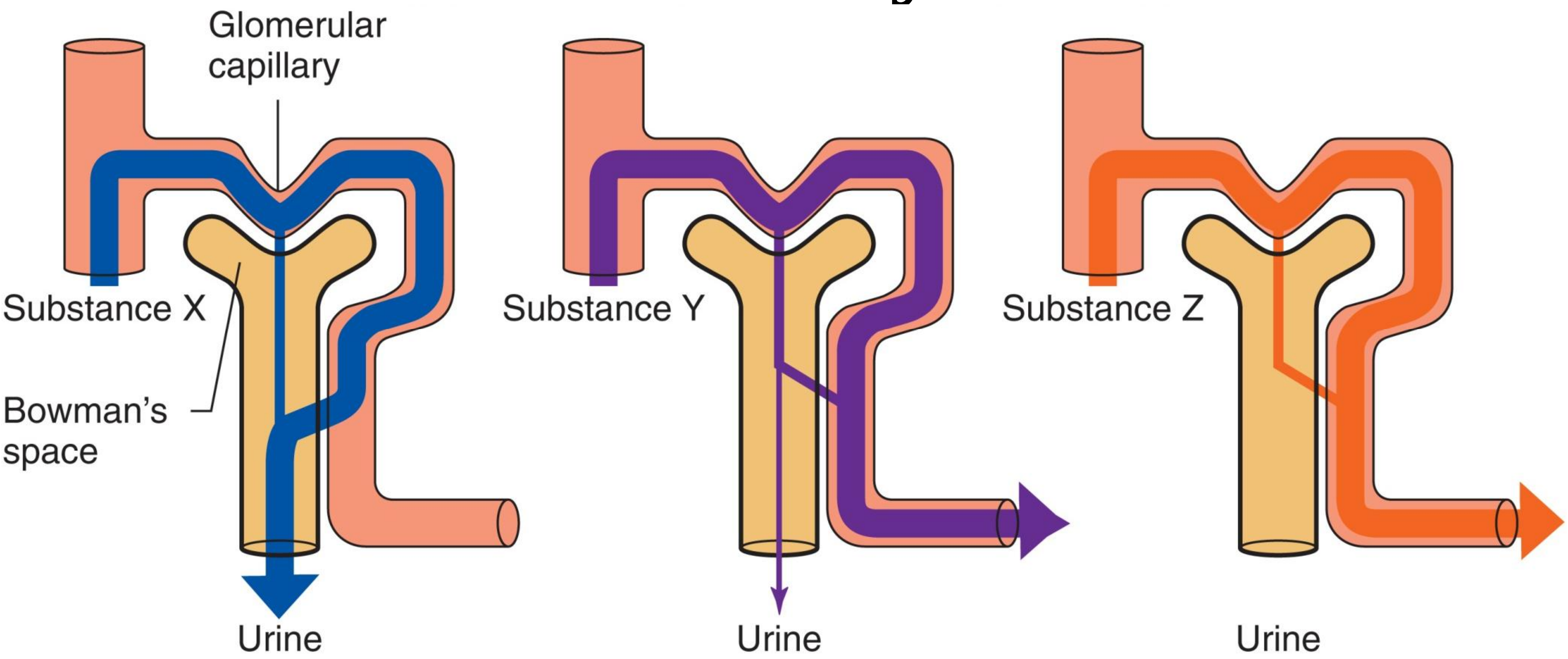
Tubular Secretion

Secretion of NH_3 and NH_4^+ /PCT

- **Urea and ammonia** in the blood are both filtered at the glomerulus and secreted by ***proximal convoluted tubule cells*** into the tubules
- The **deamination** of the amino acid ***glutamine by PCT cells*** generates both **NH_3 and new HCO_3^-**
- At the pH inside tubule cells, most NH_3 quickly binds to H^+ and becomes **NH_4^+**
- NH_4^+ can substitute for H^+ aboard **Na^+/H^+ antiporters** and be secreted into tubular fluid
- **Na^+/HCO_3^- symporters** provide a route for reabsorbed Na^+ and newly formed HCO_3^- to enter the bloodstream



Differential Handling in the Kidney



- ➢ *Substance X is filtered and secreted but not reabsorbed*
- ➢ *Substance Y is filtered and some of it is reabsorbed*
- ➢ *Substance Z is filtered and completely reabsorbed*

Regional Specialization of Renal Tubules

Tubule segment	Substances reabsorbed		Substances secreted
Proximal tubule	Na^+	Glucose	H^+
	Cl^-	Amino acids	
	K^+	Vitamins	
	Ca^{2+}	Urea	
	HCO_3^-	Choline	
	Water		
Loop of Henle (descending limb)	Water		
Loop of Henle (ascending limb)	Na^+	Mg^{2+}	
	Cl^-	Ca^{2+}	
	K^+		
Distal tubule	Na^+		K^+
	Ca^{2+}		H^+
	Cl^-		
	Water		
Collecting duct	Na^+	HCO_3^-	K^+
	K^+	H^+	H^+
	Cl^-	Urea	
	Ca^{2+}	Water	

- **Non-regulated reabsorption in proximal tubule**
  - --70% water and sodium
  - --100% glucose
- **Regulated reabsorption and secretion in the distal tubule and collecting duct**
- **Water conservation (concentrate urine) in the loop of Henle**

Summary

PROXIMAL CONVOLUTED TUBULE

Reabsorption (into blood) of filtered:

Water	65% (osmosis)
Na^+	65% (sodium-potassium pumps, symporters, antiporters)
K^+	65% (diffusion)
Glucose	100% (symporters and facilitated diffusion)
Amino acids	100% (symporters and facilitated diffusion)
Cl^-	50% (diffusion)
HCO_3^-	80–90% (facilitated diffusion)
Urea	50% (diffusion)
Ca^{2+}, Mg^{2+}	variable (diffusion)

Secretion (into urine) of:

H^+	variable (antiporters)
NH_4^+	variable, increases in acidosis (antiporters)
Urea	variable (diffusion)
Creatinine	small amount

At end of PCT, tubular fluid is still isotonic to blood (300 mOsm/liter).

LOOP OF HENLE

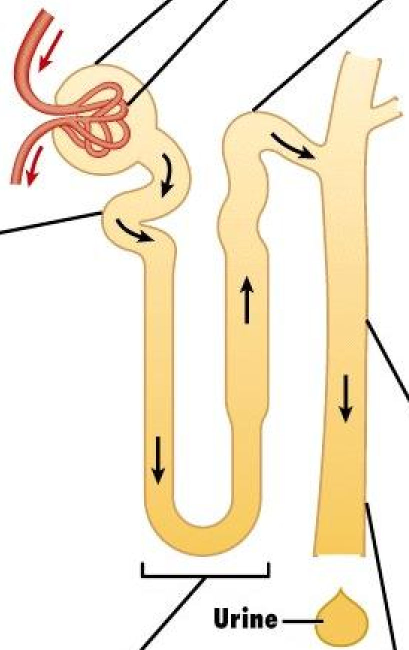
Reabsorption (into blood) of:

Water	15% (osmosis in descending limb)
Na^+	20–30% (symporters in ascending limb)
K^+	20–30% (symporters in ascending limb)
Cl^-	35% (symporters in ascending limb)
HCO_3^-	10–20% (facilitated diffusion)
Ca^{2+}, Mg^{2+}	variable (diffusion)

Secretion (into urine) of:

Urea	variable (recycling from collecting duct)

At end of loop of Henle, tubular fluid is hypotonic (100–150 mOsm/liter).



RENAL CORPUSCLE

Glomerular filtration rate: 105–125 mL/min of fluid that is isotonic to blood

Filtered substances: water and all solutes present in blood (except proteins) including ions, glucose, amino acids, creatinine, uric acid

DISTAL CONVOLUTED TUBULE

Reabsorption (into blood) of:

Water	10–15% (osmosis)
Na^+	5% (symporters)
Cl^-	5% (symporters)
Ca^{2+}	variable (stimulated by parathyroid hormone)

PRINCIPAL CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT

Reabsorption (into blood) of:

Water	5–9% (insertion of water channels stimulated by ADH)
Na^+	1–4% (sodium-potassium pumps)
Urea	variable (recycling to loop of Henle)

Secretion (into urine) of:

K^+	variable amount to adjust for dietary intake (leakage channels)

Tubular fluid leaving the collecting duct is dilute when ADH level is low and concentrated when ADH level is high.

INTERCALATED CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT

Reabsorption (into blood) of:

HCO_3^- (new)	varible amount, depends on H^+ secretion (antiporters)
Urea	variable (recycling to loop of Henle)

Secretion (into urine) of:

H^+	variable amounts to maintain acid-base homeostasis (H^+ pumps)

Hormonal Regulation of Tubular Reabsorption and Secretion

- **Angiotensin II (AII) - when blood volume and BP decrease**

  --Decreases GFR (vasoconstricting AA)

  --Promotes aldosterone production (sti. RAA System)

  --Enhances reabsorption of Na^+, Cl^- and water in PCT

- **Aldosterone - when blood volume and BP decrease**

  --Stimulates ***principal cells in collecting duct*** to ***reabsorb more Na^+, Cl^- and water, and secrete more K^+ and H^+***

- **Atrial natriuretic peptide (ANP) - when blood volume and BP increase**

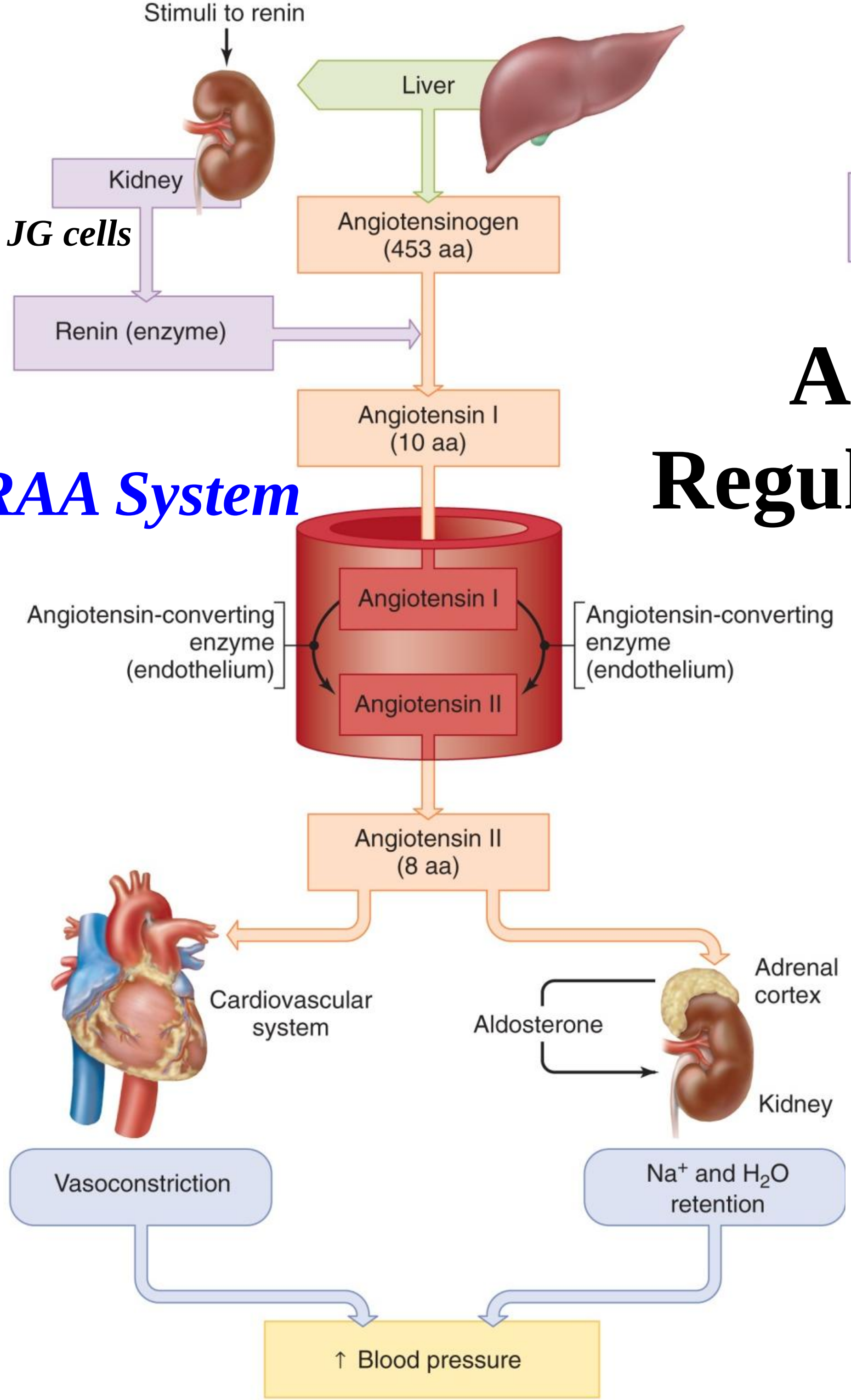
  --Inhibits reabsorption of Na^+ and water in PCT & suppresses secretion of aldosterone & ADH

  --Increase excretion of Na^+ which increases urine output and decreases blood volume

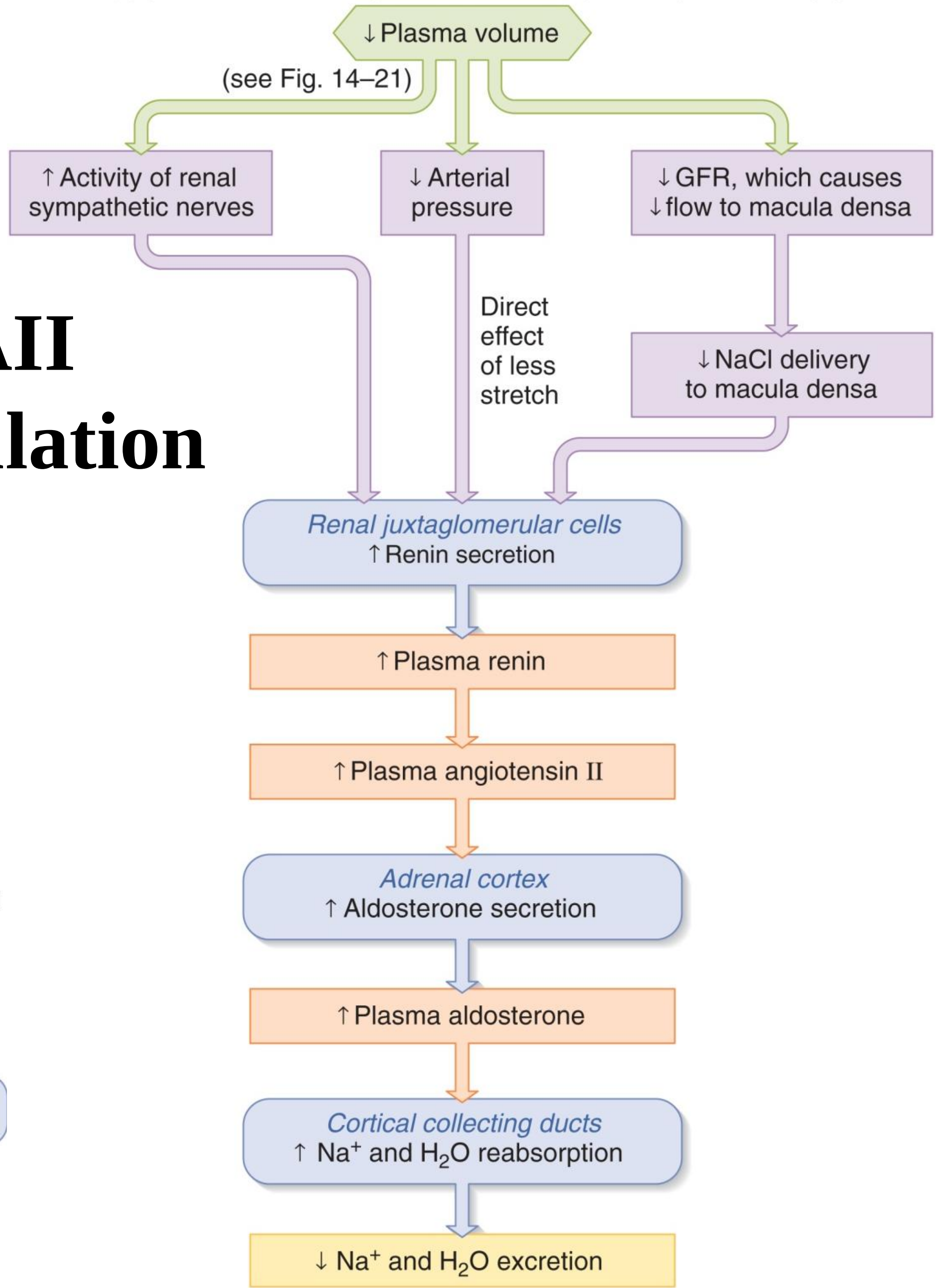
- **Parathyroid hormone (PTH)**

  --Stimulates cells in DCT to reabsorb more Ca^{2+}

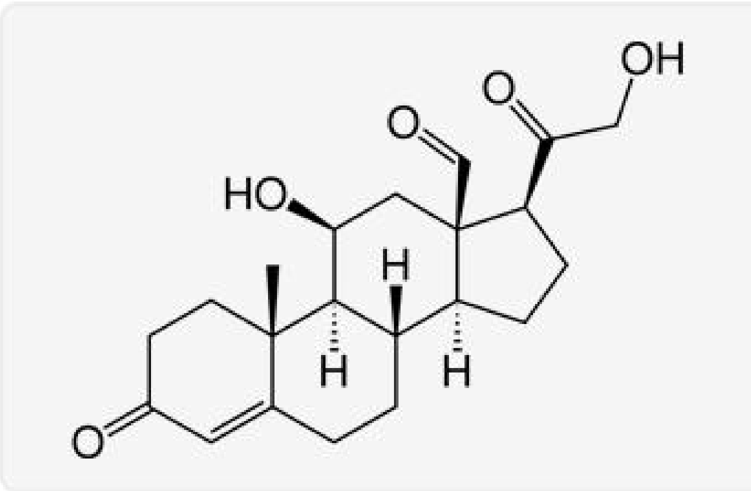
RAA System



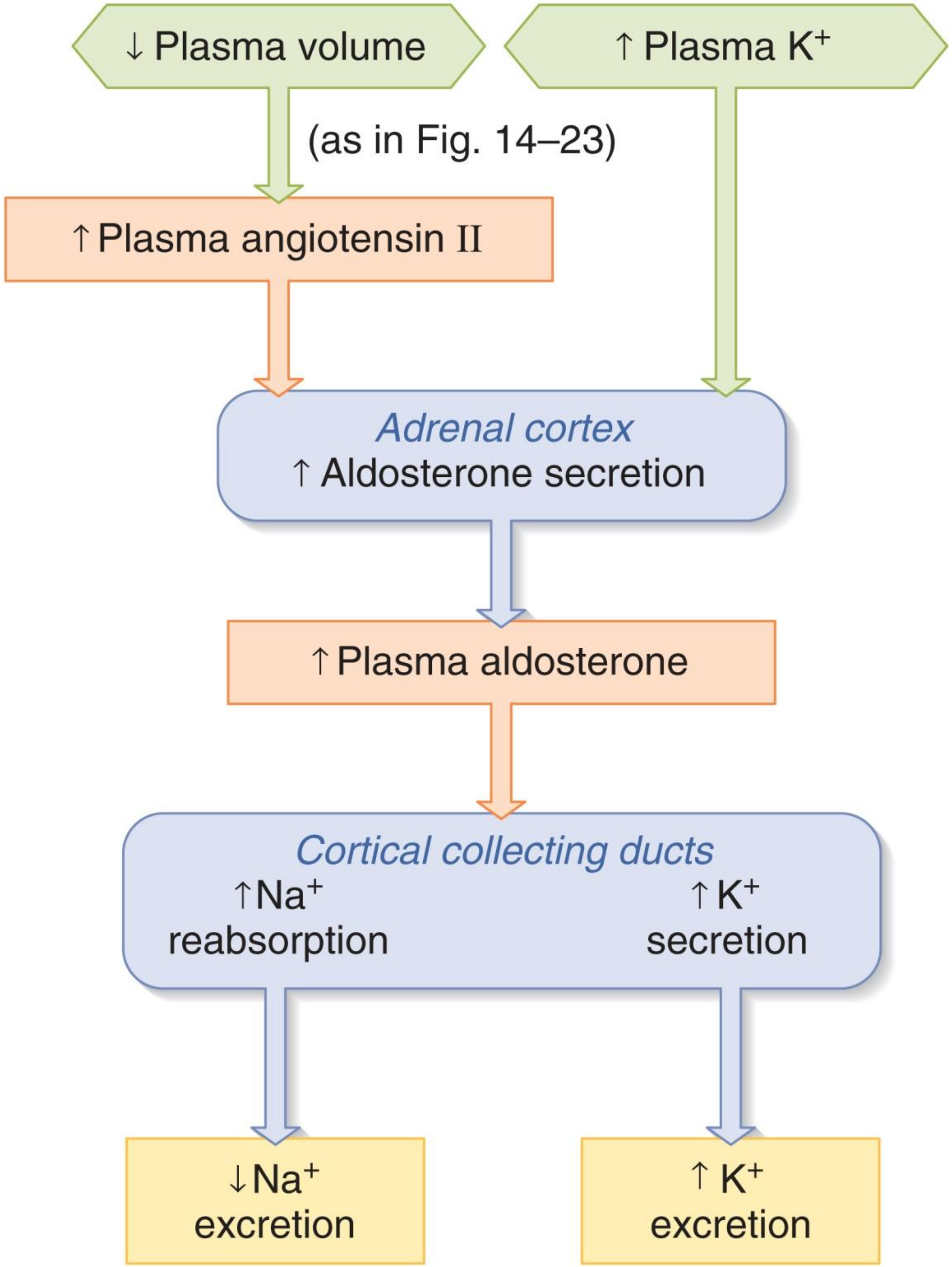
AII Regulation



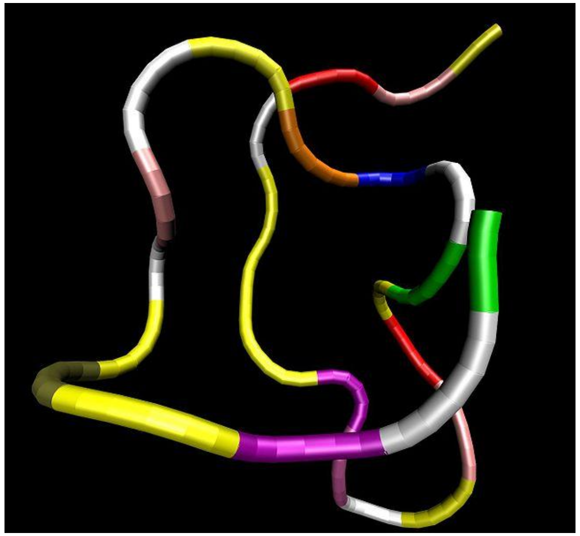
Aldosterone Regulation



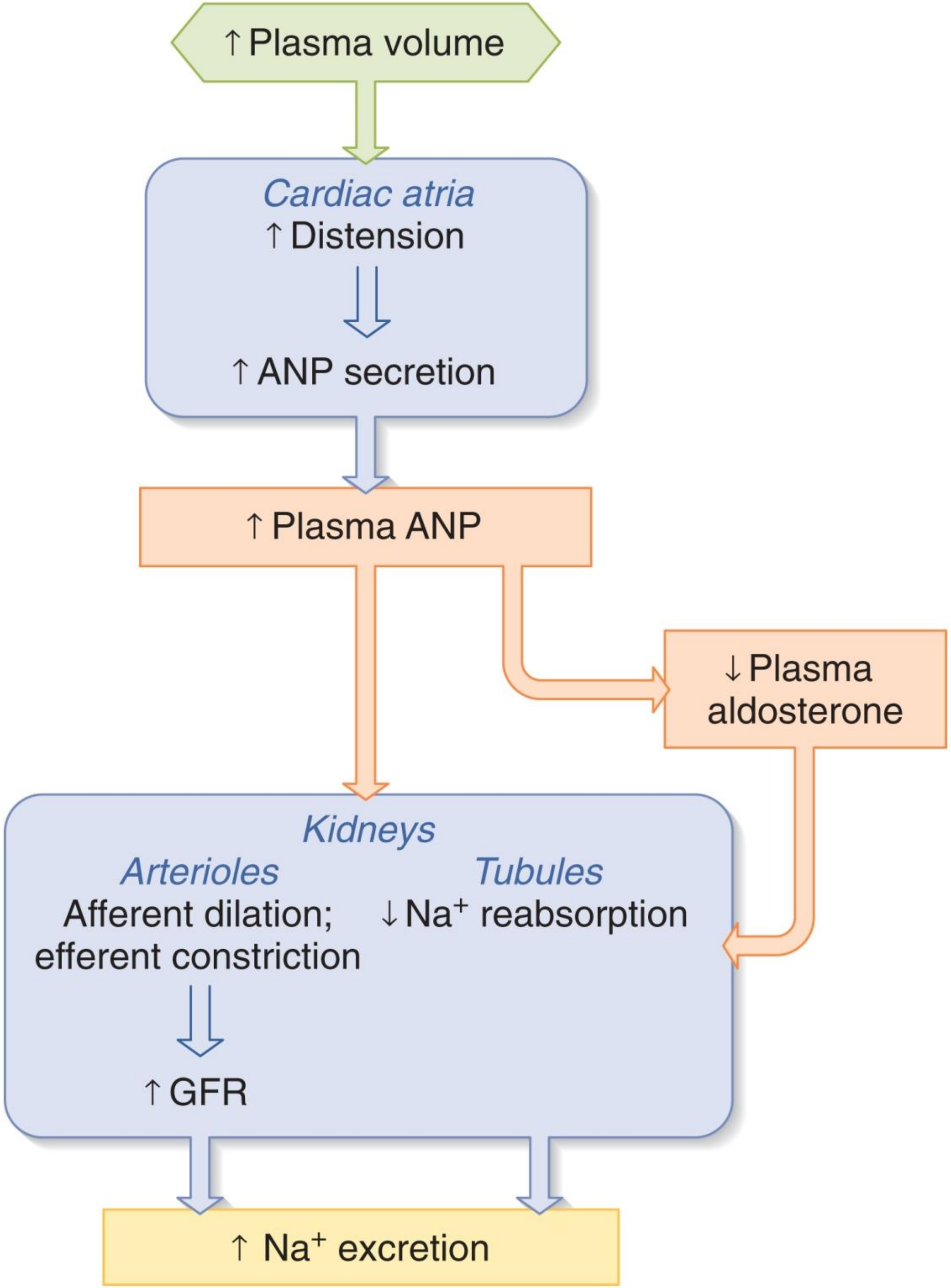
Steroid hormone



ANP Regulation



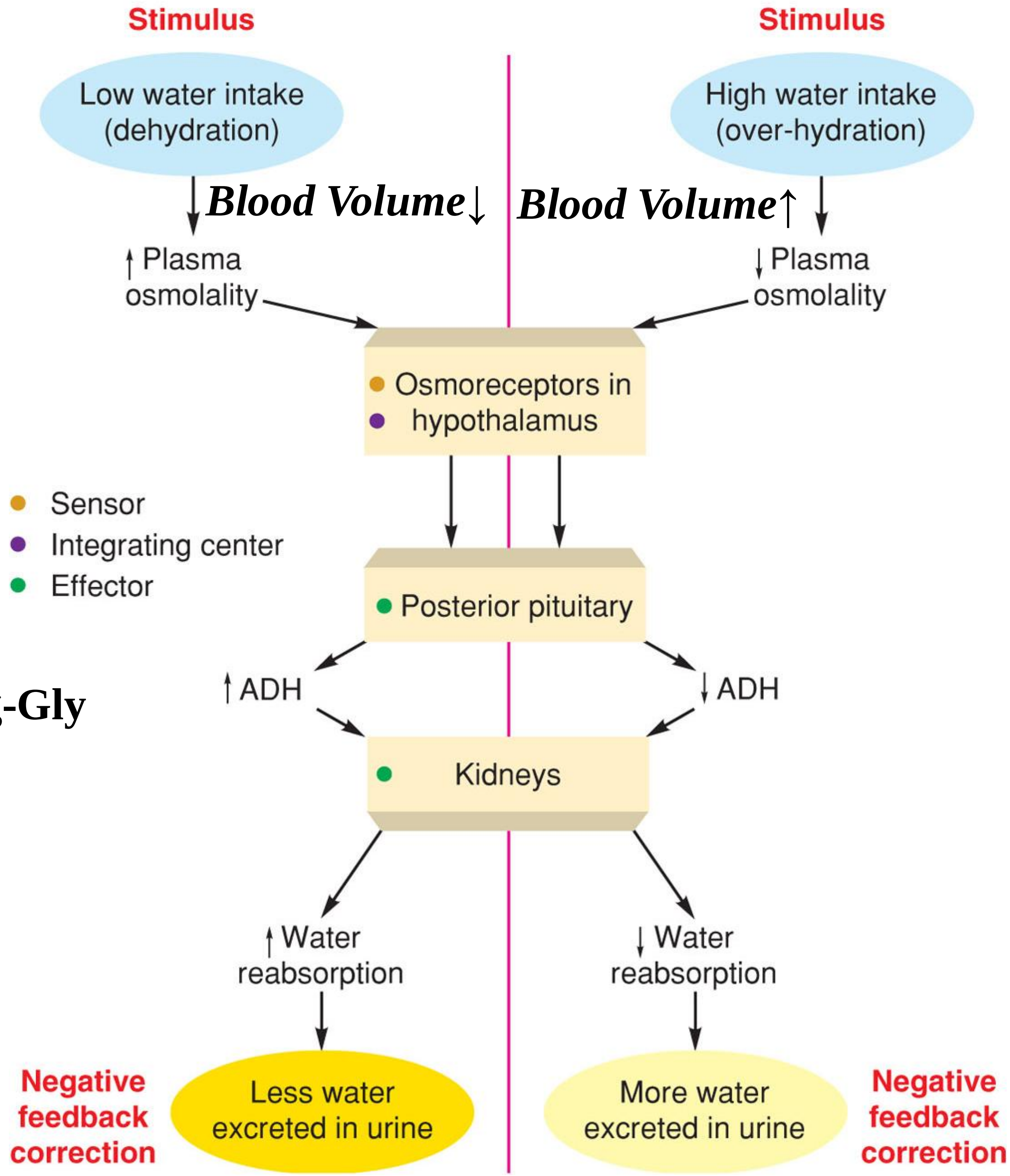
28-amino acid peptide



ADH Regulation

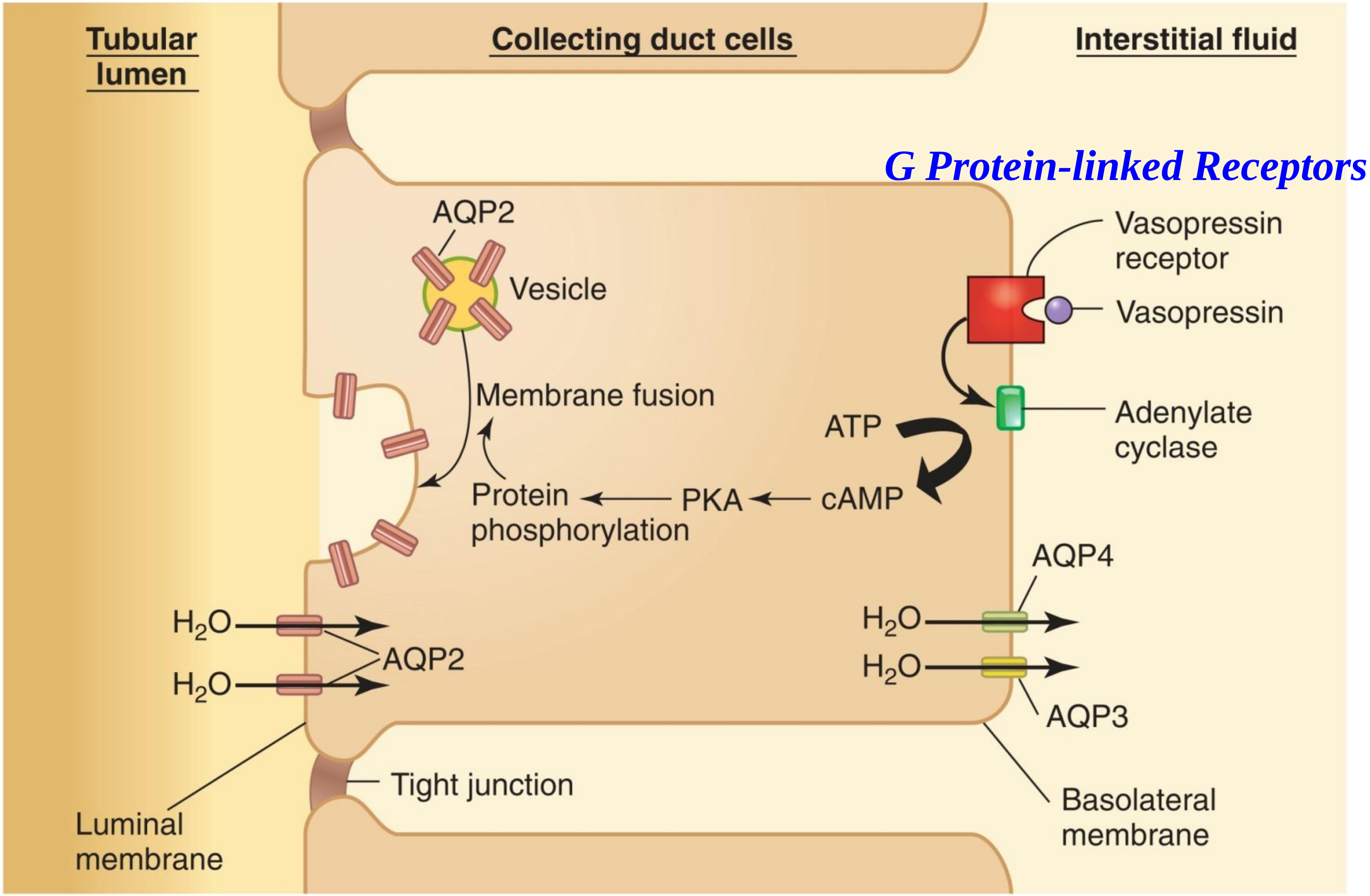
Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly

9-amino acid peptide



ADH Regulation/Collecting Duct

Aquaporin-2 (AQP2)



ADH Secretion & Action

Stimulus	Receptors	Secretion of ADH	Effects on Urine Volume	Effects on Blood
↑Osmolality (dehydration)	Osmoreceptors in hypothalamus	Increased	Decreased	Increased water retention; decreased blood osmolality
↓Osmolality	Osmoreceptors in hypothalamus	Decreased	Increased	Water loss increases blood osmolality
↑Blood volume	Stretch receptors in left atrium	Decreased	Increased	Decreased blood volume
↓Blood volume	Stretch receptors in left atrium	Increased	Decreased	Increased blood volume

Hormonal Regulation of Tubular Reabsorption and 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.
Aldosterone	Increased angiotensin II level and increased level of plasma K^+ promote release of aldosterone by adrenal cortex.	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.
Antidiuretic hormone (ADH) or vasopressin	Increased osmolarity of extracellular fluid or decreased blood volume promotes release of ADH from the posterior pituitary gland.	Stimulates insertion of water-channel proteins (aquaporin-2) into the apical membranes of principal cells.	Increases facultative reabsorption of water, which decreases osmolarity of body fluids.
Atrial natriuretic peptide (ANP)	Stretching of atria of heart stimulates secretion of ANP.	Suppresses reabsorption of Na^+ and water in proximal tubule and collecting duct; also inhibits secretion of aldosterone and ADH.	Increases excretion of Na^+ in urine (natriuresis); increases urine output (diuresis) and thus decreases blood volume.
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+}.

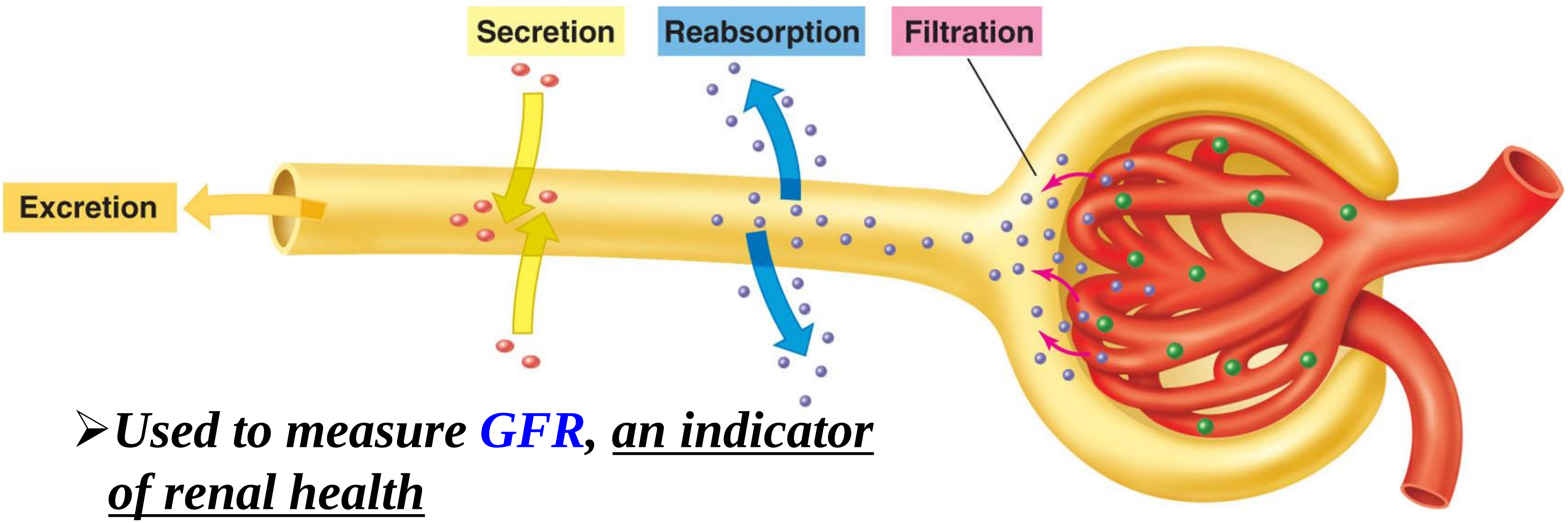
Excretion

- **Excretion rate (moles/min)** = ***filtration rate + secretion rate – reabsorption rate***

 = $U_x \times V$ = ***urinary conc.(moles/L) × urine flow rate (L/min)***

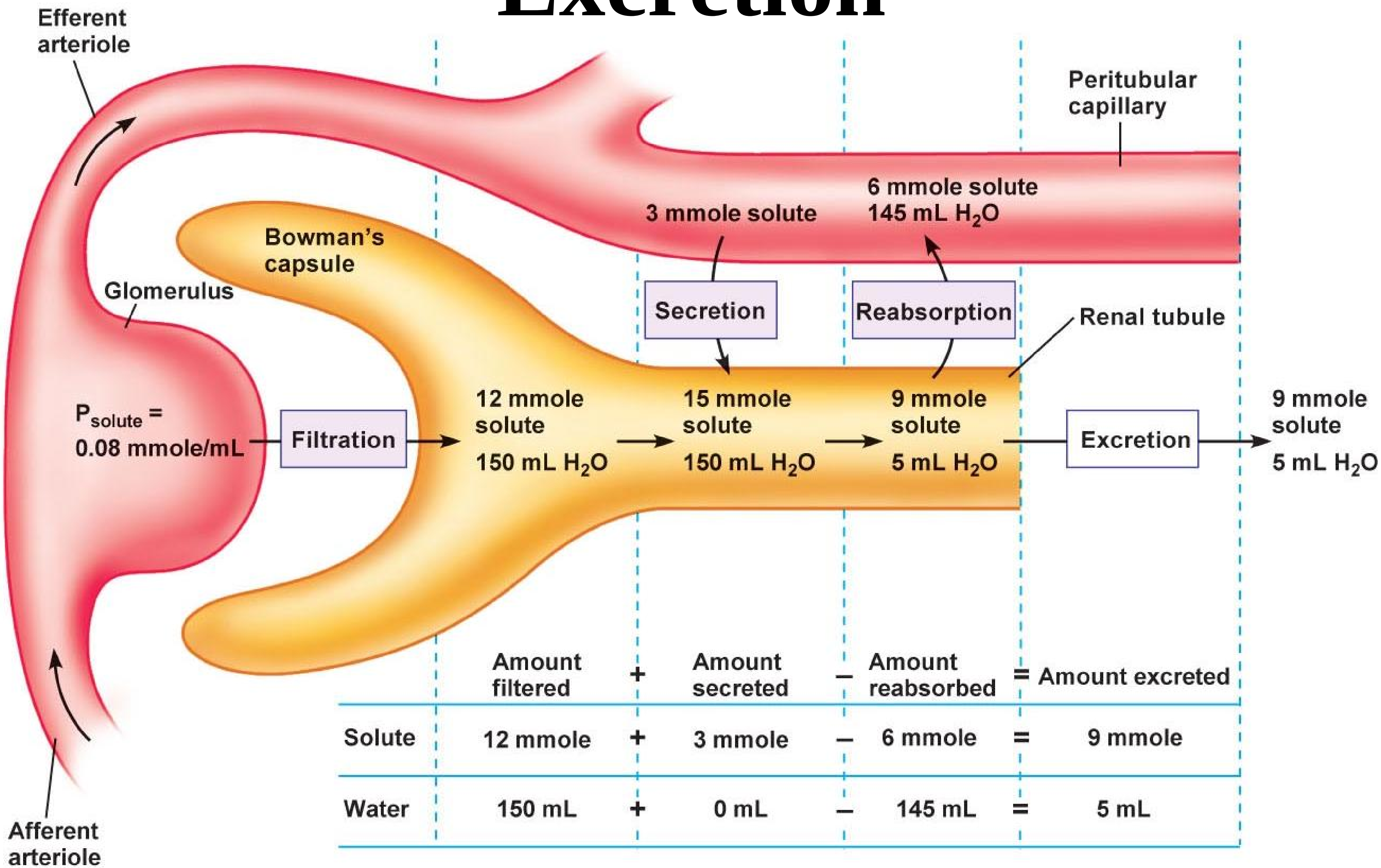
 --Amount excreted depends on

 ➢ ***Filtered load, Secretion rate and Reabsorption rate***



➢ ***Used to measure GFR, an indicator of renal health***

Excretion



- ***Amount of solute excreted/min < filtered load → solute was reabsorbed***
- ***Amount of solute excreted/min > filtered load → solute was secreted***

Clearance

- **Clearance** = excretion rate of a solute
- **Renal plasma clearance** = volume of plasma from which a substance has been removed by kidneys per unit time (mL/min or L/h)
- Tells us how urinary excretion affects the plasma conc. of one solute ***relative to another***
- Used clinically to estimate ***GFR and renal blood flow rate***

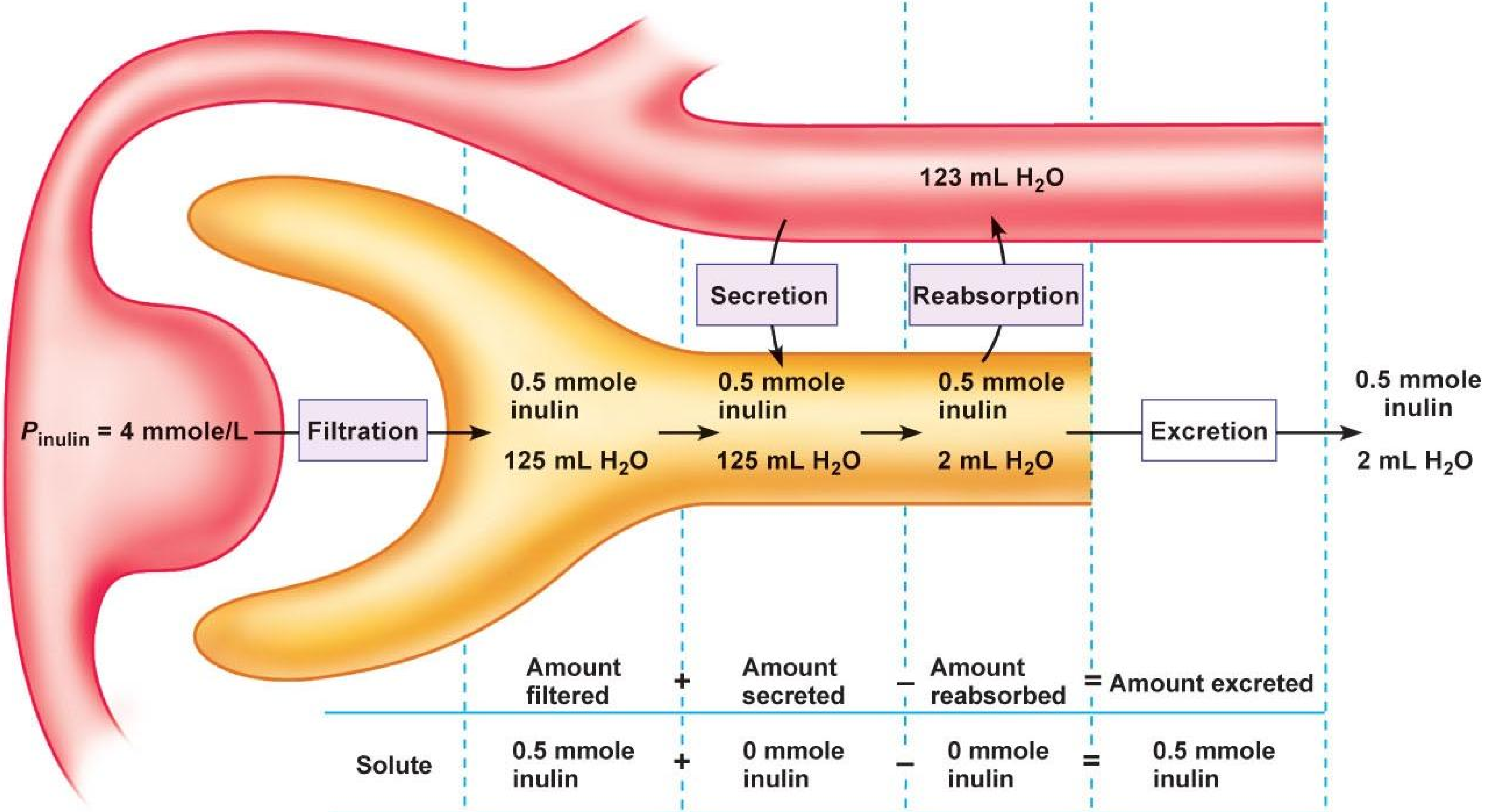
$$\text{Clearance} = \frac{\text{excretion rate}}{\text{plasma concentration}} = \frac{U_x \times V}{P_x}$$

Clearance of Inulin = GFR

- **Inulin is polysaccharide** found in garlic, onion, and artichokes that is not produced in the body but can measuring the **GFR** (via iv.)
- Clearance of substance ***freely filtered*** and ***neither reabsorbed nor secreted* = GFR**
- Amount of inulin excreted in urine **= amount that was filtered = filtered load *(Excretion rate = filtered load = GFR × P_i)***

$$\text{Clearance}_i = \frac{\text{excretion rate}}{\text{plasma concentration}} = \frac{\text{GFR} \times P_i}{P_i} = \text{GFR}$$

Clearance of Inulin = GFR



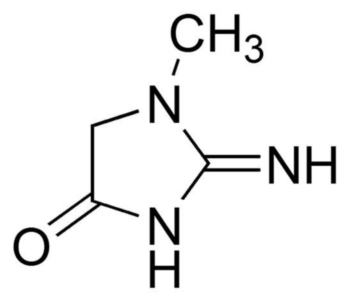
	Amount filtered	+	Amount secreted	−	Amount reabsorbed	=	Amount excreted
Solute	0.5 mmole inulin	+	0 mmole inulin	−	0 mmole inulin	=	0.5 mmole inulin
Water	125 mL	+	0 mL	−	123 mL	=	2 mL

Clearance of inulin = Volume of plasma that contained the amount of inulin excreted = Volume of plasma filtered = GFR

= 125 mL/min

Use of Creatinine to Estimate GFR

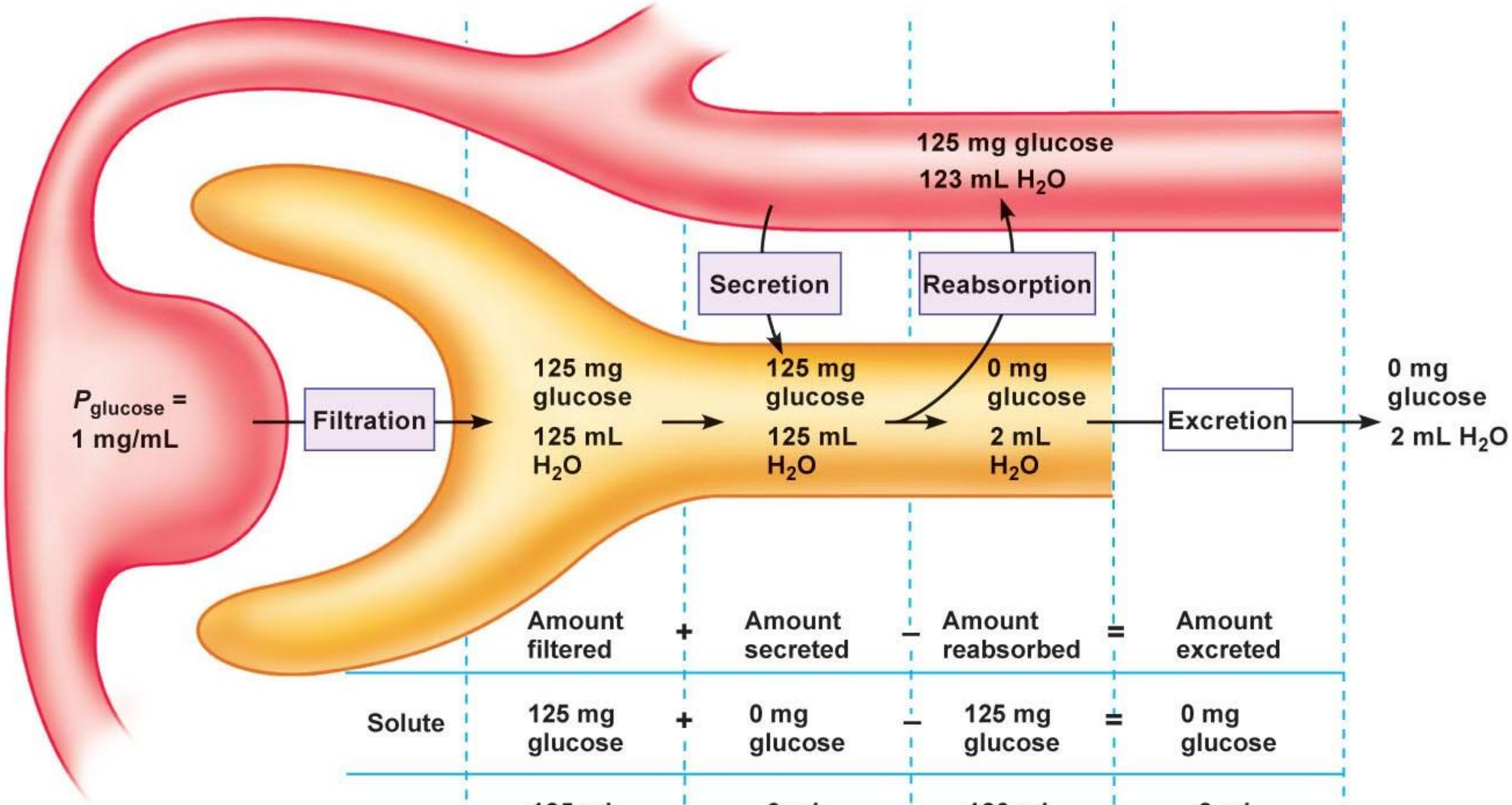
- Creatinine = by-product of **muscle metabolism**
- Produced in body, ***freely filtered***
- ***Not reabsorbed***
- ***Small amount secreted***



- Clearance = “estimate” of **GFR (renal function)**

  --Clearance a little greater than GFR, ***140 mL/min***
- Filtering of the kidney is deficient (renal function↓), creatinine blood levels ↑
- Creatinine levels in blood and urine may be used to calculate the ***creatinine clearance = reflects the GFR***

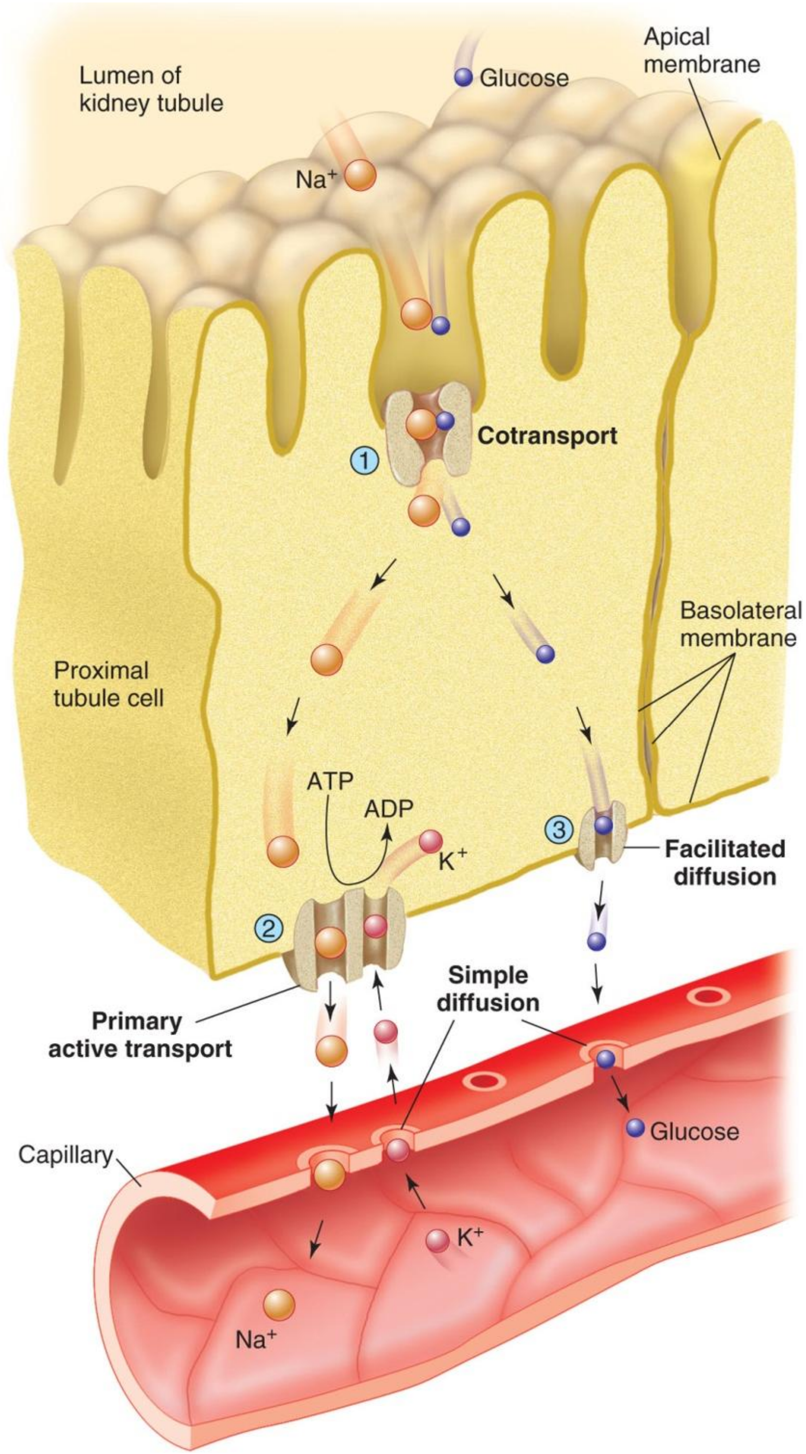
Clearance of Glucose = 0



	Amount filtered	+	Amount secreted	–	Amount reabsorbed	=	Amount excreted
Solute	125 mg glucose	+	0 mg glucose	–	125 mg glucose	=	0 mg glucose
Water	125 mL H_2O	+	0 mL H_2O	–	123 mL H_2O	=	2 mL H_2O

Clearance of glucose = Volume of plasma that contained 0 mg glucose/min = 0 mL/min

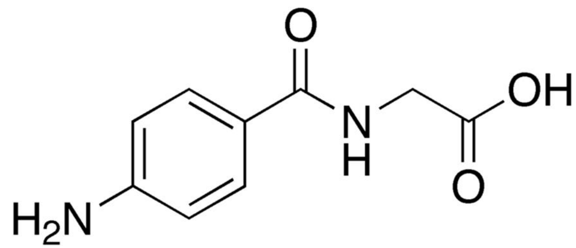
(a) Clearance of glucose



Reabsorption of Glucose

- Glucose and aa. ***easily filtered*** out in the glomerular capsule
- ***Completely reabsorbed*** in the proximal tubule via ***secondary active transport*** with sodium (Na-glucose cotransport), ***facilitated diffusion***, and ***simple diffusion***

Clearance of PAH



- **PAH (para-aminohippuric acid 對胺基馬尿酸)**

  --Foreign substance used clinically to measure ***renal blood flow***

  --Clearance of substance ***freely filtered***, ***fully secreted***, and ***not reabsorbed*** **= *renal plasma flow rate***

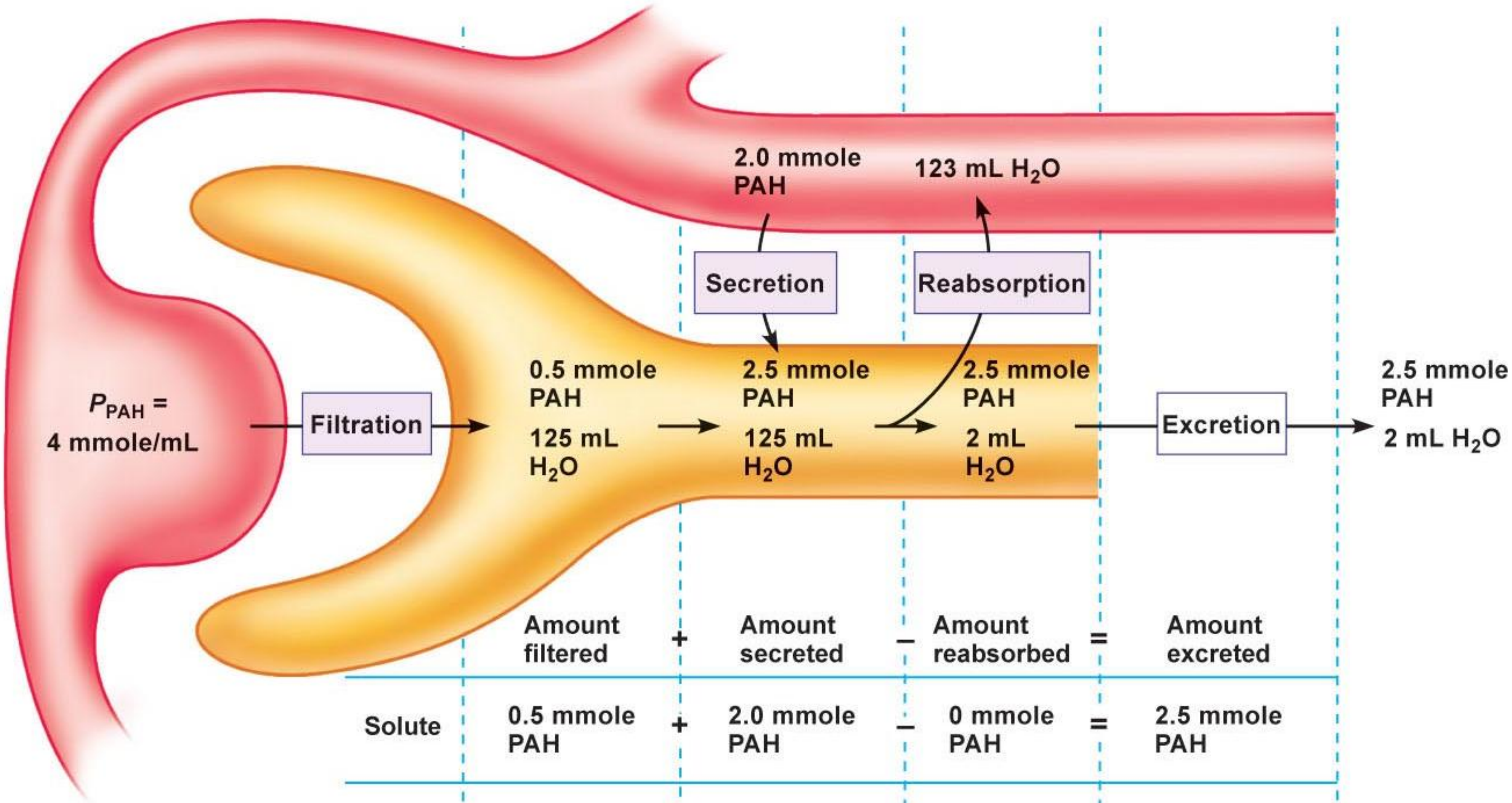
  --Amount excreted = amount contained in volume of plasma that entered the kidneys (***renal plasma flow***)

  --Convert plasma flow to blood flow (**Blood is 55% plasma**)

$$\textbf{Renal blood flow} = \frac{\text{clearance PAH}}{\text{1-hematocrit}} = \frac{\text{625 mL/min}}{0.55} = \text{1136 mL/min}$$

(1/5-1/4 of CO)

Clearance of PAH



	Amount filtered	+	Amount secreted	−	Amount reabsorbed	=	Amount excreted
Solute	0.5 mmole PAH	+	2.0 mmole PAH	−	0 mmole PAH	=	2.5 mmole PAH
Water	125 mL H_2O	+	0 mL H_2O	−	123 mL H_2O	=	2 mL H_2O

Clearance of PAH = Volume of plasma that contained 2.5 mmole PAH = $\frac{\text{2.5 mmole PAH/min}}{\text{4 mmole PAH/1000 mL } H_2O}$ = 625 mL/min

(b) Clearance of PAH

Clearance of Common Substances

Substance	Clearance rate (mL/min)	Net renal processing (reabsorption or secretion)*
PAH	650	Secretion
Creatinine	140	Secretion
Inulin	125	None
Potassium	12.0	Reabsorption
Chloride	1.3	Reabsorption
Sodium	0.9	Reabsorption
Glucose	0	Reabsorption

*GFR = 125 mL > min. If clearance is greater than GFR, net secretion has occurred; if clearance is less than GFR, net reabsorption has occurred.

Renal Plasma Clearance

Effects of Filtration, Reabsorption, and Secretion on Renal Plasma Clearance

Term	Definition	Effect on Renal Clearance
Filtration	A substance enters the glomerular ultrafiltrate.	Some or all of a filtered substance may enter the urine and be "cleared" from the blood.
Reabsorption	A substance is transported from the filtrate, through tubular cells, and into the blood.	Reabsorption decreases the rate at which a substance is cleared; clearance rate is less than the glomerular filtration rate (GFR).
Secretion	A substance is transported from peritubular blood, through tubular cells, and into the filtrate.	When a substance is secreted by the nephrons, its renal plasma clearance is greater than the GFR.

Renal "Handling" of Different Plasma Molecules

If Substance Is:	Example	Concentration in Renal Vein	Renal Clearance Rate
Not filtered	Proteins	Same as in renal artery	Zero
Filtered, not reabsorbed or secreted	Inulin	Less than in renal artery	Equal to GFR (115–125 ml/min)
Filtered, partially reabsorbed	Urea	Less than in renal artery	Less than GFR
Filtered, completely reabsorbed	Glucose	Same as in renal artery	Zero
Filtered and secreted	PAH	Less than in renal artery; approaches zero	Greater than GFR; up to total plasma flow rate (~625 ml/min)
Filtered, reabsorbed, and secreted	K^+	Variable	Variable

Urine Transportation, Storage, and Elimination

- Urine drains through papillary ducts into ***minor calyces***, which joint to become ***major calyces*** that unite to form the ***renal pelvis***
- ***Renal pelvis → ureters → urinary bladder → urethra***
- **Ureters**

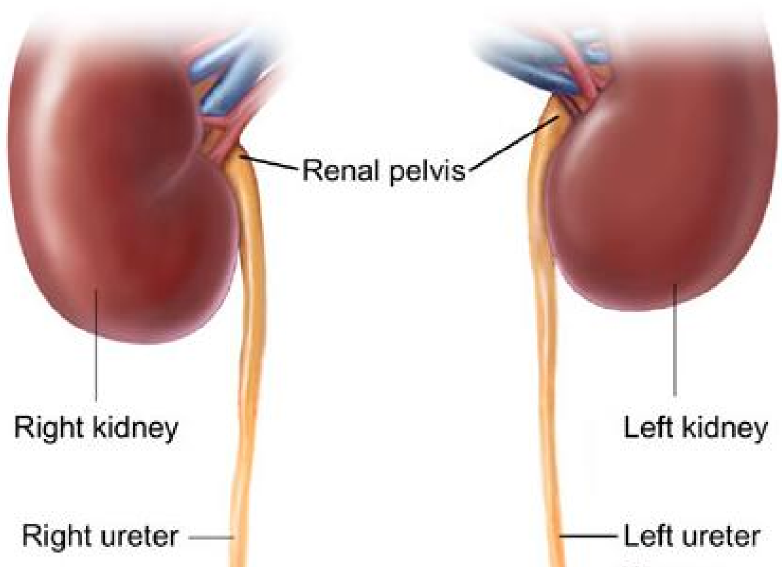
  --Each of **2 ureters** transports urine from renal pelvis of one kidney to the bladder

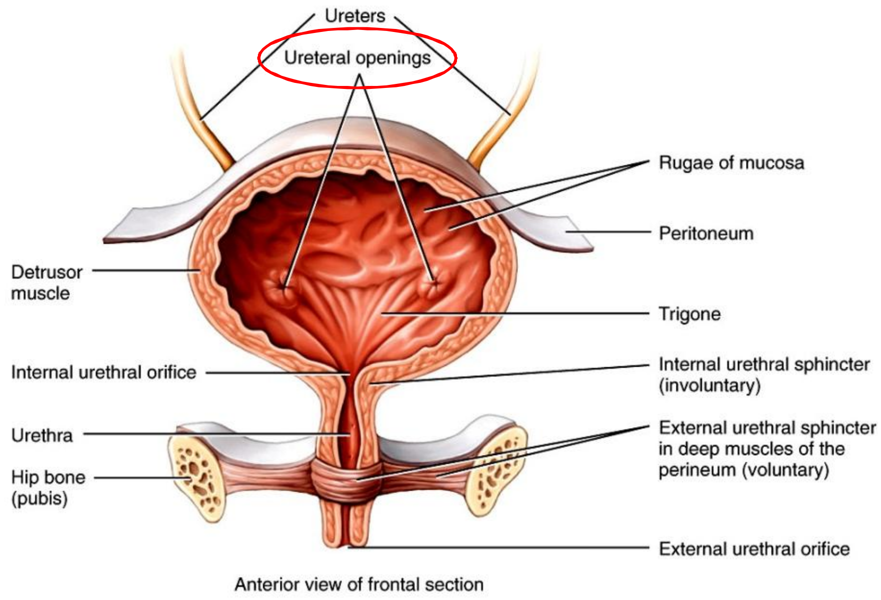
  --**Peristaltic waves**, **hydrostatic pressure** and **gravity** move urine

  --**No anatomical valve** at the opening of the ureter into bladder – when bladder fills it compresses the opening and ***prevents backflow***

Anatomy of Ureters

- Tubes made of ***smooth muscle cells*** that propel urine from the kidneys to the urinary bladder
- In the adult, the ureters are usually ***25-30 cm long*** and ***~3-4 mm in diameter***
- Ureters are ***retroperitoneal*** and consist of a ***mucosa, muscularis, and fibrous coat***
- Ureter contains ***transitional epithelium (mucosa)*** and an additional ***smooth muscle layer*** in the more distal one-third to assist with peristalsis (urine flow)
- Enters ***posterior wall*** of bladder





Urinary Bladder & Urethra

- **Urinary bladder**

  --Hollow, distensible muscular organ situated in the pelvic cavity ***posterior to the pubic symphysis***

  --Capacity averages ***700-800 mL***

  --In the floor of the urinary bladder is a small, **smooth triangular area = *trigone***

  --The ureters enter the urinary bladder near **two posterior points** in the triangle; the urethra drains the urinary bladder from the **anterior point** of the triangle

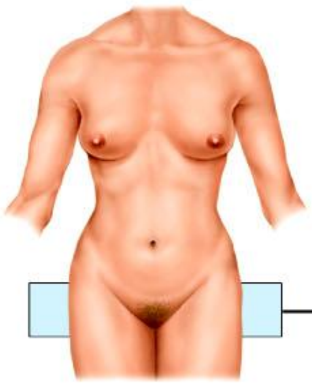
  --**Micturition** – discharge of urine from bladder

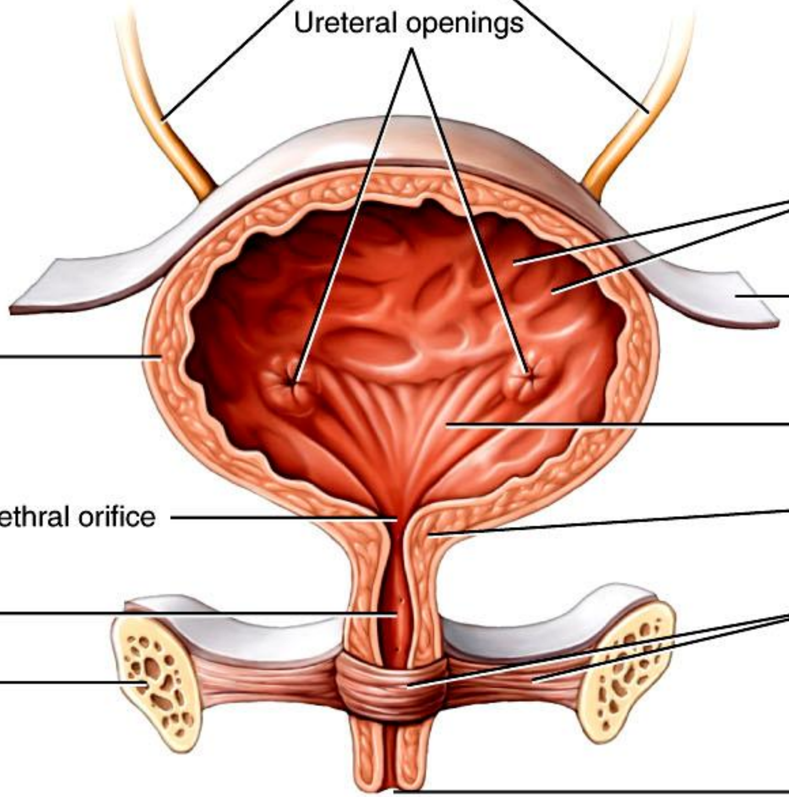
- **Urethra**

  --Small tube that connects ***the urinary bladder to the genitals*** for the removal of fluids from the body

  --In males, the urethra travels through the ***penis***, and discharges semen as well as urine

Anatomy of Urinary Bladder

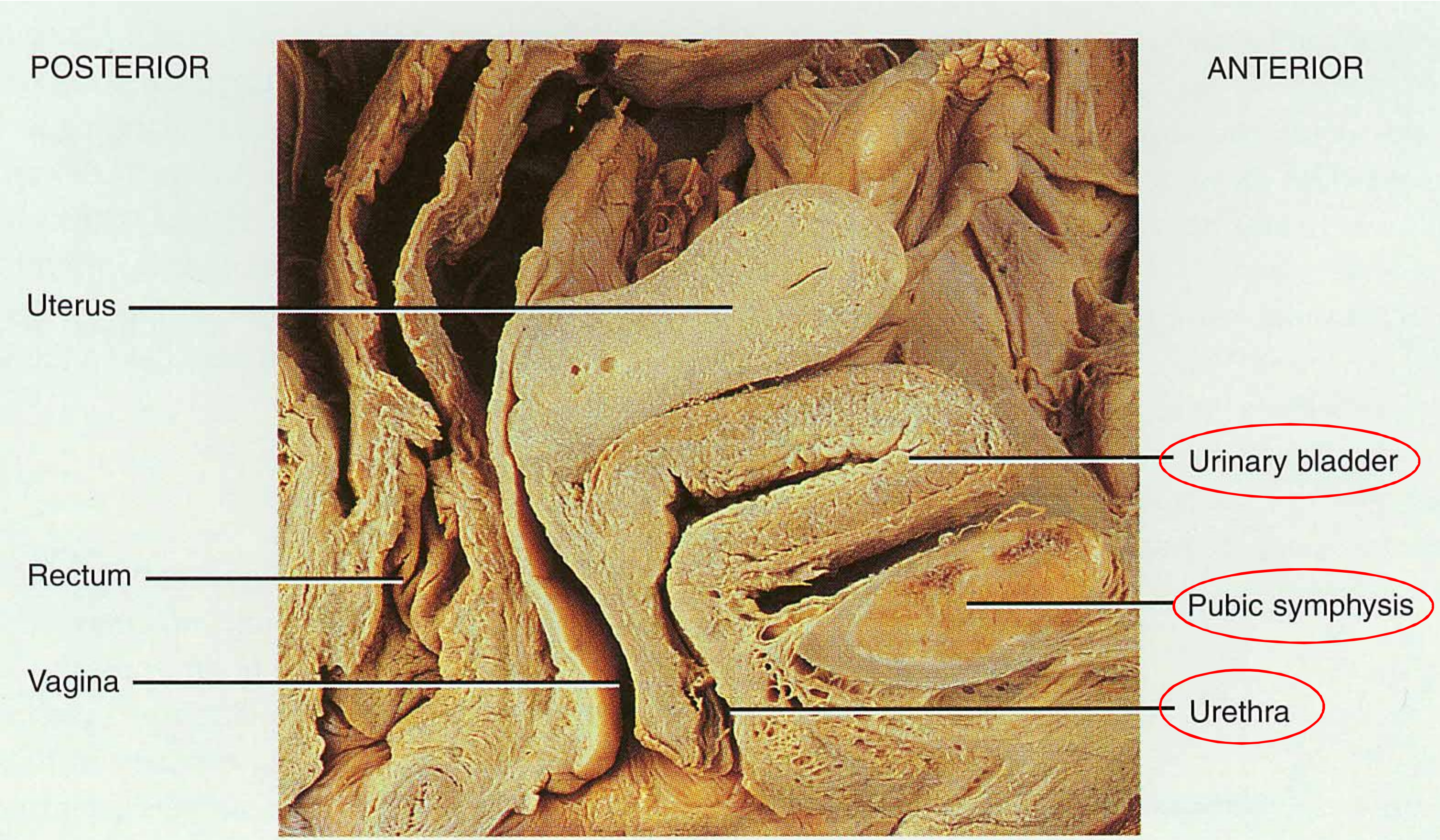




Anterior view of frontal section

- ***Hollow, distensible muscular organ with capacity of 700 - 800 mL***
- ***Trigone is smooth flat area bordered by 2 ureteral openings and one urethral opening***

Location of Urinary Bladder



- ***Posterior to pubic symphysis***
- ***In females is anterior to vagina & inferior to uterus***
- ***In males lies anterior to rectum***

Anatomy of the Urethra

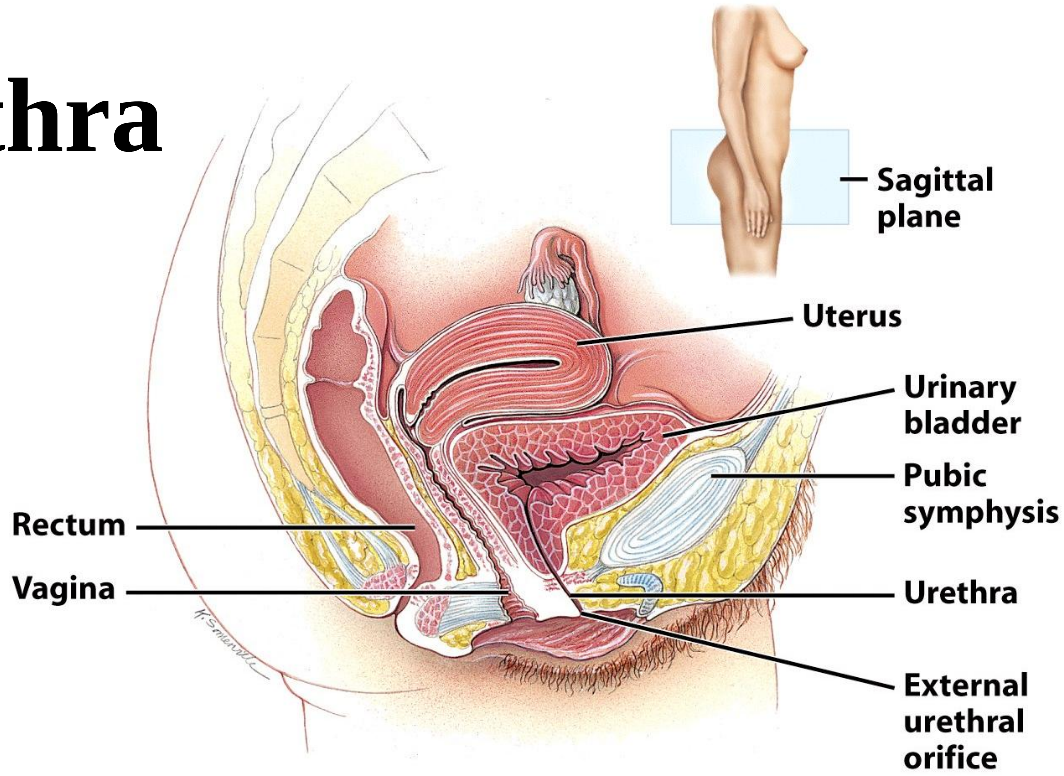
- **Females**

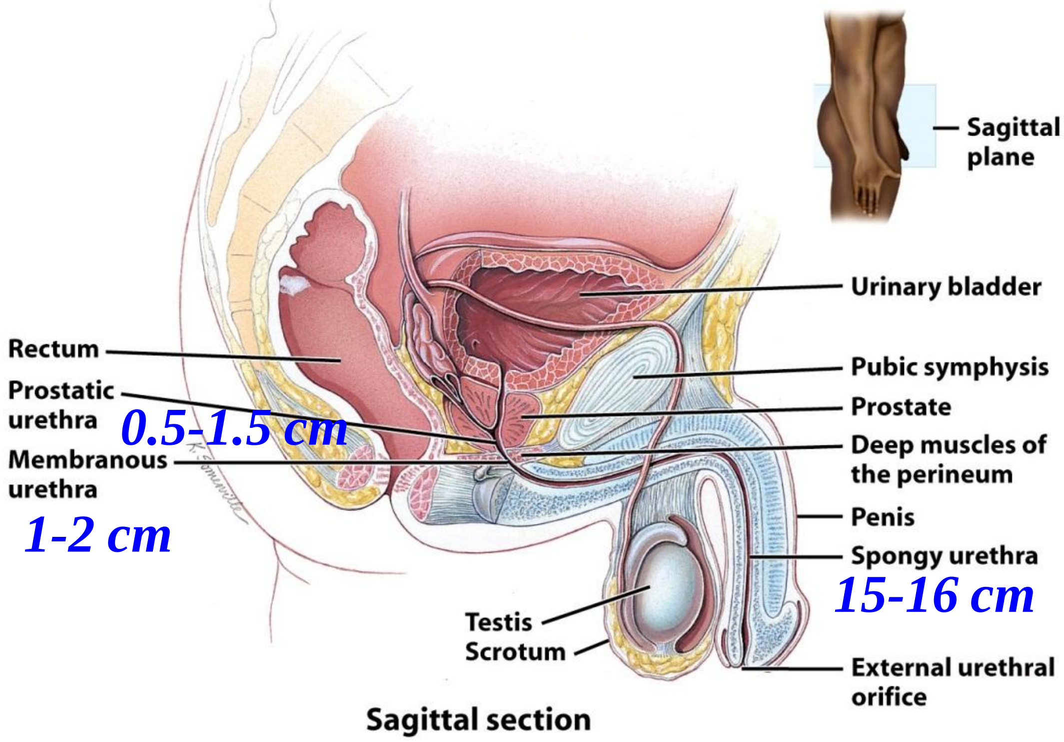
  --Length of ***3.8-5 cm***, orifice between ***clitoris & vagina***

- **Males**

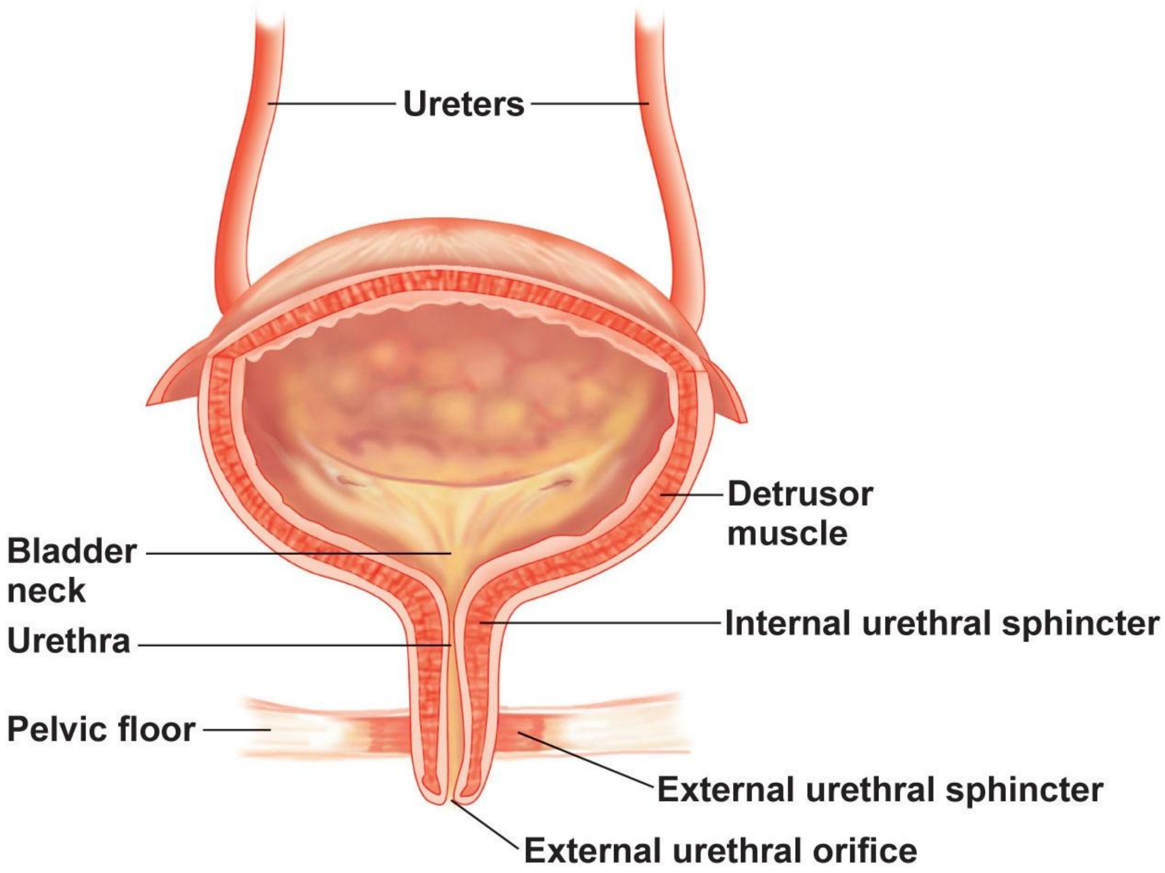
  --Length of ***20 cm***, tube passes through ***prostate, external urethral sphincter & penis***

  --3 regions of urethra: ***Prostatic urethra***, ***membranous urethra*** & ***spongy urethra***





Micturition = Urination



- **Detrusor muscles** line the wall of the urinary bladder
  - --***Gap junctions*** connect smooth muscle cells
  - --Innervated by ***parasympathetic neurons***, which release ACh onto ***muscarinic*** ACh receptors
- **2 Sphincters** surround urethra
  - --***Internal urethral sphincter***: ***smooth muscle (involuntary)***
  - --***External urethral sphincter***: ***skeletal muscle (voluntary)***

Control of Micturition

- **Stretch receptors** in the bladder send information to **S2−S4 regions** of the sacral spinal cord (**micturition center**)

  --These neurons normally ***inhibit*** ***parasympathetic*** nerves to the detrusor muscles, while ***somatic motor*** neurons to the ***external urethral sphincter are stimulated***

  --Called the ***guarding reflex***

  --Prevents involuntary emptying of bladder

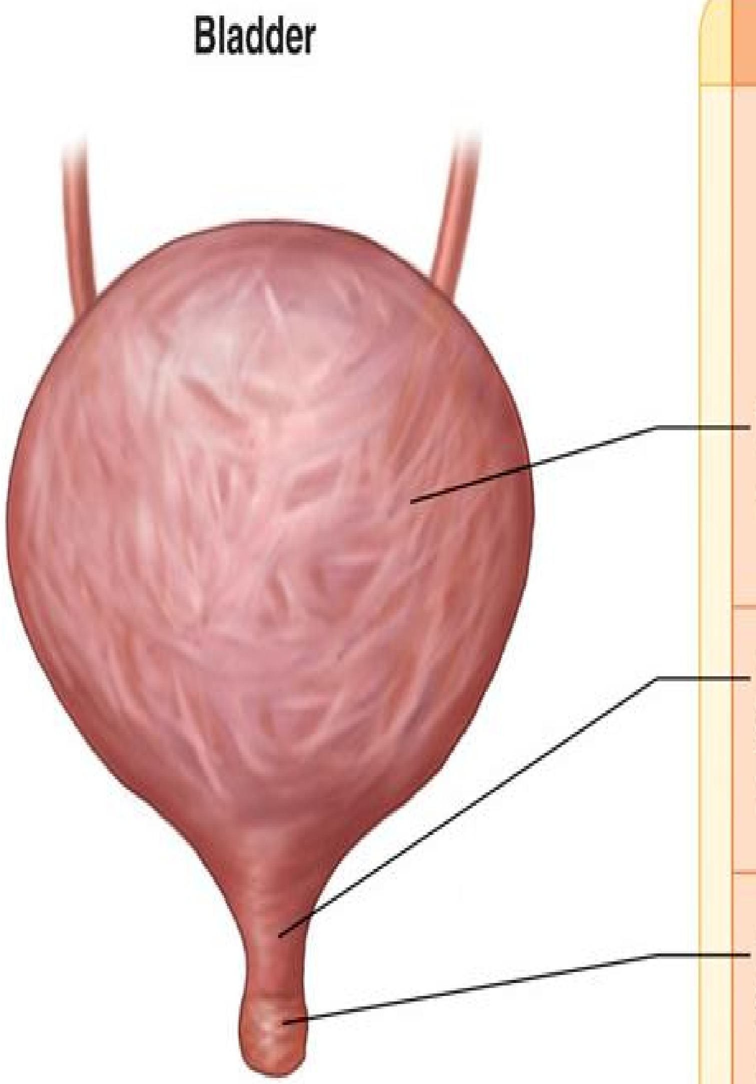
  --Micturition involves coordination between the ***central***, ***autonomic***, and ***somatic nervous systems***

  --Brain centers that regulate urination include the pontine micturition center, periaqueductal gray and the cerebral cortex

Control of Micturition

- Stretch of the bladder (urine 200-400 ml) initiates the ***voiding reflex = micturition reflex***
  - --Information about stretch passes up the spinal cord to the **micturition center** of the **pons**
  - --**Parasympathetic** neurons cause ***detrusor muscles to contract*** ***(autonomic control)***
  - --**Sympathetic** innervation of the ***internal urethral sphincter causes it to relax*** ***(autonomic control)***
  - --Person feels the need to urinate and can control when with ***external urethral sphincter*** ***(voluntary control)***

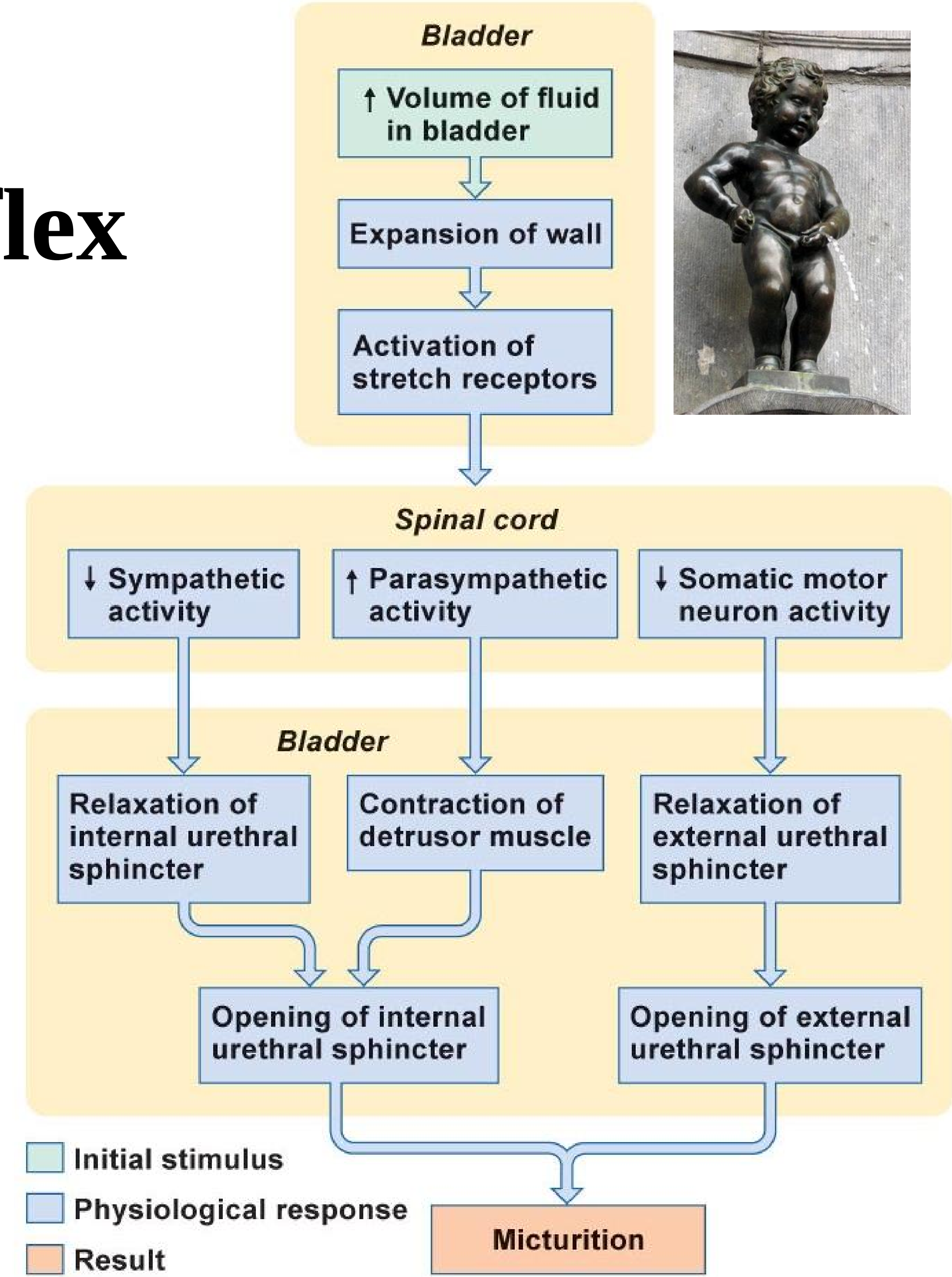
Control of Micturition



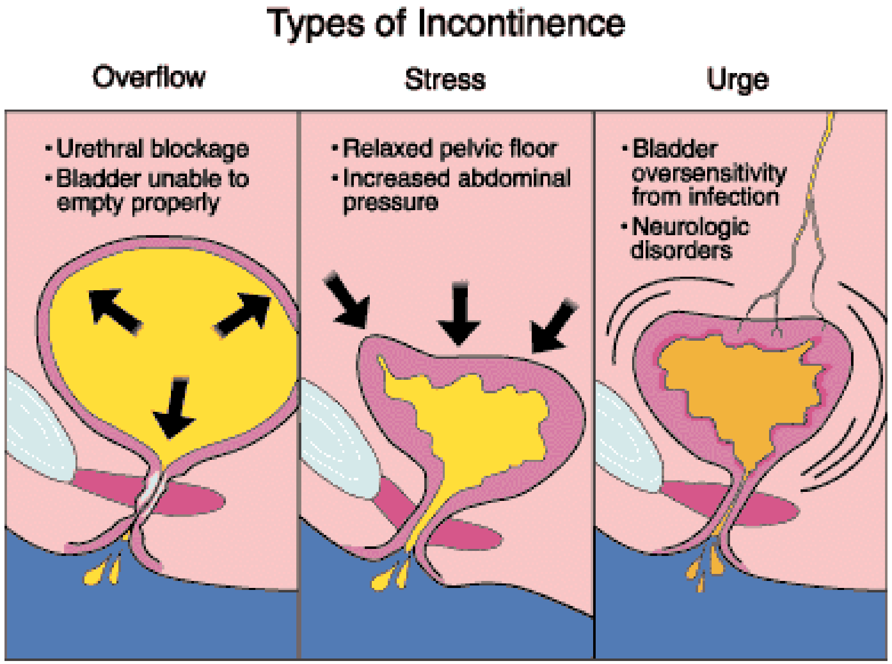
Muscle	Innervation			
	Type	During filling	During micturition	
Detrusor (smooth muscle)	Parasympathetic (causes contraction)	Inhibited	Stimulated	***M3-R***
Internal urethral sphincter (smooth muscle)	Sympathetic (causes contraction)	Stimulated	Inhibited	***α1-R***
External urethral sphincter (skeletal muscle)	Somatic motor (causes contraction)	Stimulated	Inhibited	***N-R***

Micturition Reflex

- Micturition is regulated by ***a spinal reflex*** that can be overridden by ***voluntary control*** in a trained children and adult
- In infants, the pathway is ***purely reflexive***



Clinical Application: Urinary Incontinence



- ***Urinary incontinence*** is the ***involuntary*** release of urine and more common in ***women*** ***(result of childbirth)***

  --Normal in ***2 or 3 year olds*** because neurons to sphincter muscle is not developed

- 2 most common types

  --***Stress incontinence*** (due to abdominal pressure ↑ ex. sneezing, coughing, laughing, walking or exercise; injury to the nerves, loss of bladder flexibility, or damage to the sphincter)

  --***Urge incontinence*** (associated with suddenly urge to urinate)

Clinical Application: Urinary Incontinence

- Medications such as ***estrogen replacement therapy*** to improve vaginal tone can often relieve stress incontinence

  --***Anticholinergic medication*** used to relieve urinary and bladder difficulties

  --Severe cases may require ***surgery*** to improve vaginal support of the bladder and urethra

- Any irritation to the bladder or urethra ex. ***bacterial infection*** can cause urge incontinence

  --Urge incontinence can be treated with ***anticholinergic drugs*** such as ***tolterodine or oxybutynin (M3 ACh antagonist on the detrusor muscle)***

  --These drugs can have side effects such as ***blurred vision, constipation, and increased heart rate***

Evaluation of Kidney Function

- **Urinalysis**

  --Analysis of the ***volume and physical, chemical and microscopic*** properties of urine

  --**Water** accounts for ***95%*** of total urine volume

  --Typical solutes are filtered and secreted substances that are not reabsorbed

  --If **disease** alters metabolism or kidney function, traces if substances normally not present or normal constituents in abnormal amounts may appear

Evaluation of Kidney Function

- **Blood tests**

  --***Blood urea nitrogen (BUN)*** – measures blood nitrogen that is part of the urea resulting from catabolism and deamination of amino acids

  --***Plasma creatinine*** results from catabolism of creatine phosphate in skeletal muscle – measure of renal function

- **Renal plasma clearance**

  --More useful in diagnosis of kidney problems than above

  --Volume of blood cleared of a substance per unit time

  --**High** renal plasma clearance indicates **efficient excretion** of a substance into urine

  --***PAH*** administered to measure ***renal plasma flow***

Characteristics of Normal Urine

CHARACTERISTIC	DESCRIPTION
Volume	One to two liters in 24 hours but varies considerably.
Color	Yellow or amber but varies with urine concentration and diet. Color is due to urochrome (pigment produced from breakdown of bile) and urobilin (from breakdown of hemoglobin). Concentrated urine is darker in color. Diet (reddish-colored urine from beets), medications, and certain diseases affect color. Kidney stones may produce blood in urine.
Turbidity	Transparent when freshly voided but becomes turbid (cloudy) upon standing.
Odor	Mildly aromatic but becomes ammonia-like upon standing. Some people inherit the ability to form methylmercaptan from digested asparagus that gives urine a characteristic odor. Urine of diabetics has a 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	Specific gravity (density) is the ratio of the weight of a volume of a substance to the weight of an equal volume of distilled water. In urine, it ranges from 1.001 to 1.035. The higher the concentration of solutes, the higher the specific gravity.

Abnormal Constituents in Urine

ABNORMAL CONSTITUENT	COMMENTS
Albumin	A normal constituent of plasma, it usually appears in only very small amounts in urine because it is too large to pass through capillary fenestrations. The presence of excessive albumin in the urine—**albuminuria** (al′-bū-mi-NOO-rē-a)—indicates an increase in the 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	The presence of glucose in the urine is called **glucosuria** (gloo-kō-SOO-rē-a) and usually indicates diabetes mellitus. Occasionally it may be caused by stress, which can cause excessive amounts of epinephrine to be secreted. Epinephrine stimulates the breakdown of glycogen and liberation of glucose from the liver.
Red blood cells (erythrocytes)	The presence of red blood cells in the urine is called **hematuria** (hēm-a-TOO-rē-a) and generally indicates a pathological condition. One cause is acute inflammation of the urinary organs as a result of disease or irritation from kidney stones. Other causes include tumors, trauma, and kidney disease, or possible contamination of the sample by menstrual blood.
Ketone bodies	High levels of ketone bodies in the urine, called **ketonuria** (kē-tō-NOO-rē-a), may indicate diabetes mellitus, anorexia, starvation, or simply too little carbohydrate in the diet.
Bilirubin	When red blood cells are destroyed by macrophages, the globin portion of hemoglobin is split off and the heme is converted to biliverdin. Most of the biliverdin is converted to bilirubin, which gives bile its major pigmentation. An above-normal level of bilirubin in urine is called **bilirubinuria** (bil′-ē-roo-bi-NOO-rē-a).
Urobilinogen	The 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 the shape of the lumen of the tubule in which they formed. They are then flushed out of the tubule when filtrate builds up behind them. Casts are named after the cells or substances that compose them or based on their appearance. For example, there are white blood cell casts, red blood cell casts, and epithelial cell casts that contain cells from the walls of the tubules.
Microbes	The number and type of bacteria vary with specific infections in the urinary tract. One of the most common is *E. coli*. The most common fungus to appear in urine is the yeast *Candida albicans*, a cause of vaginitis. The most frequent protozoan seen is *Trichomonas vaginalis*, a cause of vaginitis in females and urethritis in males.

Aging and the Urinary System

- ***After age 40***, the effectiveness of kidney function begins to decrease ***1%***
- **Anatomical changes**

  --2 kidney shrink in size from ***260 g to 200 g***
- **Functional changes**

  --***Lowered*** blood flow & filter less blood (50%)

  --***Diminished*** sensation of thirst (dehydration ↑)
- **Diseases common with age**

  --Acute and chronic inflammations

  --Infections, nocturia, polyuria, dysuria, retention or incontinence and hematuria
- **Cancer of prostate** is common in elderly men

Disorders of Urinary System

- ***Urinary tract infection (UTI)***

  --**An infection** of a part of the urinary system or the presence of large numbers of microbes in urine

  --UTIs include ***urethritis*** (inflammation of the urethra), ***cystitis*** (inflammation of the urinary bladder), ***pyelonephritis*** (inflammation of the kidneys), and ***pyelitis*** (inflammation of the renal pelvis and its calyces)

- ***Glomerulonephritis (Bright's disease)***

  --**An inflammation** of the glomeruli of the kidney

  --One of the most common causes is an ***allergic reaction*** to the toxins given off by ***steptococcal bacteria***

  --The glomeruli may be permanently damaged, leading to ***acute or chronic renal failure***

Disorders of Urinary System

- ***Chronic renal failure***

    --A progressive and generally irreversible decline in ***GFR***

    --May result from ***chronic glomerulonephritis***, ***pyelonephritis***, ***polycystic disease***, or ***traumatic loss of kidney tissue***

- ***Polycystic kidney disease***

    --One of the ***most common inherited disorders***

    --**In infants** it results in death at birth or shortly thereafter

    --**In adults**, it accounts for 6-12% of kidney transplantations

    --***Kidney tubules*** (hundreds or thousands of cysts) + ***noncystic tubules*** (inappropriate apoptosis of cells) → renal function ↓ and renal failure ↑